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Reaction of Benzoylnitrene with Anions: Formation of an Intermediate in the Hofmann Rearrangement

Sarah M. Mandel and Matthew S. Platz*

Department of Chemistry, The Ohio State University, 100 West 18th Avenue, Columbus, Ohio 43210

platz.1@osu.edu

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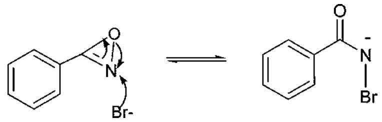
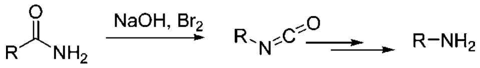
ABSTRACT

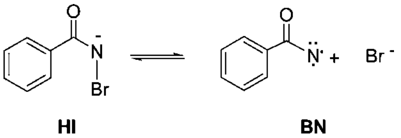


Nucleophilic anions react rapidly with benzoylnitrene to form a species involved in the Hofmann rearrangement. This species has been detected by time-resolved infrared spectroscopy.

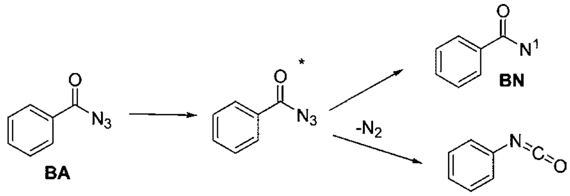
Treatment of a primary amide with base and bromine induces the Hofmann rearrangement (HR).[1]



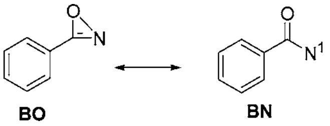
The HR involves the formation of an *N*-haloamide anion, which may form a nitrene that subsequently isomerizes, or as suggested by the work of Imamato,[2] the rearrangement and loss of bromide ion may be concerted. In this paper, we report the reaction of halide ions with benzoylnitrene to form the initial anionic Hofmann intermediate (HI).



Photolysis of benzoyl azide (BA) produces an excited state which both fragments to form benzoylnitrene (BN) or fragments in concert with Curtius rearrangement to form isocyanate.[3]



Theory predicts that there is a bonding interaction between the oxygen and nitrogen atoms of BN leading to an NCO bond angle of nearly 90° in a benzoxazirine (BO)-like resonance structure.[4−6]



The reactive intermediate is actually a resonance hybrid of an oxazirine and a carbonylnitrene. Because of this

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[1] For a review, see: Wallis, L. *Org. React.* **1946**, *3*, 267.

[2] (a) Imamoto, T.; Kim, S.-G.; Tsuno, Y.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1632. (b) Imamoto, T.; Kim, S.-G.; Tsuno, Y.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1639. (c) Imamoto, T.; Kim, S.-G.; Tsuno, Y.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1644. (d) Imamoto, T.; Kim, S.-G.; Tsuno, Y.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2776.

[3] Autrey, T.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *109*, 5814.

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interaction, benzoylnitrene, unlike phenylnitrene[7] **5**, has a closed-shell singlet ground state.

Laser flash photolysis (LFP) of BA (308 nm, 17 ns) in acetonitrile produces BN, which absorbs broadly at 305 nm and has a lifetime τ of 238 ns at ambient temperature.[5,6]

The observed first-order decay of BN, k_{obs}, is accelerated by the presence of lithium halide salts as shown in eq 1, where k is the absolute second-order rate constant of reaction of BN with lithium halide.

$$k_{obs} = 1/\tau + k[\mathrm{LiX}] \qquad (1)$$

A typical plot of k_{obs} versus [LiX] is given in Figure 1; values of k are collected in Table 1.

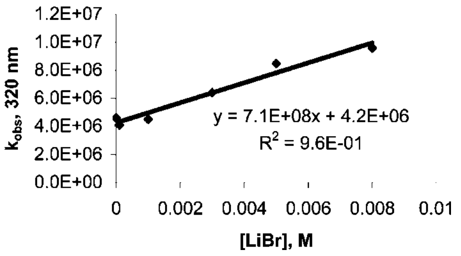

Figure 1. First-order kinetics of singlet benzoyl nitrene (7 mM in CH_3CN) decay with [LiBr] (266 nm excitation, 320 nm detection).

