

Oxoammonium Salt Oxidations of Alcohols in the Presence of Pyridine Bases

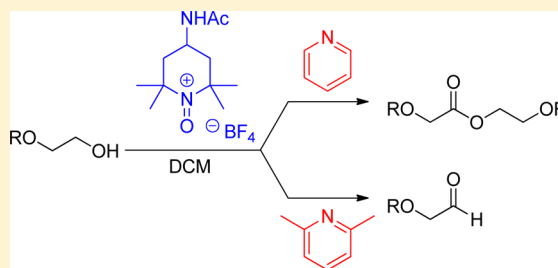
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S Supporting Information

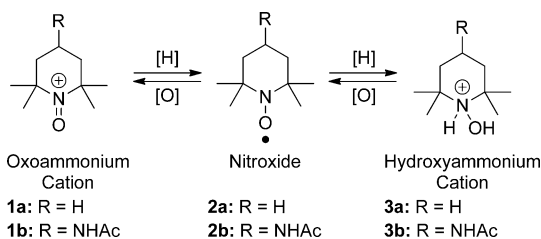
ABSTRACT: Oxoammonium salt oxidations (using 4-acetylamino-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate) of alcohols containing a β -oxygen atom in the presence of pyridine yield dimeric esters, while in the presence of 2,6-lutidine the product is a simple aldehyde. The formation of a betaine between pyridine and an aldehyde is presented to explain this disparity in reactivity. The betaine is oxidized by the oxoammonium salt to give an *N*-acetylpyridinium ion that serves as an acylating agent for ester formation. Steric effects deter the formation of such a betaine with 2,6-disubstituted pyridines. A series of alcohols containing a β -oxygen substituent were oxidized to aldehydes in the presence of 2,6-lutidine, and a short study of the relative reactivity of various alcohols is given. An overall mechanism for oxoammonium cation oxidations is suggested, premised on nucleophilic additions to the oxygen atom of the positively charged nitrogen–oxygen double bond. Possible mechanisms for both dimeric oxidations and simple oxidations are given.



INTRODUCTION

The oxoammonium cation, **1**, along with various anions (commonly tetrafluoroborate) can be used to oxidize primary and secondary alcohols to aldehydes or ketones in high yield and with convenient isolation procedures.¹ Overall oxoammonium ion chemistry can be summarized as shown in Scheme 1

Scheme 1. Overall Oxidation and Reduction of Oxoammonium Compounds^a



^aThe R group and the anion are highly variable. In most of our work, R = NHAc, and the anion is tetrafluoroborate.

for the TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl, **2a**) derived compounds. The oxidant **1a/b** can be reduced either to the nitroxide **2a/b** or to the hydroxyamine tetrafluoroborate **3a/b**. The nitroxide, **2a** or **2b**, itself, can be used as a catalyst for a large number of oxidations using various secondary oxidants.² In addition, **2b** can be used with *p*-toluenesulfonic acid as a stoichiometric oxidant.³ There are several miscellaneous oxidations using these reagents and several different nitroxide

systems. These have been summarized in our chapter in *Organic Reactions*,² in recent papers,^{4,5} and in several recent reviews.^{6–11}

In this paper, we are concerned with oxoammonium oxidations in the presence of various pyridine bases. In 1998, we reported that, although most alcohols were smoothly oxidized to aldehydes or ketones with oxoammonium salts such as **1a** or **1b**, alcohols containing a β -oxygen substituent were not oxidized at all.^{1,12} In 2004, we reported that these alcohols were oxidized by **1b** to dimeric esters in good yields in the presence of pyridine (**4**), and that alcohols without a β -oxygen substituent (such as 1-octanol) could be oxidized to dimeric esters in the presence of pyridine, albeit in low yield.¹³ Later, we reported that oxidations with **1b** in the presence of 2,6-lutidine (**5**), gave good yields of aldehydes; this chemistry is summarized in Scheme 2 and in more detail in a previous paper.^{13,14}

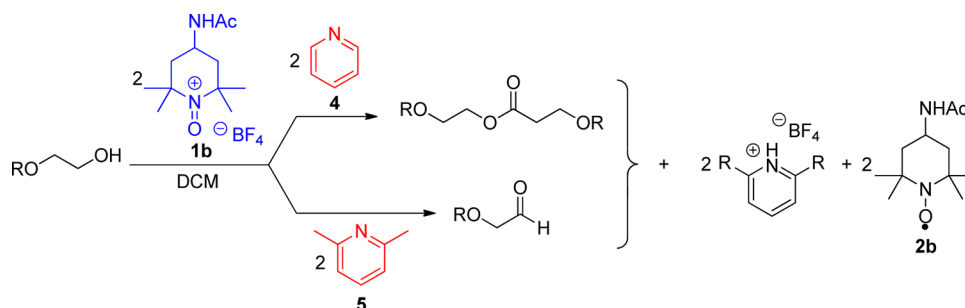
The use of pyridine bases in oxoammonium oxidations is not unprecedented. The first use of this chemistry involved electrochemical oxidations of alcohols and amines catalyzed with TEMPO (**2a**).^{15–17} These reactions were carried out in the presence of 2,6-lutidine (**5**). More recently, other electrooxidations in the presence of **5** have been reported.^{18–21}

Electrooxidations using nitroxides immobilized on a polymer in the presence of **5** have also been discovered.^{18,22–24} 2,6-

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Scheme 2. Overall Oxidation of β -Oxygen Alcohols in the Presence of Pyridine Bases

Lutidine (5) has been used in stoichiometric oxoammonium oxidations of trifluoromethyl carbinols²⁵ and carbohydrates.²⁶

Pyridine (4) itself has been used in conjunction with oxoammonium salt **1b** for the stoichiometric oxidation of carbohydrates,²⁷ β -oxygen alcohols,¹³ and long chain unsaturated alcohols.²⁸ It has also been recently used in TEMPO catalyzed oxidations of alcohols and aldehydes.^{29,30} Alternatively, 2,2'-bipyridine (Bipy) can be used in place of 4 for catalyzed reactions.^{31,32}

In this paper, we present the experimental details related in our initial presentation,¹⁴ and the mechanistic details of the oxidations of β -oxygen alcohols in the presence of pyridine (4) or 2,6-lutidine (5). In addition, we report the preparative oxidations of β -oxygen alcohols with **1b** in the presence of 5 and some relative reactivities of various alcohols under these oxidizing conditions. Finally, we suggest an overall mechanism for oxoammonium oxidations based upon steric effects. Plausible mechanisms for the oxidations of simple alcohols to aldehydes in the presence of pyridine bases are discussed.

