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Chain-Amplified Photochemical Fragmentation of *N*-Alkoxypyridinium Salts: Proposed Reaction of Alkoxyl Radicals with Pyridine Bases To Give Pyridinyl Radicals

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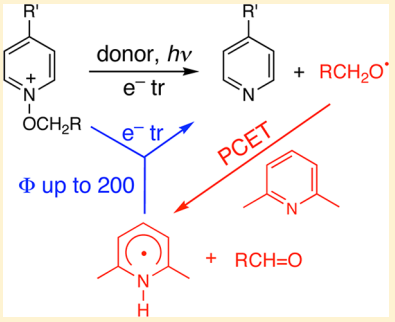
Supporting Information

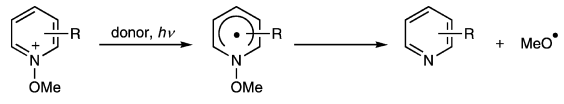
ABSTRACT: Photoinduced electron transfer to *N*-alkoxypyridiniums, which leads to N−O bond cleavage and alkoxyl radical formation, is highly chain amplified in the presence of a pyridine base such as lutidine. Density functional theory calculations support a mechanism in which the alkoxyl radicals react with lutidine via proton-coupled electron transfer (PCET) to produce lutidinyl radicals (BH•). A strong electron donor, BH• is proposed to reduce another alkoxypyridinium cation, leading to chain amplification, with quantum yields approaching 200. Kinetic data and calculations support the formation of a second, stronger reducing agent: a hydrogen-bonded complex between BH• and another base molecule (BH•···B). Global fitting of the quantum yield data for the reactions of four pyridinium salts (4-phenyl and 4-cyano with *N*-methoxy and *N*-ethoxy substituents) led to a consistent set of kinetic parameters. The chain nature of the reaction allowed rate constants to be determined from steady-state kinetics and independently determined chain-termination rate constants. The rate constant of the reaction of $CH_3O^•$ with lutidine to form BH•, k_1, is ∼6×10^6 M^{-1} s^{-1}; that of $CH_3CH_2O^•$ is ∼9 times larger. Reaction of $CD_3O^•$ showed a deuterium isotope effect of ∼6.5. Replacing lutidine by 3-chloropyridine, a weaker base, decreases k_1 by a factor of ∼400.



INTRODUCTION

Reactions of alkoxyl radicals have received considerable attention because of their importance in a variety of organic,[1] biological,[2] and atmospheric[3] processes. These radicals undergo a variety of inter- and intramolecular reactions such as unimolecular fragmentation,[4] hydrogen atom abstraction,[5] addition to unsaturated compounds,[6] and isomerization.[7] Hydrogen atom abstraction reactions by alkoxyl radicals are of particular interest because of their importance in enzymatic and biological systems.[8] Alkoxyl radicals also play an important role in atmospheric oxidation of volatile organic compounds, where isomerization, fragmentation, and reaction with O_2 are the dominant reactions.[3] Intramolecular isomerization of alkoxyl radicals via 1,5-hydrogen shift to the corresponding hydroxyalkyl radicals is well-known in solution,[7a−c] and similar reactions are also proposed to take place in the gas phase.[3] The isomerization of methoxyl radical to hydroxymethyl radical via 1,2-hydrogen shift is thermodynamically favorable but has a high barrier,[9] although the isomerization has been shown to be catalyzed by water,[7d−f] alcohols,[7g] and acid.[7h]

In this paper we describe the novel reaction of methoxyl and ethoxyl radicals with pyridine bases. The alkoxyl radicals were conveniently generated by photoinduced electron transfer to *N*-alkoxypyridinium salts, which leads to fast N−O bond cleavage, eq 1.[10] *N*-Alkoxypyridinium salts undergo a range of photochemical reactions that have been exploited in a variety of ways.



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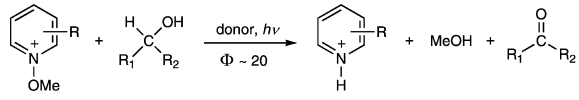

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For example, alkoxyl radicals generated from alkoxypyridinium salts have been used to initiate free radical polymerization, which extended the photosensitivity of these polymerizations to light throughout the visible region.[11] In addition, an interesting aspect of electron transfer reactions of the alkoxypyridiniums is their ability to lead to chain amplification, as in the oxidation of alcohols to ketones or aldehydes, eq 2.[12] Another dramatic example of chain amplification is described in the present work. Importantly, the chain nature of the reaction was instrumental in the determination of kinetic parameters for the methoxyl and ethoxyl radicals, which otherwise would not have been

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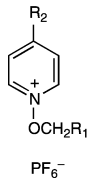
accessible through conventional flash photolysis because of their lack of a convenient absorption chromophore.

RESULTS AND DISCUSSION

The photoreductions of four *N*-alkoxypyridinium salts (**1a–d**) were examined: the substituent in the 4-position was either phenyl or cyano, and the alkoxy substituent was either methoxy or ethoxy. No reversible potential can be obtained for these pyridiniums by using conventional electrochemical methods due to fast fragmentation of the N–O bond upon one electron reduction. Nonetheless, estimates of the reduction potentials of the 4-phenyl and 4-cyano derivatives of −1.0 and −0.5 V vs SCE in acetonitrile have been previously made[11a] based on a comparison between charge transfer absorption bands of the *N*-alkoxy and the corresponding *N*-alkyl pyridinium salts, which show reversible potentials.[13]

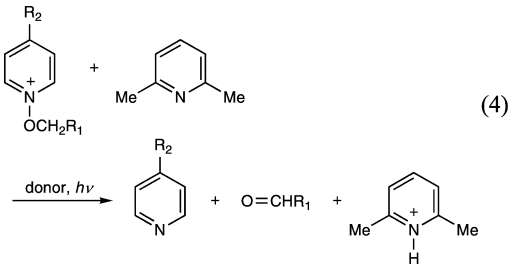


	R_1	R_2
1a	H	Ph
1b	Me	Ph
1c	H	CN
1d	Me	CN

Electron transfer to *N*-alkoxypyridinium salts can be induced by either singlet or triplet excited donors.[12a] The energetic requirements are given by eq 3, where $(E_{excit})_D$ is the excitation energy of the sensitizing donor (singlet or triplet, depending on which state reacts with the pyridinium), $(E_{ox})_D$ is the oxidation potential of the donor, $(E_{red})_A$ is the reduction potential of the pyridinium, and Δ is an energy increment varying from tens of meV in acetonitrile[14] to ca. 0.3 eV in nonpolar media.[15] Triplet sensitizers are more efficient in reducing the pyridinium salts because energy-wasting return electron transfer within the geminate pair is spin forbidden. Thioxanthone, which has an intersystem crossing (ISC) efficiency of 0.88 in acetonitrile,[12a] has proven to be effective for these reactions.[12a] In the current work 2-chlorothioxanthone (CTX) was used, which has an ISC efficiency very close to unity[16] and still meets the requirements of eq 3.[17] Consistent with this conclusion, triplet CTX is quenched by **1a** with a rate constant of 4.7×10^9 M^{-1} s^{-1} and by **1c**, a 0.5 eV more exergonic reaction, with a rate constant of 8.3×10^9 M^{-1} s^{-1}.

$$(E_{excit})_D > (E_{ox})_D - (E_{red})_A + \Delta \quad (3)$$

The fragmentation quantum yields for **1a–d** induced by triplet CTX are ∼1 in acetonitrile. Depending on the starting pyridinium salt, the reaction product is 4-phenyl- or 4-cyanopyridine. A dramatic increase in the quantum yield (up to ∼200) was observed in the presence of lutidine. In these latter cases, the reaction products were the pyridine derived from the pyridinium salt, formaldehyde or acetaldehyde, and the protonated lutidinium cation, eq 4. The mass balances for conversion of the pyridiniums to their pyridine products were uniformly >95%.