To determine whether the product of reaction of BN with LiBr is a nitrenoid (N) or a Hofmann intermediate (HI), the kinetics of reaction of BN with tetraalkylammonium halides and lithium tetrafluoroborate were studied.

Table 1. First-Order Rates of BN Quenching with Various Salts (308 nm Excitation, 320 nm Detection in CH_3CN)

salt	k, CH_3CN (M^{-1} s^{-1})
LiBr	7.15×10^8
LiCl	1.56×10^8
NEt_4F	6.79×10^9
NEt_4Cl	3.09×10^9
NEt_4Br	6.59×10^9
NEt_4I	1.19×10^{10}

Tetraalkylammonium halides react faster with benzoylnitrene than do the analogous lithium halides. This demonstrates the lack of involvement of lithium ion in this reaction and indicates that the reaction product is a Hofmann intermediate. The halide counterions of the ammonium salts must be more nucleophilic than their lithium counterparts, which suffer ion pairing in acetonitrile (Figure 2).

Lithium tetrafluoroborate does not quench singlet benzoylnitrene. Only nucleophilic anions quench benzoylnitrene, further evidence that a Hoffmann intermediate, and not a nitrenoid, is formed in the reaction.

The disappearance of the UV−vis spectrum of benzoylnitrene in the presence of halide ion is not accompanied by the growth of a new transient UV−vis absorption. The Hofmann intermediate is not observed by time-resolved electronic spectroscopy. Similar results were reported by Moss and co-workers, who reported that quenching of chlorophenylcarbene with lithium salts failed to produce the UV−vis spectra of carbenoids.[8] The Moss group did, however, detect the formation of $PhCCl_2^-$ and $PhCBr_2^-$ anions upon LFP of halophenyldiazirines in the presence of tetrabutylammonium halide.[9]

LFP (266 nm) of benzoyl azide in acetonitrile produces the transient IR spectrum[5] of BN (1760 cm^{-1}). A very different spectrum is observed in the presence of lithium or tetraalkylammonium halide (Figure 2).

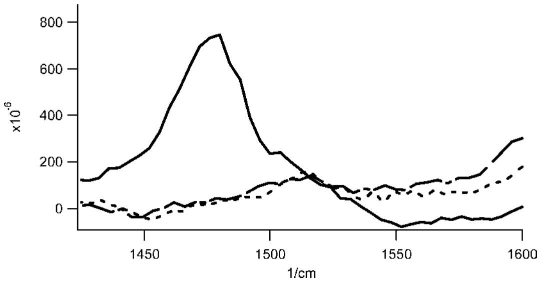

Figure 2. Transient IR spectrum observed 1.2 μs after photolysis (266 nm in CD_3CN) of BA (7 mM), - - -; BA (7 mM) with $LiBF_4$ (0.01 M), – –; and BA (7 mM) with NEt_4Br (0.01 M), —).

In the presence of halide ion an intense new band is observed which we assign to the Hofmann intermediate (HI). The position of the carbonyl vibration (1470 cm^{-1}) is consistent with the predictions of density functional theory (DFT)[10] for the HI (1471 cm^{-1}) in the lower energy syn conformation (Figure 3) but agrees less well with the

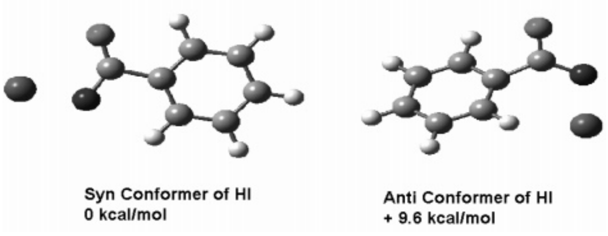

Figure 3. Geometries of the syn and anti conformers of HI at the B3LYP-6-31G* level of theory in the gas phase.

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predicted vibrational frequency of the analogous nitrenoid (Figure 4, predicted stretch at 1538 cm^{-1}; Supporting Information, Figures S1 and S2).