RESULTS AND DISCUSSION

Oxidation of a Representative β -Oxygen Alcohol, 2-Butoxyethanol (6), in the Presence of Various Pyridine Bases.¹⁴ The oxidation of 2-butoxyethanol (6) with **1b** in the presence of various pyridine bases was explored. The results are summarized in Table 1 and in Scheme 2. Bases with substituents in the 2- and 6-positions predominantly gave aldehydes, while bases with no substituents in these positions gave dimeric esters. Since the difference in pK_b 's among the bases is minor,³³ the controlling factor is likely steric. This is supported by the fact that 2,6-di-*tert*-butylpyridine (entry 6, Table 1) gives only the ester product despite being close in basicity to pyridine. However, in the other cases, a mixture of ester and aldehyde were obtained, implying that methyl groups cannot completely impede the oxidative esterification pathway.

Oxidation of Mixtures of 2-Butoxyethanol (6) and 1-Nonanol (9) in the Presence of Pyridine (4) or 2,6-Lutidine (5). We further confirmed the results in Table 1 by conducting a study of the relative oxidation reactions of 2-butoxyethanol (6) in the presence of a suitable long-chain primary alcohol, 1-nonanol (9). This was done by half-oxidations of an equimolar mixture of the two alcohols in the presence of 4 and in the presence of 5. The equations are given in Scheme 3, and the results are shown in Figure 1.

All of the peaks in the scans in Figure 1 were confirmed by comparison with authentic samples. Compounds 6, 7, 9, 10, and 13 are commercially available samples. Compound 8 was prepared in our original paper.¹³ This leaves the two unsymmetrical esters 11 and 12, of which, 11 has not been reported and was prepared from butoxyacetic acid and 1-

Table 1. Oxidation of 6 in the Presence of Various Pyridine Bases

entry	pyridine base	$pK_b^{a,b}$	aldehyde (%) ^c	ester (%) ^c
1		8.75	0	100
2		7.98	27	73
3		7.01	72	28
4		7.35	93	7
5		6.57	85	15
6		9.05 ^d	100	0

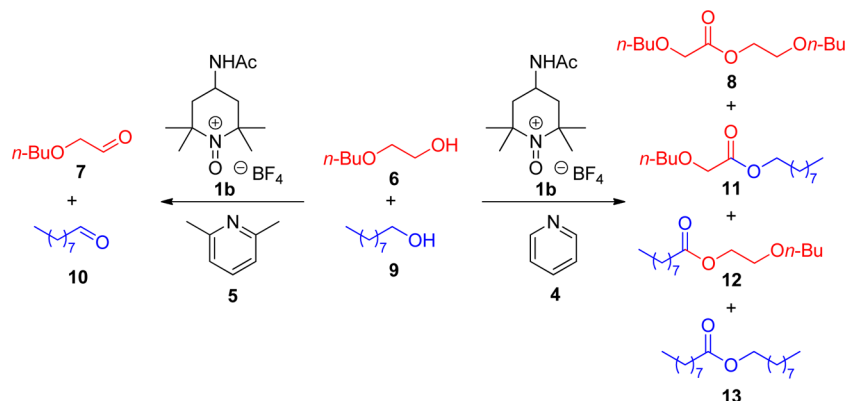
^a pK_b in H_2O . ^bUnless otherwise noted, values obtained from ref 33.

^cYields were determined by GC analysis of product mixtures and corrected for detector response. ^dTaken from Hopkins, H. P and co-workers, *J. Am. Chem. Soc.*, **1984**, 106, 4341.

nonanol (exact details provided in Experimental Section). Compound 12 is known and was prepared as described in the Experimental Section.

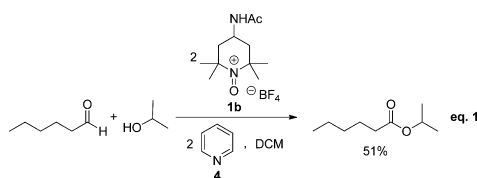
It is apparent from Figure 1 that the structure of the pyridine base is crucial to product formation. The oxidations of the alcohols 6 and 9 give only aldehydes in the presence of 2,6-lutidine (5), implying that they are equally liable toward oxidation (Figure 1a). In Figure 1b with pyridine, aldehyde 7 is consumed quite rapidly and the two resulting esters 8 and 11 are observed. Compound 10 reacts significantly slower to give the nonacyl esters 12 and 13. If the reaction is carried to completion (Figure 1c), all four possible esters (8, 11–13) are clearly observed. In Figure 1c, a small peak at 14.6 min corresponds to nonanonic anhydride (14). The presence of this side product is in agreement with a recent paper describing the TEMPO (2a)-catalyzed direct oxidation of aldehydes to mixed anhydrides.³⁰

Scheme 3. Half-Oxidation of a Mixture of 2-Butoxyethanol (6) and 1-Nonanol (9)



From the results of Table 1 and Figure 1, we were able to deduce a plausible mechanistic rationale, shown in Scheme 4. The first step in the sequence is the oxidation of the β -oxygen alcohol to its corresponding aldehyde, as expected. However, the aldehyde then reacts with pyridine (4) to form, reversibly, a betaine. Such a betaine does not form readily with 2,6-lutidine (5) due to the steric constraints of the methyl groups flanking the pyridine nitrogen. We suggest that the rapidity in which 2-butoxyacetaldehyde (7) is converted into its corresponding ester product 8 may be attributed to the neighboring group participation of the β -oxygen atom with the free 2-position of pyridine. This interaction acts to stabilize the pyridinium species, thereby enhancing its lifetime. Such participation has been noted in carbocationic oxygen structures; therefore, a similar interaction in this system is reasonable.^{34,35} This betaine is then rapidly and irreversibly oxidized by **1b** to an *N*-acylpyridinium species, a highly reactive acylating agent. This species is commonly cited as the key intermediate in nucleophilic acyl substitution reactions.^{36–38} Such a mechanistic path involving oxoammonium salts has not, to the best of our knowledge, been proposed elsewhere in the literature.