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1. Substituents Effect. The dependence of the fragmentation quantum yields on the concentration of lutidine was investigated with a starting concentration of the pyridinium salts of 0.02 M. Irradiations were carried out to ∼20% conversion. The quantum yields were determined by using NMR spectroscopy from the ratio of the pyridine product to the starting pyridinium salt. The estimated error in the quantum yields is 5–10%. As shown in Figure 1, there is a sharp increase in the quantum yields with increasing [lutidine] up to ∼0.2 M, followed by a modest increase at higher concentrations. The highest attainable quantum yield increases by a factor of ∼2 upon changing the *N*-alkoxy group from methoxy to ethoxy (cf. **1a** vs **1b** and **1c** vs **1d**) and also by changing the 4-substituent from phenyl to cyano (cf. **1a** vs **1c** and **1b** vs **1d**). Thus, there is a ∼4-fold increase in the limiting quantum yield between 4-phenyl-*N*-methoxypyridinium (**1a**, Φ_{lim} ∼50) and 4-cyano-*N*-ethoxypyridinium (**1d**, Φ_{lim} ∼200).

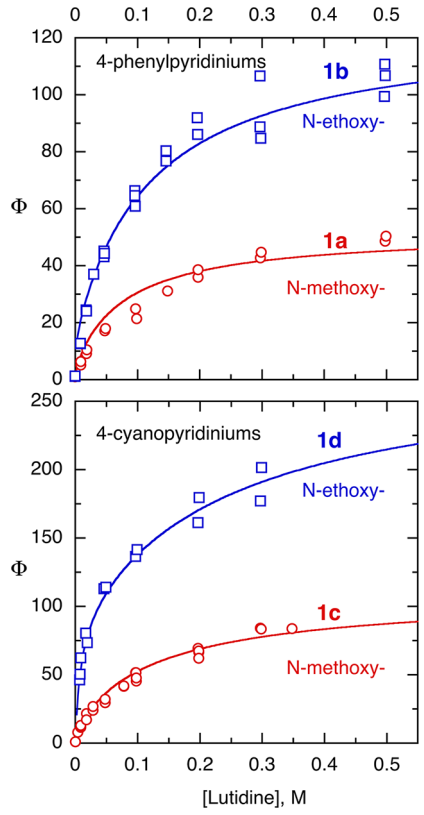

Figure 1. Fragmentation quantum yields of the pyridinium salts (**1a–d**), eq 4, in CD_3CN as a function of lutidine concentration. The average concentration of **1** between the start and end of irradiation is ∼0.018 M. 2-Chlorothioxanthone (CTX), 2 mM, was used as sensitizer; excitation at 405 nm. See text for details regarding the fitting curves.

Increasing the concentration of the pyridinium salts also leads to an increase in quantum yield, but the effect is much less pronounced than that of increasing [lutidine]. For example, at [lutidine] of 0.3 or 0.5 M, the quantum yield for **1b** increases upon increasing its concentration from 0.02 to 0.05 M by only ∼25% and, within the experimental error, stays at that level at concentrations as high as 0.2 M (see the Supporting Information). As described below, the differing sensitivities of the quantum yield to the changes in lutidine and pyridinium

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concentrations are consistent with different contributions from chain termination reactions.

2. Deuterium Isotope Effect. The deuterium isotope effect on the α-hydrogens of the alkoxy group was evaluated by comparing the reactions of **1a** to an analogue in which the OCH_3 group was replaced by OCD_3. As shown in Figure 2, as a function of the concentration of lutidine or of the pyridinium salt, the deuterated compound exhibited considerably lower quantum yields. The magnitude of the deuterium isotope effect of ~6.5 was determined by globally fitting both sets of data (see kinetics section).

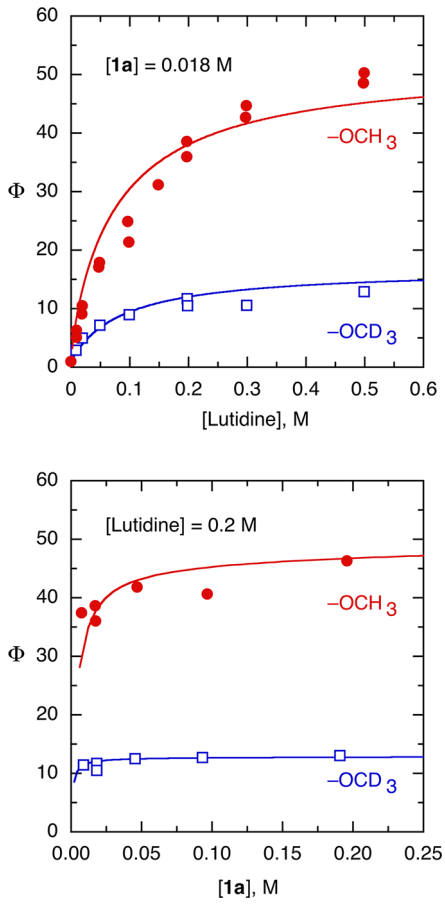


Figure 2. Deuterium isotope effect on the fragmentation quantum yields (Φ) of 4-phenyl-*N*-methoxypyridinium (**1a**) as a function of the lutidine concentration (top) and of the pyridinium concentration (bottom). Methoxy group: OCH_3 (red, filled circles); OCD_3 (blue, unfilled squares). The fitting curves are based on a deuterium isotope effect for reaction of the methoxyl radical with lutidine (k_1) of 6.5.

3. Basicity of the Pyridine. To examine the effect of the basicity of the pyridine, the reaction of **1b** with 3-chloropyridine (pK_a ~10)[18] was compared to that described above with lutidine (pK_a ~14).[18] As shown in Figure 3, the weaker base is much less effective in propagating the chain reaction. The lack of leveling off in quantum yield at higher concentrations of 3-chloropyridine and the fitting curves in Figure 3 are discussed in the kinetics section.

4. Reaction Intermediates and Kinetic Scheme. As shown above, the photosensitized fragmentation of *N*-alkoxypyridinium cations (P^+) proceeds by a chain reaction mechanism in the presence of pyridine bases. It is plausible to conclude that alkoxyl radicals generated by reduction of P^+ (eq 1) react with the added base (B) to give a second reaction intermediate that is capable of transferring an electron to another P^+, thus propagating the chain reaction. To efficiently reduce the 4-phenylpyridiniums (**1a** or **1b**), the secondary intermediate must have an oxidation potential similar to or more negative than the reduction potential of the pyridiniums ($E_{red} \approx -1$ V vs SCE).