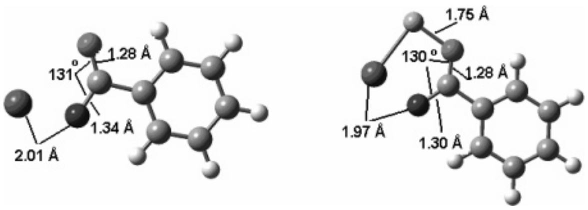

Figure 4. Geometries of HI and N as determined by DFT calculations at the UB3LYP 6-31G* level of theory using the PCM model of acetonitrile.

Lithium tetrafluoroborate does not quench singlet benzoylnitrene as measured by time-resolved UV−vis or IR spectroscopy. Only nucleophilic anions quench benzoylnitrene and form a new TRIR band at 1470 cm^{-1}.

The concentration of benzoyl azide has no effect on the lifetime of the Hoffmann Intermediate, but increasing concentrations of LiBr extend the lifetime of HI (Supporting Information, Figure S3).

Sequesteration of the lithium ion with crown ether (12-crown-4)[11] increases the observed rate constants of reaction of the halide ion with the Hofmann intermediate in acetonitrile (constant [LiBr] = 0.01M) (Figure 5) as determined by monitoring the lifetime of the HI at 1470 cm^{-1}.

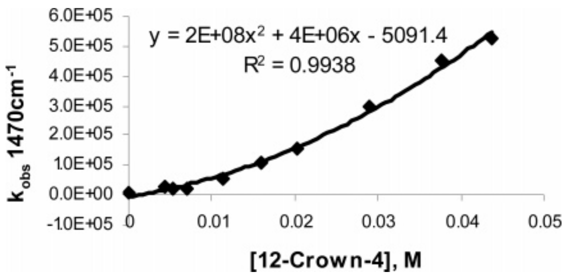

Figure 5. Observed rate constant of decay of HI in the presence of 12-crown-4 ether in CH_3CN (7 mM benzoyl azide, 0.01 M LiBr, 266 nm excitation, 1470 cm^{-1} detection).

In acetonitrile solution, benzoylnitrene is known to react with solvent to form an ylide,[5] which has a strong IR band at 1635 cm^{-1}. The lifetime of the ylide has been found to be approximately 50 μs by TRIR spectroscopy.[5] The presence of LiBr suppresses the yield of the ylide, measured at 1635 cm^{-1}, but does not change the lifetime of the ylide (Supporting Information, Figure S4). This demonstrates that X$^-$ is reacting directly with BA and not with the solvent-derived ylide.

It was not possible to study the kinetics of reaction of HI with alkenes or amines because these reagents scavenge BN before it can form the HI at moderate halide ion concentration.

As we do not detect a growth of isocyanate concurrent with the decay of the 1470 cm^{-1} band, we conclude that the HI is not fragmenting to isocyanate under our experimental conditions. The rate constant of this process is less than 5 × 10^3 s^{-1}, the intercept of Figure 5, under the experimental conditions.

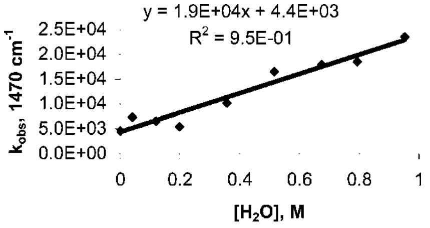

Figure 6. Quenching of the signal at 1470 cm^{-1} of HI (7 mM BA) with LiBr (0.1 M) in CD_3CN by water (266 nm excitation, 1470 cm^{-1} detection).

Water reacts slowly with the HI ($k = 1.9 \times 10^4$ M^{-1} s^{-1}). The HI reacts more slowly with water than does benzoylnitrene ($k = 3.8 \times 10^6$ M^{-1} s^{-1}) (Figure 6).[6]

In summary, benzoylnitrene reacts rapidly with halide ions to produce the nitrogen centered anion thought to be involved in the Hofmann rearrangement.

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Supporting Information Available: Protocols for Time-resolved UV and IR spectroscopy along with a Stern−Volmer plot of the quenching of the yield of the band at 1635 cm^{-1} by LiBr and the predicted IR spectra of *syn*-HI and N. This material is available free of charge via the Internet at http://pubs.acs.org.

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