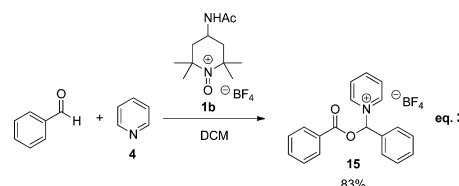
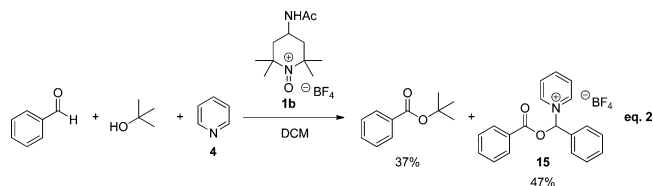
Considering the two separate steps, oxidation and esterification, we hoped to find a method to prepare unsymmetrical esters from aldehydes and alcohols. To this end, we investigated a wide range of alcohols in the presence of benzaldehyde and hexanal. Unfortunately, yields were unacceptably low. The best result was the oxidative esterification of hexanal with isopropanol in 51% yield, eq 1.



There are two explanations for the low yield of these oxidative esterifications. The first possibility is that the alcohol is oxidized to its corresponding carbonyl species before it can react with the acylpyridinium intermediate. This possibility is supported by a recent paper in which hexafluoroisopropanol (HFIP) can be used successfully in the oxidative esterification of aldehydes in the presence of **1b** and pyridine.³⁹ This fluorinated alcohol reacts very slowly, if at all, with the oxoammonium salt and therefore the alcohol is free to react with the acylpyridinium intermediate to give HFIP esters.

These fluoroesters are formed in good yield and are themselves good acylating agents.³⁹

The second possibility is more complex and was discovered in an experiment using a nonoxidizable alcohol, *tert*-butyl alcohol. When benzaldehyde was oxidized in the presence of pyridine and *tert*-butyl alcohol, we expected to get solely *tert*-butyl benzoate, and we did observe the formation of the ester in 37% yield by GC/MS. However, a solid product that was later found to be 1-[benzoyloxy-*N*-(1-phenylmethyl)]-piperidinium tetrafluoroborate (**15**) was obtained in a 47% isolated yield, (eq 2). When a similar oxidation was carried out in the absence of any alcohol, compound **15** was isolated in 83% yield, (eq 3).



The structure of compound **15** was proven by an independent synthesis utilizing the method of French and Adams,⁴⁰ which produces the analogous chloride salt of **15**, **19**. The chloride was converted to the tetrafluoroborate by an anion-exchange reaction (eqs 4 and 5 in Scheme 5). One final point is that benzoyl fluoride was observed as a very minor product in these aldehyde oxidations. This fluoride has been noted as a decomposition product of *N*-acylpyridinium tetrafluoroborate.⁴¹

We envision **15** as being formed from benzaldehyde and pyridine through the betaine **16**, oxidized by oxoammonium salt to the acylpyridinium salt **17** and thence to **15** by reaction with a second benzaldehyde (dotted arrows). This supports our proposed intermediacy of a betaine in the oxidative esterification pathway.

Preparative Oxidations in the Presence of 2,6-Lutidine (5). There are appreciable differences between the neutral/silica gel-catalyzed oxidations¹ and oxidation reactions in the presence of 2,6-lutidine (5). First, product isolation is