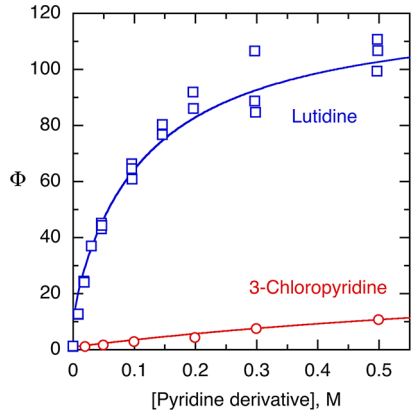
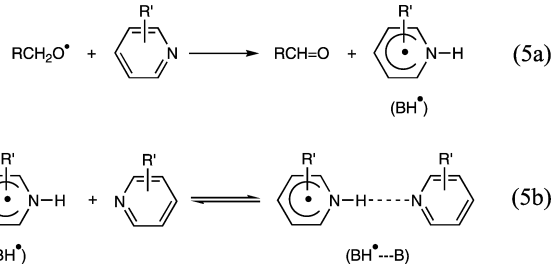


Figure 3. Comparison between the fragmentation quantum yields of **1b** in the presence of 3-chloropyridine versus lutidine. The reaction conditions are the same as in Figure 1. See text for details regarding the fitting curves.

In principle, the reaction of the methoxyl or ethoxyl radical with B could lead to several possible products. For example, proton transfer from the alkoxyl radicals to B would generate the radical anions of formaldehyde or acetaldehyde, both of which could reduce P^+ to propagate the chain. As discussed in the next section, these proton transfers are kinetically incompetent, i.e., the endergonicities for the proton transfers exceed the activation barriers estimated for reaction of the alkoxyl radicals with B based on the kinetic scheme used to fit the quantum yield data. The reaction of methoxyl or ethoxyl radical with B could alternatively result in their isomerization to the corresponding α-hydroxy radicals, $RCH^{\bullet}-OH$ (R = H or CH_3). Although these radicals have estimated oxidation potentials[19] less negative than −0.5 V vs SCE, making electron transfer to the pyridinium cations energetically unfavorable, the intermediates could react with the pyridine bases to form an intermediate ($RCH^{\bullet}-OH\cdots B$) that is capable of energetically favorable electron transfer to the alkoxypyridiniums.[20] As described in detail below, quantum chemical calculations instead predict that methoxyl (ethoxyl) radicals react with lutidine or 3-chloropyridine to give formaldehyde (acetaldehyde) and the lutidinyl or 3-chloropyridinyl radical ($BH^{\bullet}$), eq 5a. To test whether these pyridinyl radicals are capable of



reducing the pyridinum cations, leading to chain propagation, their oxidation potentials were estimated from the reduction potentials of the corresponding protonated bases. The cyclic

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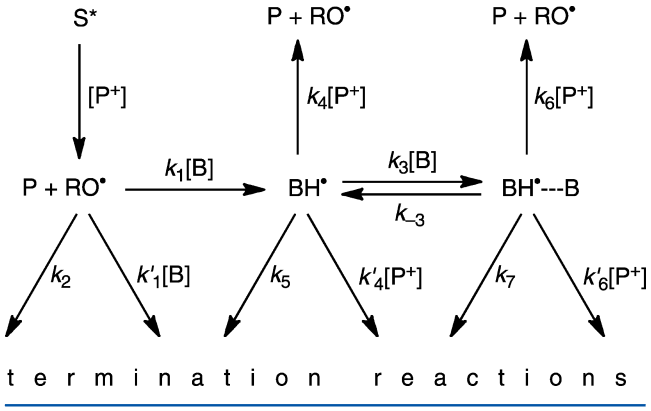
voltammograms of protonated lutidine and 3-chloropyridine showed irreversible reductions in acetonitrile with peak potentials at −1.58 and −1.16 V vs SCE, respectively (see Supporting Information), indicating that reduction of the pyridinium cations by both pyridinyl radicals ($BH^{\bullet}$) is energetically favorable.

Quantum chemical calculations also revealed that the pyridinyl radicals ($BH^{\bullet}$) were capable of forming hydrogen-bonded complexes ($BH^{\bullet}\cdots B$) with their pyridine precursors, eq 5b, and that these complexes were *stronger* reducing agents than $BH^{\bullet}$ alone (see Section 6). Importantly, a consistent set of kinetic parameters to model the experimental quantum yields over the entire range of base concentrations could not be obtained for all four pyridinium cations **1a**−**d** unless the $BH^{\bullet}\cdots B$ complexes were included in the kinetic analysis.

Scheme 1 shows the full range of kinetic processes needed to globally fit the combined quantum yield data. In addition to

Scheme 1



initiation and propagation reactions, several chain-termination steps are included in the kinetic scheme. Two of them, k'_1 and k_2, involve the alkoxyl radicals. Competing with the reaction of $RO^{\bullet}$ with the pyridine bases that leads to the formation of $BH^{\bullet}$, k_1, there is a minor, chain-terminating hydrogen atom abstraction from the methyl groups of lutidine, k'_1, when this base is used. The other termination rate constant, k_2, is analogous to that encountered in a related system.[12a] The k_2 step represents the sum of two reactions: deuterium atom abstraction from the solvent CD_3CN and a minor reaction between $RO^{\bullet}$ and the photosensitizer, 2-chlorothioxanthone (CTX).[12a] Competing with the propagation reaction of $BH^{\bullet}$, k_4, are two possible termination reactions, k'_4 and k_5. The corresponding reactions for $BH^{\bullet}\cdots B$ are k_6, k'_6, and k_7. In both cases k'_4 and k'_6 represent reactions with trace impurities in P^+ and/or minor reactions of the radicals with P^+, other than the chain-propagating electron transfer. As explained in Section 5, the termination steps k_5 and k_7 with lutidine as base can predominantly be attributed to electron transfer to the sensitizer, CTX.

Based on Scheme 1, the quantum yield for consumption of the *N*-alkoxypyridininium salt (P^+) can be expressed in terms of eq 6 (see Supporting Information for derivation). Because the quantum yield depends only on ratios of rate constants and not on their absolute values, it was convenient to use fractionation factors (α−ε), which in turn can be expressed in terms of rate constants ratios (a−h).

$$\Phi = \frac{1}{1 - \frac{\alpha\beta + \alpha\gamma\delta}{1 - \gamma\varepsilon}} \tag{6}$$

where

$$\alpha = \frac{k_1[B]}{k_1[B] + k'_1[B] + k_2} = \frac{1}{1 + a + b[B^{-1}]}$$

$$\beta = \frac{k_4[P^+]}{k_4[P^+] + k'_4[P^+] + k_5 + k_3[B]} = \frac{1}{1 + c + d[P^+]^{-1} + e[B][P^+]^{-1}}$$

$$\gamma = \frac{k_3[B]}{k_4[P^+] + k'_4[P^+] + k_5 + k_3[B]} = \frac{e[B][P^+]^{-1}}{1 + c + d[P^+]^{-1} + e[B][P^+]^{-1}}$$

$$\delta = \frac{k_6[P^+]}{k_6[P^+] + k'_6[P^+] + k_7 + k_{-3}} = \frac{1}{1 + f + g[P^+]^{-1} + h[P^+]^{-1}}$$

$$\varepsilon = \frac{k_{-3}}{k_6[P^+] + k'_6[P^+] + k_7 + k_{-3}} = \frac{h[P^+]^{-1}}{1 + f + g[P^+]^{-1} + h[P^+]^{-1}}$$

$$a = \frac{k'_1}{k_1} \quad b = \frac{k_2}{k_1}$$

$$c = \frac{k'_4}{k_4} \quad d = \frac{k_5}{k_4} \quad e = \frac{k_3}{k_4}$$

$$f = \frac{k'_6}{k_6} \quad g = \frac{k_7}{k_6} \quad h = \frac{k_{-3}}{k_6}$$

Although there are several fitting parameters (a−h), global analysis was helpful in limiting their range because some of the rate constant ratios are constrained by being common among certain pairs of the four pyridiniums **1a**−**d**. For example, the rate constant for reaction of the methoxyl radical with lutidine $(k_1)_{MeO}$ does not depend on the starting pyridinium (**1a** or **1c**); thus, a and b were kept constant for these two compounds. The same applies for the reaction of the ethoxyl radical $(k_1)_{EtO}$, whether from **1b** or **1d**. In addition, the ratio $a/b = k'_1/k_2$ is expected to be constant for all reactions with lutidine. Because k'_1/k_2 is the ratio of rate constants for hydrogen abstraction from lutidine to the sum of deuterium abstraction from the solvent and reaction with the sensitizer, it is unlikely that it will differ between methoxyl and ethoxyl radicals.