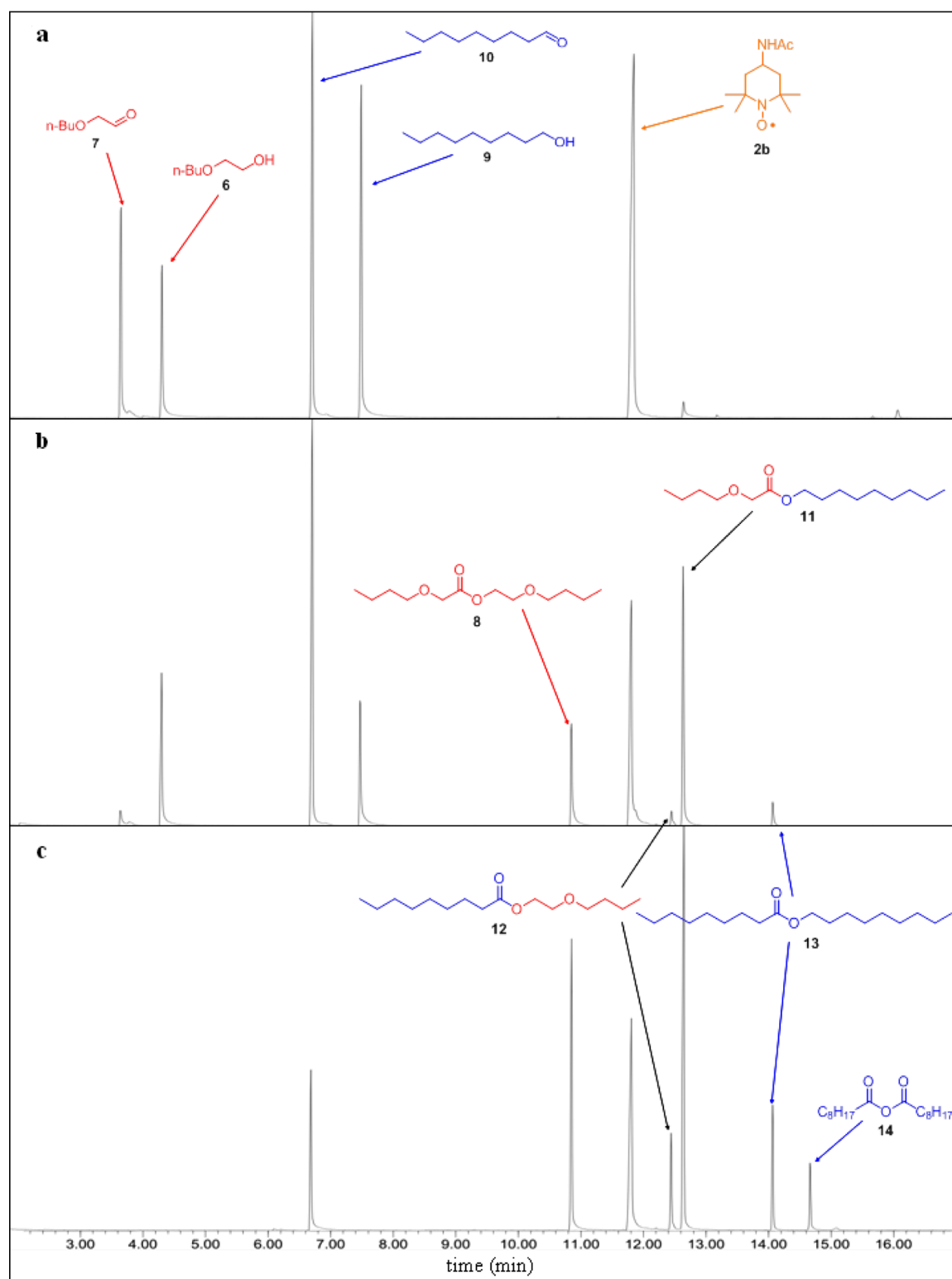


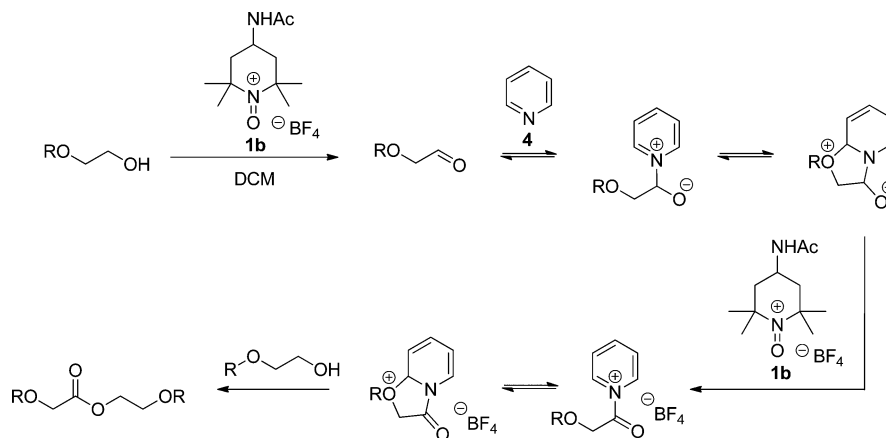
Figure 1. The oxidations of a mixture of 2-butoxyethanol (6) and 1-nonanol (9) in the presence of 5 (a ~ half oxidation) and 4 (b ~ half oxidation and c ~ complete oxidation).

trivial in the simple neutral reactions¹ and somewhat more complex in the pyridine-mediated (“basic”) oxidation reactions. In base reactions, one must remove the products, nitroxide 2b, and lutidinium tetrafluoroborate. This is done by partially evaporating the DCM, followed by precipitation of the byproducts with dry Et₂O. The ether solution is passed through silica gel to remove any remaining byproducts. GC/

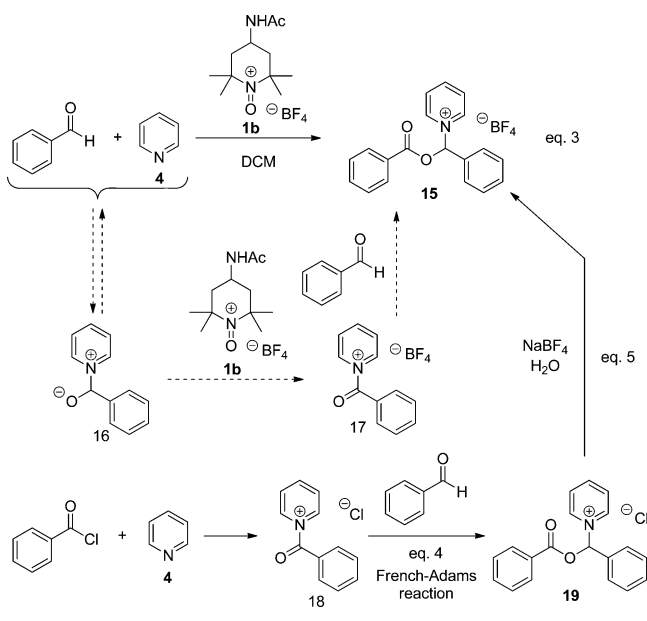
MS scans of these ether solutions are given in the Supporting Information [SI].

The base-catalyzed reactions are, in general, capable of oxidizing a much wider array of alcohols including the β -oxygen alcohols in this paper, those with an electron-withdrawing group in the 2- or 3-position,⁴² and those whose oxidations are nontrivial (e.g., trifluoromethyl carbinols²⁵). With the knowl-

Scheme 4. Plausible Mechanistic Pathway to Explain Ester Formation



Scheme 5. Identification of 15



edge that oxidations in the presence of 2,6-lutidine (5) would give primarily aldehydes rather than esters in basic oxidative reactions, we screened a number of β -oxygen alcohols. To further minimize the formation of dimeric esters, the reaction mixtures were made dilute, (20 mL of DCM per mmol of alcohol). The results of the oxidations are given in Table 2. By monitoring the progress of these reactions by NMR and GC/MS, it was apparent that the oxidation was complete in about 1 h, although the subsequent reactions to give the byproducts (Scheme 2 and Scheme 6, mechanism 2) was not complete for about 4 h. Like the neutral reactions, which are colorimetric, turning from yellow to white, these oxidation are also colorimetric, but turn from yellow to red.

^1H NMR spectra are given in the SI for all of the crude reaction mixtures described in Table 2. Integration of the aldehyde peak against the peak for the C-4 proton in lutidinium tetrafluoroborate tells whether the reaction did indeed take place and the approximate conversion to the aldehyde.

Low-molecular-weight aldehydes were somewhat problematic due to their volatility, and diminished yields were obtained (entry 4). While these aldehydes can be isolated, the final ethereal solutions obtained after silica gel chromatography are

Table 2. Oxidations of Various Alcohols In the Presence of 2,6-Lutidine^a

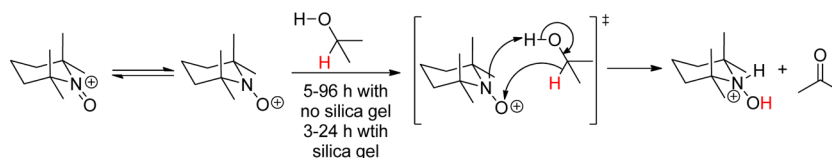
entry	alcohol	aldehyde	time (h) ^b	yield (%)
1			4	96
2			4	87
3			4	84
4			4	70
5			4	98
6			48	97

^aConditions unless otherwise noted: alcohol (1 equiv), 2,6-lutidine (2.2 equiv), oxoammonium salt (2.4 equiv), DCM (0.05 M in starting alcohol). ^bReaction progress was followed by ^1H NMR.

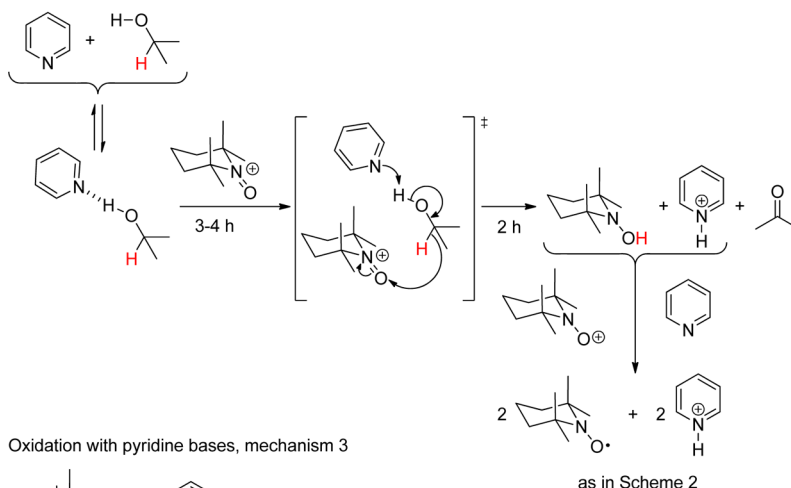
suitable for tandem reactions since the products are free of any other contaminants at this point. Accurate determination by weight percent assay would be required in this case to determine the yield of the aldehyde, although one can assume that the yield is at least as good as the isolated yields. Less

Scheme 6. Oxidations of Alcohols to Aldehydes or Ketones^a

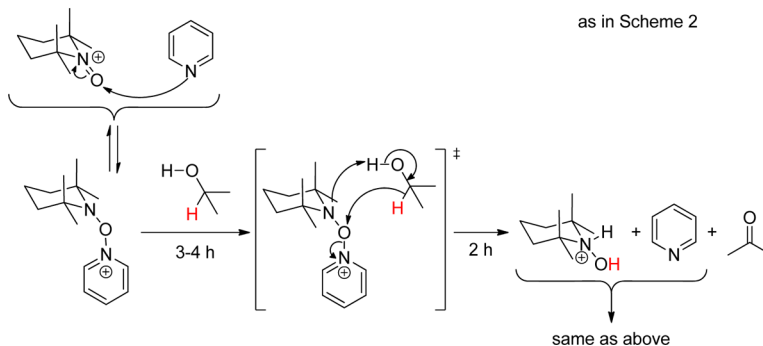
Oxidation in neutral systems, mechanism 1



Oxidation with pyridine bases, mechanism 2



Oxidation with pyridine bases, mechanism 3

^aThe hydrides shifting are in red.

volatile, higher molecular weight aldehydes gave far better isolated yields (entries 1–3, 5, 6).

When these oxidation reactions are combined with our original paper on neutral, silica gel oxidations¹ and the recent paper on the preparation of HFIP esters,³⁹ one can imagine a tandem series of oxidations of almost any primary alcohol to aldehydes and subsequently to HFIP esters, which themselves can be further functionalized.³⁹

Relative Reactivities of Some Alcohols in the Presence of 2,6-Lutidine (5). Finally, we have measured the relative reactivities in some miscellaneous oxidations in the presence of 2,6-lutidine (5) in Table 3. The primary alcohols, interestingly, have negligible differences in reactivities and are all set to a reactivity of 1 (Table 3, entries 2–4). This is in sharp contrast to the rates noted by us in our preceding paper, where benzyl alcohols and secondary alcohols were 10 and 2 times more reactive, respectively, as compared to primary alcohols.^{1,43} However, there are small differences in benzyl alcohols with varying ring electron densities (Table 3, entries 1, 2, 5), in general accord with the earlier papers. Interestingly, secondary alcohols are quite slow (Table 3, entries 6, 7), and this allows good selectivity for primary alcohols. This has been observed extensively in carbohydrate chemistry.² Moreover, the sterically

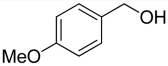
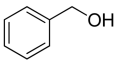

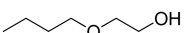
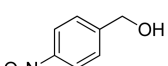
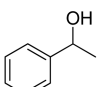
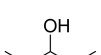
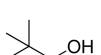
hindered neopentyl alcohol (Table 3, entry 8) was 10 times less prone to oxidation, despite being a primary alcohol.

GENERAL MECHANISTIC CONSIDERATIONS

There are two mechanistic aspects at work in the oxidations presented in this paper. The first was previously discussed and addressed differences in product formation in pyridine (4)- and 2,6-lutidine (5)-mediated oxidations (Scheme 4). The second aspect is more general and involves the simple oxidation of alcohols to aldehydes or ketones in the presence of pyridine bases. There have been at least four general mechanistic studies of oxoammonium ion oxidations.^{15,44–46} Two of the studies explored deuterium isotope effects and indicated that the rate determining step was the breaking of the α -hydrogen bond of the carbinol. One study suggested that it was a proton cleavage pathway,¹⁵ and one preferred a hydride transfer.⁴⁴ We prefer the hydride-transfer mechanism.