The electron transfer rate constants to 4-phenylpyridiniums, $(k_4)_{Ph}$ and $(k_6)_{Ph}$, are assumed to be the same for the *N*-methoxy- and *N*-ethoxy-pyridiniums, **1a** and **1b**; thus, the ratios d, e, g, and h were kept constant for these two compounds. The same applies to $(k_4)_{CN}$ and $(k_6)_{CN}$, the corresponding electron transfer reactions of the 4-cyanopyridiniums, **1c** and **1d**. Another constraint derives from the reactant independence of the equilibration rate constants between $BH^{\bullet}$ and $BH^{\bullet}\cdots B$, k_3 and k_{-3}, which are common for all pyridiniums reacting with a

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single pyridine base. The rate constants k_5 and k_7, which represent termination reactions, are also common for all pyridiniums. Therefore, $e/d = k_3/k_5$ and $h/g = k_{-3}/k_7$ should be the same for all pyridiniums with lutidine as base.[21] Values of all the global-fitting parameters are listed in the Supporting Information.

5. Rate Constants. *Reaction of Alkoxyl Radicals with the Base, k_1.* As indicated in the Introduction, a key aspect of this work is the reaction of alkoxyl radicals with pyridine bases that is proposed to lead to the reducing radical BH$^\bullet$, k_1. Although, the quantum yield data afford only ratios of rate constants, an estimate of k_1 can be obtained from the ratio $b = k_2/k_1$ because the value of k_2 (4.2×10^3 s^{-1}) is available from previous work.[22]

To ensure internal consistency, we first checked if the kinetic analyses led to congruent relationships between the independently determined value of k_2 and that of k'_1, the other termination rate constant of the alkoxyl radical. As mentioned above, the ratio $a/b = k'_1/k_2$ was kept constant for all reactions with lutidine. The best value for this ratio from the global fitting was 10 M^{-1}, which corresponds to k'_1 of 4.2×10^4 M^{-1} s^{-1} for reaction of the alkoxyl radicals with lutidine. For comparison, the rate constant for hydrogen abstraction from toluene by *tert*-butoxyl radical is $\sim 2 \times 10^5$ M^{-1} s^{-1}.[5a] Considering there are two methyl groups in lutidine versus one in toluene leads to a ~10-fold difference in the rate constants for hydrogen atom abstraction, or ~1.3 kcal/mol in activation barrier. However, hydrogen atom abstraction by *tert*-butoxyl radical from toluene is 3 kcal/mol more favorable than hydrogen atom abstraction by methoxyl (or ethoxyl) radical from lutidine,[23] which could readily account for the lower reactivity of lutidine. This comparatively good agreement with independent literature data supports the general reliability of the fitting procedure.

Fitting the kinetic data for methoxypyridiniums **1a** and **1c** in Figure 1 gave k_2/k_1 of 7.2×10^{-4} M. Based on the value of k_2 mentioned above, k_1 for the reaction of $CH_3O^\bullet$/lutidine, $(k_1)_{MeO}$, is estimated to be 5.8×10^6 M^{-1} s^{-1}. Fitting the kinetic data for the ethoxypyridiniums, **1b** and **1d**, required k_2/k_1 of 8×10^{-5} M, yielding $(k_1)_{EtO}$ of 5.3×10^7 M^{-1} s^{-1}.

The significant decrease in quantum yield upon replacing the CH_3O group in **1a** by CD_3O shown in Figure 2 is reflected in a factor of 6.5 increase in k_2/k_1 required to fit the data, which can most plausibly be attributed to a 6.5-fold decrease in k_1. This is clearly a primary isotope effect, consistent with the proposed hydrogen atom transfer from the methoxyl radical to lutidine.

The precipitous decrease in quantum yield using 3-chloropyridine instead of lutidine in the reaction of **1b** (Figure 3) required a ~400-fold decrease in k_1 to fit the data. As expected, because of the absence of abstractable hydrogen in chloropyridine the best fit was obtained with no contribution from k'_1 in this case. The absence of chain termination via k'_1 with 3-chloropyridine explains the lack of leveling off in the quantum yields at high base concentrations (Figure 3). The leveling off in quantum yield is a dominant feature of the reactions with lutidine (Figure 1), where the plateau is defined largely by $1/a$ or k_1/k'_1.

As mentioned above, the rate constant k_1 for reaction of $CH_3O^\bullet$ with lutidine can be used to evaluate the kinetic competence of the proton transfer mechanism to form formaldehyde radical anion and the lutidinium cation. The pK_a of $CH_3O^\bullet$ in acetonitrile is estimated to be ~25.[24] Based on the pK_a of the lutidinium cation in acetonitrile (~14),[18] proton transfer from $CH_3O^\bullet$ to lutidine is estimated to be endergonic by ~14 kcal/mol (ΔG°_{pt}). This corresponds to the *minimum* activation free energy for the proton transfer reaction. The experimental activation free energy ($\Delta G^\ddagger_{exp}$) can be estimated from the rate constant k_1 at 295K to be ~8 kcal/mol. That $\Delta G^\circ_{pt} \gg \Delta G^\ddagger_{exp}$ excludes proton transfer for the k_1 step in Scheme 1. As discussed below, computational results provide independent evidence against a proton transfer mechanism for the reaction of the alkoxyl radicals with pyridine bases.

Propagation Reactions k_4 and k_6. Based on the parameters derived from the data fitting (see the Supporting Information), $(k_4)_{Ph} = 0.15 \times (k_4)_{CN}$ and $(k_6)_{Ph} = 0.6 \times (k_6)_{CN}$. Being rate constants for strongly exergonic electron transfer reactions (driving force >1 eV), which are likely to proceed over long distance, both $(k_4)_{CN}$ and $(k_6)_{CN}$ are expected to be $\sim 1.2 \times 10^{10}$ M^{-1} s^{-1}.[25] This value yields $(k_4)_{Ph}$ of $\sim 2 \times 10^9$ M^{-1} s^{-1} and $(k_6)_{Ph}$ of $\sim 7 \times 10^9$ M^{-1} s^{-1}, which are reasonable for the reactions of **1a** and **1b** that are 0.5 eV less exergonic than those of **1c** and **1d**. The larger value of $(k_6)_{Ph}$ compared to $(k_4)_{Ph}$ can be attributed to the ~0.15 eV greater reducing power of BH$^\bullet\cdots$B compared to that of BH$^\bullet$ (see Section 6).

From the ratio d, the pseudo first-order rate constant of the termination reaction k_5 is $\sim 1.8 \times 10^6$ s^{-1}. More than one reaction may be represented by k_5, for example, electron transfer to residual oxygen, oxidant impurities, and/or the sensitizer, CTX. The last reaction, however, is most likely the main contributor. CTX has reduction potential of −1.53 V vs SCE,[17a] which allows for energetically favorable electron transfer from BH$^\bullet$ and at [CTX] = 0.002 M can account for the observed rate constant for k_5.[26]

With 3-chloropyridine as base, there are insufficient quantum yield data to obtain reliable estimates for k_4 and k_6. The reducing power of BH$^\bullet$ in this case is certainly less than when the base is lutidine. Combined with a relatively large driving force to form the hydrogen-bonded complex, BH$^\bullet\cdots$B, which is a stronger reducing agent than BH$^\bullet$ (see Section 6), it is likely that chain-propagating electron transfer to the pyridinium cation **1b** proceeds predominantly via k_6 in this case.

Equilibrium Constant (k_3/k_{-3}). Based on the assumption that $(k_4)_{CN} \approx (k_6)_{CN} \approx 1.2 \times 10^{10}$ M^{-1} s^{-1}, the ratios e and h for these reactions, 0.3 and 0.0072, respectively, yield k_3 of 3.6×10^9 M^{-1} s^{-1} and k_{-3} of 8.7×10^7 s^{-1}. From these values (k_3/k_{-3}) is ~40, i.e., BH$^\bullet\cdots$B is more stable than BH$^\bullet$ by 0.094 eV; the computed stabilization energy is 0.076 eV (see below).

6. Computational Results. As described above, the quantum yield for the chain fragmentation of *N*-alkoxypyridinium cations is strongly dependent on the basicity of the pyridine base. This observation is consistent with the reaction of the alkoxyl radicals and the bases having some proton-transfer character. We therefore initiated computational studies that focused on reaction of the α-C−H bonds of the alkoxyl radicals with the nitrogen atom of the pyridine bases.

All calculations were done using the hybrid B3LYP density functional method.[27] All open-shell calculations were performed with the unrestricted UB3LYP method. Geometry optimizations, transition structure searches, and vibrational analyses were performed with a 6-311++(d,p) basis set. The polarizable continuum model (PCM)[28] was used to model the reaction solvent, acetonitrile. The Universal Force Field (UFF)[29] radii for all atoms, including hydrogen atoms, were used in cavity building. All of the calculations were carried out with the Gaussian 03 suite of programs.[30] Vibrational frequencies were determined by using the analytic Hessian, calculated for each local minimum and each transition state structure. In all cases, local minima had positive vibrational

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frequencies and transition state structures had only one imaginary frequency.

Calculations on the reactions of the alkoxyl radicals with the pyridine bases showed that a weakly bound reactant complex is formed (see Figure 4), where the α-C−H bond of the alkoxyl

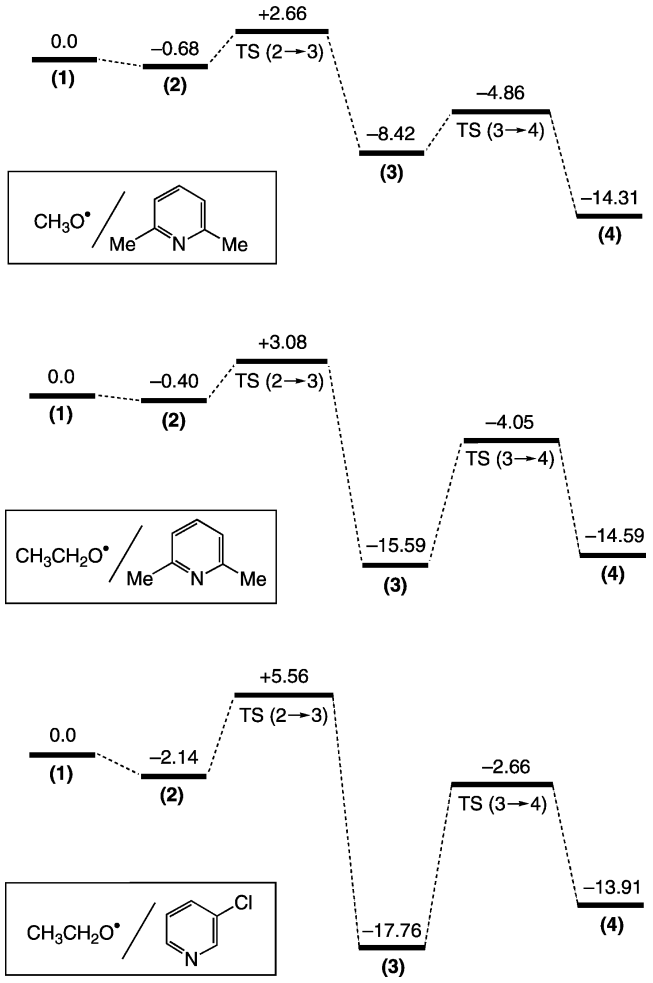

Figure 4. Calculated energy differences (in kcal/mol) between intermediates relative to that of an alkoxyl radical plus a pyridine base (1). Interaction between the pair (see inserts) leads to a hydrogen-bonded complex (2). Hydrogen atom transfer from (2) leads to a pyridinyl radical, hydrogen-bonded to an aldehyde (3). Return hydrogen atom transfer from (3) leading to a hydrogen-bonded complex between an α-hydroxy radical and the corresponding pyridine (4). Energies of the transition states for the conversion of (2) to (3) and (3) to (4) are marked by TS. Structures and bond lengths are given in the Supporting Information. Calculational details are given in the text.

radical is hydrogen-bonded to the nitrogen atom of the pyridine base.[31] Interestingly, reaction of this complex leads, in all cases, to transfer of a *hydrogen atom* rather than a proton from the alkoxyl radical to the nitrogen of the pyridine base, resulting in the formation of formaldehyde (or acetaldehyde) and an *N*-hydropyridinyl radical. As described above, the oxidation potentials of both the lutidinyl and the 3-chloropyridinyl radicals are sufficiently low to be capable of reducing the *N*-alkoxypyridinium cations used in this work, thus promoting chain propagation. As shown in Figure 4, the energy barriers for the hydrogen atom transfers are predicted to be relatively low for the reactions of methoxyl and ethoxyl radicals with lutidine (2.7 and 3.1 kcal/mol, respectively) and significantly higher for reaction of ethoxyl radical with 3-chloropyridine (5.6 kcal/mol). The higher calculated barrier for the reaction of ethoxyl radical with 3-chloropyridine is in agreement with experiment. The predicted barriers for reaction of methoxyl and ethoxyl radical with lutidine are reversed relative to the experimental data, although the energetic differences are relatively small.

Before discussing the detailed nature of the hydrogen atom transfer reactions, we note that our calculations show that deprotonation of the alkoxyl radicals by the pyridine bases are energetically unfavorable relative to the hydrogen atom transfer reactions. For example, deprotonation of the methoxyl and ethoxyl radicals by the stronger base, lutidine, are both predicted to be endothermic relative to the reactant complexes by ∼10−11 kcal/mol (see Supporting Information). Thus, deprotonation of the alkoxyl radicals is *not* expected to measurably compete with the hydrogen atom transfer reactions. This conclusion is consistent with the kinetic competence test described above that similarly excluded a proton transfer mechanism.