The Unique Oxoammonium Cation. Oxoammonium cation oxidations are unique reactions characterized by high yields, few side reactions, and readily isolable products. In this section, we will explore the ramifications and principles of these reactions. Although there are many reported nitroxides and oxoammonium salts,^{2,47,48} this discussion will be limited to

Table 3. Relative Reactivities of Various Alcohols in the Presence of 1b and 2,6-Lutidine (5)^a

entry	alcohol	relative reactivity ^b
1		1.2
2		1
3		1
4		1
5		0.5
6		0.2
7		0.1
8		0.1

^aThe two alcohols being compared (both 1 equiv), 2,6-lutidine (2 equiv), oxoammonium salt (2 equiv), DCM (0.04 M in the alcohols).

^bReaction progress was followed by ¹H NMR and used to determine the ratios between oxidized species.

the 2,2,6,6-tetramethylpiperidine system (as in compounds 1, 2, and 3). Most, or all, of these oxidations are characterized by the interaction of the oxoammonium cation with a nucleophile (hydrides as well as other nucleophiles documented below). Then, the question arises as to where nucleophiles might attack the cation. In the cation, the nitrogen is surrounded by two quaternary carbon groups and a double bond to oxygen. Thus, for steric reasons, it is very likely that the nucleophilic attack is on the oxygen in the positively charged nitrogen–oxygen bond (N=O⁺).^{2,3,14,46} This situation is clearly shown in Figure 2, which includes a space-filling picture of a typical oxoammonium ion.

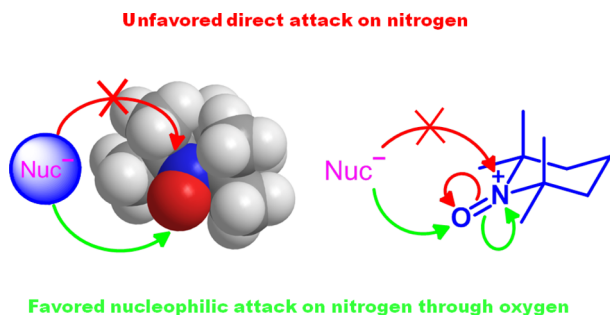


Figure 2. Reaction of the oxoammonium cation with nucleophiles.

A simple analogous functional grouping is the nitronium cation NO₂⁺ (O=N⁺=O), usually sold as its tetrafluoroborate salt. This cation contains two nitrogen–oxygen double bonds, but has no steric hindrance. Hence nucleophiles react with the nitrogen to yield nitro compounds in many reactions.⁴⁹

The oxoammonium cation can therefore behave as though the positive charge is on the oxygen, effectively giving rise to an electrophilic oxygen. This concept was originally suggested by Golubev⁴⁴ and discussed in detail in our review,² but without serious considerations of the steric substitution effects. It is shown in Scheme 6 in mechanism 1. Such an effective electrophilic oxygen is a rare situation in organic chemistry.

In most alcohol oxidation mechanisms, the electrons used to form the carbonyl double bond come from the α -hydrogen bond of the carbinol.^{50,51} In oxoammonium oxidations, the electrons used to form the carbonyl double bond come from the hydrogen–oxygen bond of the hydroxyl group by means of a hydride transfer.⁴⁴

Other oxidations involving hydride transfers (i.e. when electrons used to form the carbonyl double bond come from the hydroxyl group of the carbinol) are known. Three oxidation systems involving a hydride transfer similar to the oxoammonium system exist: the Oppenauer oxidation,⁵² the Canizzaro⁵³ reaction, and in the action of alcohol dehydrogenase⁵⁴ on ethanol with NAD⁺ as a cofactor. The hydride transfer model of oxoammonium cation oxidation implies that a transient carbocation is formed at the α -carbon during the course of an oxidation. Factors which seem to influence oxoammonium oxidations of alcohols appear to be the electron density around the carbinol carbon and the steric effects surrounding it. In simple alcohols, the hydride transfer is facilitated by an electron-rich hydroxyl group. In alcohols containing an electron-withdrawing group close to the carbinol carbon such as β -oxygen systems, α -CF₃ systems, acyloxy alcohols^{42,55} and the *p*-nitrobenzyl group (Table 2 and previously cited cases^{1,43}), this electron density is reduced, as is the reactivity. The reactivity is also reduced in sterically hindered systems.

There are a number of oxidations that do not involve alcohols but do involve hydride-transfer reactions. In the case of benzyl hydrogens, activation is provided by a benzyl oxygen,^{56–58} an amide nitrogen,^{57,59,60} an anilino nitrogen in a tertiary amine,⁶¹ or in an α -position to an ester.⁵⁹ These reactions provide effective carbocations that can undergo numerous cyclization reactions, many catalyzed by metal ions. In some cases, the nucleophiles are unsaturated moieties such as a suitably activated carbon–carbon double bond (three alkyl groups),⁶² enols,^{45,63–66} enol ethers,^{67,68} enamines.^{64,69} Grignard reagents⁷⁰ (to give *N*-alkoxytetramethylpiperidines), and indole derivatives.⁷¹ For alkenes, enols, enol ethers, enamines, and Grignard reactions the products are often stable addition products.

Specific Oxidation Mechanisms. The mechanisms of pyridine base-mediated oxidations (mechanisms 2 and 3 in Scheme 6) make more sense if viewed in light of the neutral oxidations (mechanism 1 in Scheme 6).¹ Three mechanisms are shown in Scheme 6.

The oxidation of an alcohol with a neutral oxoammonium salt requires the transfer of a hydride and a proton to the salt from the alcohol (Scheme 6, mechanism 1). The hydrogen bonding in mechanism 1 was originally suggested in our review as a reasonable mechanism since it seemed to offer a six-atom transition state.² Oxoammonium oxidations in the presence of pyridine bases are quite different from the neutral reactions. They are stronger oxidation systems (see above); the relative reactivities of various alcohols are quite different (Table 2 and previous papers^{1,43}); and the isolation procedures are different.