Interestingly, our calculations reveal that the transition states for hydrogen atom transfer have a significant degree of ionic character. For example, in the reaction of the methoxyl radical with lutidine, the Mulliken charges on the formaldehyde fragment, the lutidine fragment, and the transferring hydrogen atom are −0.76, +0.21, and +0.55, respectively. Similar results were found for the other hydrogen atom transfer reactions (see Supporting Information). These group charges are consistent with a reaction that has significant proton-transfer character. In support of this idea, examination of the singly occupied molecular orbital (SOMO) for the transition state (Figure 5)

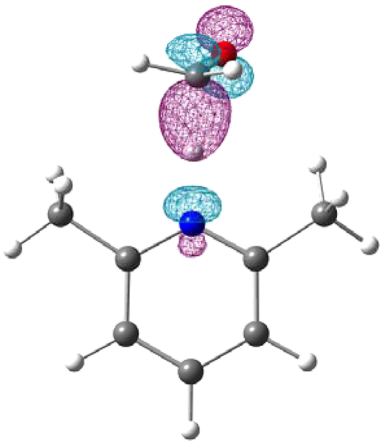

Figure 5. Singly occupied molecular orbital (SOMO) density surface of the transition state for hydrogen atom transfer from methoxyl radical to lutidine computed with an isodensity value of 0.12 au.

shows that the orbital is localized between the nitrogen of the lutidine and the methoxyl radical fragment; no occupation of the π-orbitals for the lutidine is evident, as would be expected during formation of the lutidinyl radical. The transition states for reaction of ethoxyl radical with lutidine and 3-chloropyridine showed similar results (see the Supporting Information). The combined results are consistent with these hydrogen atom transfers proceeding by a proton-coupled electron transfer (PCET) mechanism,[32] where partial proton transfer precedes electron transfer in the net hydrogen atom transfer reaction. It is worth noting that the valence bond curve-crossing model of

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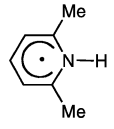
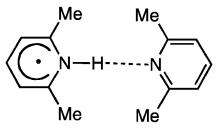
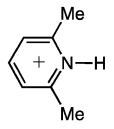
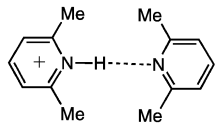
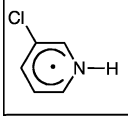
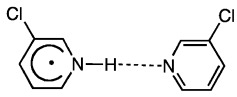
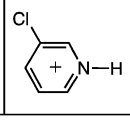
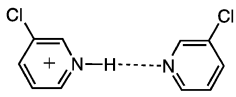
Table 1. Calculated Stabilization Energies[a]

$BH^{\bullet}$	$BH^{\bullet}$---B	$\Delta G_{(\bullet)}$	BH^{+}	BH^{+}---B	$\Delta G_{(+)}$	ΔE_{ox}
		−0.076			−0.228	−0.152
		−0.160			−0.331	−0.171

[a]Energies (in eV) of hydrogen-bonded complexes of pyridinyl radicals with the corresponding pyridine derivative relative to the separated species $\Delta G_{(\bullet)}$ and the stabilization energies for the corresponding pyridinium derivatives $\Delta G_{(+)}$. The increment $\Delta G_{(+)} - \Delta G_{(\bullet)}$ gives the difference in oxidation potential of the complex versus that of the free radical, ΔE_{ox}.

Shaik and co-workers[33] predicts that for reactions with a low-lying proton transfer state, such as the reactions of alkoxyl radicals with pyridines studied here, a PCET process is expected to have a relatively low activation energy.

Additional calculations revealed that, following the initial hydrogen atom transfer from the alkoxyl radicals to the pyridine bases, a subsequent return hydrogen atom transfer can occur from the pyridinyl radicals to the aldehydes to give the corresponding pyridines and α-hydroxy alkyl radicals. As shown in Figure 4, for the reactions of both pyridinyl radicals with acetaldehye, the return hydrogen atom transfers are predicted to have relatively large energy barriers (~11 and ~15 kcal/mol). Thus these processes are *not* expected to compete with diffusional separation of the pyridinyl radical/aldehyde complexes that are formed after the initial hydrogen atom transfer. For the reaction of methoxyl radical with lutidine, however, the second hydrogen atom transfer is predicted to have a significantly lower barrier (~4 kcal/mol), presumably due to the greater driving force of the reaction and, perhaps, less steric hindrance in the transition state. Nonetheless, the lutidinyl radical/formaldehyde pair is predicted to be bound by only 1.6 kcal/mol (see Supporting Information), thus diffusional separation is again predicted to proceed more rapidly than the return hydrogen atom transfer.

In summary, the calculational evidence leads to the prediction that the pyridinyl radicals are the principal chain-propagating species that reduce the *N*-alkoxypyridinium cations for all cases investigated here. We cannot rule out the possibility, however, that for the *N*-methoxypyridinium cation/lutidine reactions, a minor amount of hydroxymethyl radical may be formed, which leads to chain-propagating reduction of the pyridinium cation. Finally, we note that, despite considerable effort, we were unable to locate transition states wherein the pyridine bases catalyze isomerization of the alkoxyl radicals to α-hydroxy alkyl radicals in a one-step reaction.

As described above, a mechanistic model that included reduction of the *N*-alkoxypyridinium cations *only* by the pyridinyl radicals was unable to fit the experimental quantum yield data with a consistent set of kinetic parameters for the different pyridiniums over the full range of base concentrations. The data suggested that, at high concentration, the pyridine base played an additional role in promoting chain propagation. We hypothesized that the pyridinyl radicals might react with the pyridines to form hydrogen-bonded complexes that were more strongly reducing than the pyridinyl radicals. As shown in Table 1, DFT calculations support this hypothesis. The relative reducing ability of the pyridinyl radicals versus their complexes were determined by comparing the calculated binding free energies of the pyridinyl radicals vs the corresponding pyridinium cations with the pyridine bases. The difference in the binding free energies is equal to the difference in the oxidation potentials of the unbound versus bound radicals. For the lutidine and 3-chloropyridine, the pyridinium cations were found to be more strongly bound than the pyridinyl radicals by 0.152 and 0.171 eV, respectively, consistent with the base-bound pyridinyl radicals being stronger reducing agents. These predictions are consistent with the hypothesis that, at high base concentration, pyridinyl radical-pyridine complexes are formed, which are able to more rapidly reduce the *N*-alkoxypyridinium cations and promote chain propagation.

7. Concluding Remarks. In the presence of pyridine bases, photoinduced reductions of *N*-alkoxypyridinium salts lead to highly efficient chain reactions resulting in N−O bond cleavage. A mechanism is proposed wherein alkoxyl radical intermediates react with the pyridine bases by proton-coupled electron transfer (PCET) to generate pyridinyl radicals that are capable of reducing the *N*-alkoxypyridinium salts, thereby propagating the chain reaction. The chain nature of the reaction provided an opportunity to determine rate constants for the key steps of the chain by combining rate constant ratios derived from the dependence of the reaction quantum yields on the reactant concentrations with established rate constants for termination reactions. Quantum yield data were best fit by a kinetic scheme in which reduction of the alkoxypyridinium salts occurred by pyridinyl radicals as well as by hydrogen-bonded complexes with their corresponding pyridines. Consistent with the PCET mechanism, the rate constant for the reaction of alkoxyl radicals with pyridines was found to decrease with decreasing basicity of the pyridine. Further support for the PCET mechanism was derived from computational studies, which revealed transition states for the hydrogen atom transfer reactions that resemble proton transfer, and where electron transfer to the pyridine base was found to occur along the reaction coordinate after the transition state.

It is reasonable to expect that the reaction of alkoxyl radicals with pyridine will be general for other compounds that are sufficiently basic and capable of accepting a hydrogen atom through a proton-coupled electron transfer mechanism. Potential examples include other nitrogen heterocycles, imines, azo compounds, etc. It is also intriguing to speculate that when alkoxyl radicals are generated in the proximity of appropriate

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DNA and RNA bases they may react in part by PCET resulting in net hydrogen atom transfer to the bases. If so, this would represent a nontraditional reaction of alkoxyl radicals in biology, where hydrogen atom transfer to, not from, alkoxyl radicals is the generally accepted paradigm.

EXPERIMENTAL SECTION

Materials. 4-Phenylpyridine-*N*-oxide, 4-cyanopyridine-*N*-oxide, trimethyloxonium tetrafluoroborate, triethyloxonium tetrafluoroborate, iodomethane, and iodomethane-d_3 (>99% D) were obtained from Aldrich and used as received. The *N*-alkoxypyridinium salts were prepared by minor modification of literature procedures.[10a,13a,34] 2-Chlorothioxanthone (Aldrich) was recrystallized from ethanol before use. 2,6-Lutidine (Aldrich) and 3-chloropyridine (Aldrich) were purified by passing through a short column of neutral alumina before use. Acetonitrile-d_3 (Cambridge Isotope, 99.6% D) was used as received.

*4-Phenyl-N-methoxypyridinium Hexafluorophosphate (**1a**).* To a stirred solution of 4-phenylpyridine-*N*-oxide (5.0 g, 29.24 mmol) in acetonitrile (dry, 300 mL) was added methyl iodide (12 g, 84.5 mmol), and the reaction mixture was refluxed for 6 h. After cooling, the reaction mixture was poured into rapidly stirred diethyl ether (700 mL) to obtain an off-white precipitate. The precipitate was filtered and then dissolved in water (200 mL) followed by addition of a solution of potassium hexafluorophosphate in water (7.0 g in 50 mL H_2O) to afford a white precipitate. The crude material was recrystallized twice from hot methanol to give white crystals (8 g, 83%). ^{1}H NMR (CD_3CN) δ: 8.95−8.90 (m, 2H), 8.34−8.30 (m, 2H), 7.93−7.89 (m, 2H), 7.71−7.63 (m, 3H), 4.40 (s,1H). ^{13}C NMR (CD_3CN) δ: 157.3, 141.5, 134.5, 130.9, 129.2, 127.2, 118.4, 70.9.

*4-Phenyl-N-ethoxypyridinium Hexafluorophosphate (**1b**).* To a stirred solution of 4-phenylpyridine-*N*-oxide (5.0 g, 29.24 mmol) in acetonitrile (dry, 300 mL) was added ethyl iodide (12 g, 76.9 mmol), and the reaction mixture was refluxed for 12 h. After cooling, the reaction mixture was poured into rapidly stirred diethyl ether (700 mL) to obtain an off-white precipitate. The precipitate was filtered and then dissolved in water (200 mL) followed by addition of a solution of potassium hexafluorophosphate in water (7.0 g in 50 mL H_2O) to afford a white precipitate. The crude material was recrystallized twice from hot ethanol to obtain white crystals (9 g). ^{1}H NMR (CD_3CN) δ: 8.90−8.88 (m, 2H), 8.33−8.29 (m, 2H), 7.93−7.89 (m, 2H), 7.71−7.63 (m, 3H), 4.66 (q, J = 6.96 Hz, 2H), 1.46 (t, J = 6.96 Hz, 3H). ^{13}C NMR (CD_3CN) δ: 157.3, 142.2, 133.4, 130.9, 129.2, 127.2, 118.4, 81.4, 13.4.

*4-Cyano-N-methoxypyridinium Hexafluorophosphate (**1c**).* To a stirred solution of 4-cyanopyridine-*N*-oxide (3.0 g, 25 mmol) in acetonitrile (dry, 100 mL) was added trimethyloxonium tetrafluoroborate (5g, 33.8 mmol), and the reaction mixture was refluxed for 12 h. After cooling, the reaction mixture was poured into rapidly stirred diethyl ether (400 mL) to obtain a white precipitate that was filtered and dried in air. The dried precipitate was dissolved in acetonitrile (50 mL) and then added to a solution of potassium hexafluorophosphate (5.0 g in 100 mL H_2O) to afford a white precipitate that was recrystallized twice from hot methanol. ^{1}H NMR (CD_3CN) δ: 9.15−9.12 (m, 2H), 8.47−8.44 (m, 2H), 4.45 (s, 3H). ^{13}C NMR (CD_3CN) δ: 142.9, 133.8, 128.9, 118.4, 71.1.

*4-Cyano-N-ethoxypyridinium Hexafluorophosphate (**1d**).* To a stirred solution of 4-cyanopyridine-*N*-oxide (3.0 g, 25 mmol) in acetonitrile (dry, 100 mL) was added triethyloxonium tetrafluoroborate (5 g, 33.8 mmol), and the reaction mixture was refluxed for 12 h. The reaction mixture was concentrated by partial removal of solvent (~75 mL), and then excess of diethyl ether was added into the reaction mixture to afford a pale yellow solid. The dried precipitate was dissolved in a minimum amount of acetonitrile (~25 mL) and then added to a solution of potassium hexafluorophosphate (7.0 g in 100 mL H_2O) to afford a white precipitate that was recrystallized twice from hot ethanol. ^{1}H NMR (CD_3CN) δ: 9.13−9.09 (m, 2H), 8.47−8.44 (m, 2H), 4.71 (q, J = 6.96 Hz, 2H), 1.47 (t, J = 6.96 Hz, 3H). ^{13}C NMR (CD_3CN) δ: 143.9, 133.9, 128.5, 118.4, 82.2, 13.3.

4-Phenyl-N-d_3-methoxypyridinium Hexafluorophosphate. To a stirred solution of 4-phenylpyridine-*N*-oxide (7.0 g, 40.46 mmol) in acetonitrile (dry, 400 mL) was added methyl-d_3 iodide (10 g, 68.9 mmol), and the reaction mixture was refluxed for 12 h. After cooling, the reaction mixture was poured into rapidly stirred diethyl ether (700 mL) to obtain an off-white precipitate. The precipitate was filtered and then dissolved in water (200 mL) followed by addition of a solution of potassium hexafluorophosphate in water (7.0 g in 50 mL H_2O) to afford a white precipitate. The crude material was recrystallized twice from hot methanol. ^{1}H NMR (CD_3CN) δ: 8.95−8.91 (m, 2H), 8.34−8.30 (m, 2H), 7.93−7.89 (m, 2H), 7.71−7.63 (m, 3H). ^{13}C NMR (CD_3CN) δ: 157.2, 141.5, 134.5, 133.5, 130.9, 129.2, 127.2, 118.4.

Instrumentation. Steady-state photolyses were carried out with an Oriel 200 W medium-pressure Hg lamp. The excitation wavelength (405 nm) was isolated by passing the lamp output through a Corning 5-58 bandpass filter immersed in water, followed by a 405 nm interference filter. Generally, 3 mL of an acetonitrile-d_3 solution containing 2-chlorothioxanthone (CTX, 0.002 M), an alkoxypyridinium (**1a**−**1d**), and a pyridine base (lutidine or 3-chloropyridine) in a 1 cm × 1 cm quartz cell was purged with a thin stream of argon for 3 min and then irradiated for 1−10 min to achieve ~20% conversion. Argon was continuously bubbled through the reaction mixture during photolysis to purge as well as stir the solution.

The photon flux was determined by using the photocycloaddition reaction of phenanthrenequinone to *trans*-stilbene in benzene as an actinometer.[35] The light intensity was typically 2−5 × 10^{-9} einstein s^{-1}. The quantum yield for product formation was determined from the percent conversion and the light intensity.