Two possible mechanisms for the pyridine base reactions are suggested in mechanisms 2 and 3 in Scheme 6. The electron

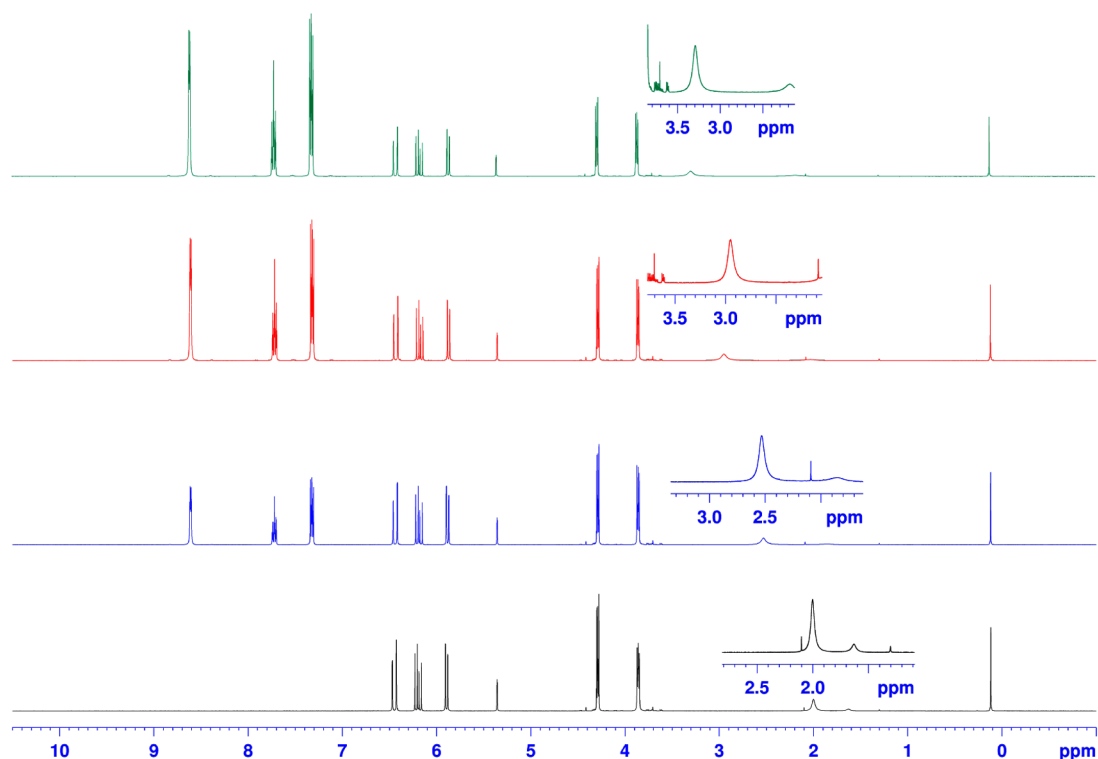


Figure 3. NMR experiment showing the shift of the OH peak of acryloxyethanol in the presence of **4**. Conditions: **Black**: 0.1 M acryloxyethanol in CD_2Cl_2 ; **Blue**: 0.1 M 2-hydroxyethyl acrylate in CD_2Cl_2 , 1 equiv **4**; **Red**: 0.1 M acryloxyethanol in CD_2Cl_2 , 2 equiv **4**; **Green**: 0.1 M acryloxyethanol in CD_2Cl_2 , 3 equiv **4**.

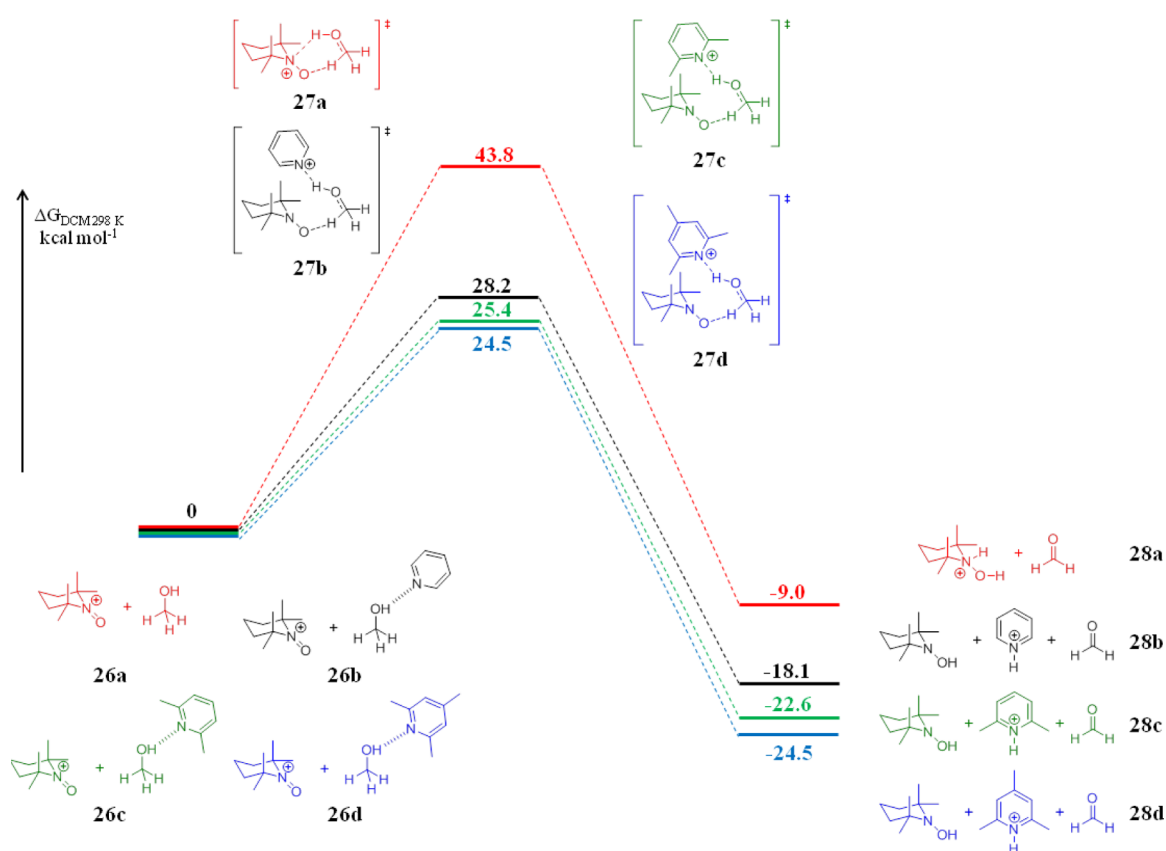


Figure 4. Reaction profiles for the oxidation reaction of the H-bonded complexes with the oxoammonium species at B3LYP/6-311++g(d,p)//B3LYP/6-31+g(d). Free energies relative to the reactants in DCM. Figures of transition-state structures can be found in the SI.

cascade leading to the product can be initiated by the pyridine base either through polarization of the alcohol (mechanism 2) or by activation of the electrophilic oxygen in the oxoammonium cation (mechanism 3). The ultimate products of the oxidations shown in mechanism 2 and 3 are the same. It should be noted that the pyridine bases serve two purposes: they mediate the reactions and they react with the spent oxidant to give tetrafluoroborate salts.