Product Analysis. After photolysis, the ^{1}H NMR spectrum of the photolysate was recorded and the percent conversion of the starting materials was determined by integration of diagnostic signals of the pyridinium reactant and the pyridine product (see Supporting Information). The mass balance was consistently high, >95%.

ASSOCIATED CONTENT

Supporting Information

Triplet energy of CTX in acetonitrile; cyclic voltammograms; fragmentation quantum yields versus pyridinium concentration; derivation of eq 6; kinetic fitting parameters; energy diagrams with selected structures for reactions of alkoxyl radicals with pyridines; singly occupied molecular orbitals of the transition states for reaction of ethoxyl radical with lutidine and 3-chloropyridine; calculated energies, expectation values of S^2 ($<S^2>$), and geometries; Mulliken population analyses of transition state structures; transition state imaginary frequencies and the corresponding vibrational modes; NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(16) (a) The intersystem crossing quantum yield for CTX of 0.98 in acetonitrile was measured as described in ref 12a by triplet-triplet energy transfer from ^{3}CTX* to 1-cyanonaphthalene using the corresponding reaction of benzophenone as an actinometer. This value is likely to be more accurate than the recently reported[16b] Φ_{isc} of 0.91, which unlike our approach uses actinometry that requires accurate knowledge of extinction coefficients. We measured a fluorescence quantum yield of 0.01 for CTX in acetonitrile, which is in agreement with the value reported in ref 16b. Thus, within the experimental error, there is practically no internal conversion from singlet excited CTX. (b) Santiago, L. E. P.; Garcia, C.; Lhiaubet-Vallet, V.; Miranda, M. A.; Oyola, R. *Photochem. Photobiol.* **2011**, *87*, 611.
(17) (a) Based on its phosphorescence spectrum in acetonitrile at room temperature, the triplet energy, E_T, of CTX is 62.1 kcal/mol (2.69 eV); details are in the Supporting Information. No well-defined oxidation wave of CTX could be determined by cyclic voltammetry. An upper limit for the oxidation potential, E_{ox}, however, can be estimated from the singlet excitation energy, E_{S*}, and the reduction potential, E_{red}, based on the relationship $E_{S*} = E_{ox} - E_{red} + C$, where the increment C, measured for many compounds, ranges between ∼0.1 and 0.4 eV.[11a,17b−d] From absorption and fluorescence spectra of CTX in acetonitrile, E_{S*} = 3.09 eV, which agrees with a literature value.[16b] Reversible reduction of CTX was observed in acetonitrile, yielding E_{red} of −1.53 V vs SCE. Thus, E_{ox} is estimated to be between 1.2 and 1.5 V vs SCE. From eq 3, electron transfer from triplet CTX to **1a** and **1b** is expected to be exothermic by at least 0.1 eV. (b) Lenhard, J. R. *J. Imaging Sci.* **1986**, *30*, 27. (c) Lenhard, J. R.; Cameron, A. D. *J. Phys. Chem.* **1993**, *97*, 4916. (d) Loutfy, R. O.; Sharp, J. H. *Photogr. Sci. Eng.* **1976**, *20*, 165.
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(19) (a) Oxidation potentials of α-hydroxy radicals are difficult to determine reliably because of sensitivity to medium effects. For example, hydrogen bonding to another alcohol molecule or water could lower the oxidation potential due to coupled electron/proton transfer.[19b] Accurately determined oxidation potentials of aryl-substituted α-hydroxy radicals were found to be the same or similar to those of the corresponding alkoxyl radical.[19c,d] Thus, the oxidation potentials of $CH_2{}^{\bullet}OMe$ and $MeCH^{\bullet}OEt$, −0.24 and −0.45 V vs SCE, respectively,[19e] can be used as reasonable estimates for those of the corresponding alcohols. Consistent with these values, the oxidation potential of $Me_2C^{\bullet}OH$ is −0.61,[19c] i.e., there are similar increments between the primary, secondary, and tertiary radicals. (b) Lilie, V. J.; Beck, G.; Henglein, A. *Ber. Bunsen-Ges. Phys. Chem.* **1971**, *75*, 458. (c) Lund, T.; Wayner, D. D. M.; Jonsson, M.; Larsen, A. G.; Daasbjerg, K. *J. Am. Chem. Soc.* **2001**, *123*, 12590. (d) Workentin, M. S.; Wayner, D. D. M. *Res. Chem. Intermed.* **1993**, *19*, 777. (e) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132.
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(21) The ratios $c = (k'_4/k_4)$ and $f = ((k'_6/k_6)$ are not expected to be the same for all pyridiniums, as these compounds may have varying amounts of minor impurities. We allowed for such differences to obtain the best fit. It should be noted, however, that these ratios are quite small (∼0 to 0.01), but whenever the quantum yields are very large, they become very sensitive to any minor differences in termination reactions. To minimize the number of variables, however, both ratios were kept constant for each pyridinium.
(22) The rate constant k_2 is a composite of deuterium abstraction from CD_3CN and reaction with the donor sensitizer (at 0.002 M).[12a]
(23) (a) The O−H BDE in *tert*-butanol is 106.3 kcal/mol, which is 1.7 kcal/mol larger than that in methanol or ethanol (104.6 kcal/mol).[23b] DFT calculation yields a 1.3 kcal/mol larger BDE (in acetonitrile) for the methyl C−H bond in lutidine than in toluene. (b) Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: Boca Raton, 2003.
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difference between $CH_3O^{\bullet}$ and $^{\bullet}CH_2OH$ can be estimated from their heats of formation (4.1 and −2 kcal/mol, respectively)[24b] and the statistical factor of 3 that favors $^{\bullet}CH_2OH$ in the equilibrium. Based on these thermodynamic quantities, the pK_a of $CH_3O^{\bullet}$ in acetonitrile is estimated to be ∼25. (b) Tsang, W. Heats of Formation of Organic Free Radicals by Kinetic Methods. In *Energetics of Organic Free Radicals*; Martinho Simões, J. A., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic and Professional: London, 1996; pp 22−58.

(25) (a) At moderate exergonicity bimolecular electron transfer requires contact interaction. With increasing driving force, however, long distance electron transfer leading directly to solvent-separated radical ion pairs dominates.[25b] As a result, the rate constant increases,[25c] and in the case of charge shift reactions it reaches 1.2×10^{10} M^{-1} s^{-1}.[25d] (b) Gould, I. R.; Young, R. H.; Moody, R. E.; Farid, S. *J. Phys. Chem.* **1991**, *95*, 2068. (c) Rosspeintner, A.; Kattnig, D. R.; Angulo, G.; Landgraf, S.; Grampp, G. *Chem.—Eur. J.* **2008**, *14*, 6213. (d) Luo, P.; Dinnocenzo, J. P.; Merkel, P. B.; Young, R. H.; Farid, S. *J. Org. Chem.* **2012**, *77*, 1632.

(26) Because of uncertainty about the exact oxidation potential of the lutidinyl radical, the rate constant for electron transfer from $BH^{\bullet}$ to CTX (k_{et}) might be less than the diffusion-controlled limit ($k_{diff} \approx 1 \times 10^{10}$ M^{-1} s^{-1}). If $k_{et} \approx k_{diff}/10$, it would correspond to the measured pseudo first-order rate constant k_S. If k_{et} is between $k_{diff}/10$ and k_{diff}, it would not necessarily contradict the experimental data: $CTX^{\bullet-}$ could propagate the chain by reducing the pyridinium and only partially lead to termination, e.g., via proton transfer from trace amounts of water.

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