Mechanisms 1 and 2 in Scheme 6 show hydrogen bonding as parts of the reactions. This is not true in mechanism 3. While there is no direct evidence for any hydrogen bonding in mechanism 1 except the convenient six-membered transition state, there is some evidence for the hydrogen bonding in mechanism 2. If one mixes an alcohol and pyridine, some heat is given off, indicating a favorable intermolecular interaction of some type is occurring. Further evidence of such an interaction is observed by ^1H NMR (Figure 3). The hydroxyl proton of acryloxyethanol (Table 2, entry 4) in CD_2Cl_2 appears at about 2.0 ppm and has a well-defined hydrogen-bonded structure given the sharpness of its signal. If one adds varying equivalents of pyridine, the hydroxyl proton is shifted consistently downfield and become far less defined, implying a mixed mode of hydrogen bonding.^{72,73}

In order to study the mechanism in base systems, we attempted to model the three mechanisms using quantum mechanical calculations with methanol as substrate and DCM as solvent. The calculations on mechanisms 1 and 2 in Scheme 6 were made assuming hydrogen bonding, represented by dotted lines, as in **26b–d** in Figure 4. The thermodynamics of these pathways were probed using B3LYP/6-311++g(d,p)/PCM(DCM)//B3LYP/6-31+g(d)/PCM(DCM) calculations; details can be found in the SI. The energy of complexation is enthalpically favorable for mechanisms 1 and 2 with DCM as the implicit solvent (See Table 2 in the SI). It was not possible to carry out calculations of mechanism 3.

A key feature of the hydrogen-bonding complexes is that it enables polarization of the bonds, possibly resulting in greater partial negative character of the α -hydrogen on the alcohol substrate. This can effectively enhance the hydridic character of the α -hydrogen and possibly lowers the activation energy of the hydride-transfer step in the oxidations. The results of these calculations are shown in Figure 4. It is clear from Figure 4 that mechanism 1 has a much higher activation energy, thereby making it a much slower reaction. This has been experimentally observed; reaction times of neutral oxidations (mechanism 1) are much longer (12–48 h) than analogous base reactions (1–4 h).³ The role of the basicity of pyridine bases was also probed in the calculations in mechanism 2. It is clear that the activation barriers decrease with increasing basicity (Table 1). Thus, the reactions should be faster for the more basic amines, which was confirmed by a recent publication.²⁵ While one cannot discount such hydrogen bonding, the reaction could also simply be written as a pyridine base-catalyzed reaction and is therefore quite similar to mechanism 1 if the pyridine is considered as an external base.

The case for mechanism 3 is more difficult to make. There are two reactions in this mechanism: (1) The reaction of pyridine with the positive oxygen; (2) The collapse of this intermediate to give products. We can find no precedence for the first reaction, although one would intuitively expect that a pyridine would react with the positive oxygen (or the oxygen–nitrogen system) rather than extract a proton from the hydroxyl group (as in mechanism 2). Such a reaction would be in accord

with the general nucleophilic attacks on oxygen described above and shown in Figure 2. It is also interesting that in the pyridine reactions, all of the primary alcohols are oxidized at about the same rate, while in neutral reactions there is a tremendous difference in the reactivities (allyl and benzyl, very fast; alkyl much slower; and finally, the fact that secondary alkyl alcohols are oxidized at almost twice the rate of similar primary alcohols).^{1,43} This implies that the electronic configurations in the alcohols are less important in the pyridine oxidations because the initial reaction is similar for all cases and may be the rate-controlling step. In essence, the pyridine facilitates the same sort of displacement (by the hydride) as is shown in acylpyridinium systems in Scheme 4 because it is a good leaving group.

NMR spectra of mixtures of pyridine and oxoammonium salt showed no evidence for the intermediate pyridinium complex in mechanism 3, nor did an MS study using electrospray ionization (ESI) measured on a Quattro II mass spectrometer.

There is some precedence for this hydride displacement reaction. Salts of the *N*-methoxypyridinium ion are stable and have been investigated in detail.^{75,76} *N*-Methoxypyridinium perchlorate was treated with NaBH_4 to give pyridine (isolated as a picrate) and, presumably, methanol.⁷⁶ This is quite similar to the hydride displacement of an oxygen-containing pyridinium as a leaving group in mechanism 3.

In most of the nitroxide-catalyzed oxidations with various secondary oxidants,² the bromide ion is a specific catalyst (not chloride or iodide).⁷⁴ Since bromide is a weak base and a good leaving group, it is possible that it serves in the same role as do the pyridine bases.

CONCLUSION

We have studied the reactions of oxoammonium cations with alcohols in the presence of pyridine and pyridine derivatives with various substitution patterns. Those pyridines having substitution in the 2- and 6-positions lead to aldehyde formation, and pyridines having little or no substitutions at these positions lead to dimeric esters. A plausible mechanism has been proposed to explain these results. We have defined experimental conditions for the alcohol–aldehyde reactions and studied the relative reactivities of several alcohols. Finally, we suggest that oxoammonium oxidations occur by nucleophilic reactions on the charged nitrogen–oxygen double bond and have suggested mechanisms for the other reactions in this paper.

EXPERIMENTAL SECTION

General Methods. Oxidations were carried out under nitrogen. Rotary evaporations of DCM and Et_2O solutions were carried out at about 80 mm (house vacuum) using a water bath at 25 °C, and with the flask just touching the water. GC/MS scans were measured on an HP-1 column (starting temp 40 °C, starting time at 40 °C for 2 min, 15 °C per min to a final temperature of 270 °C). High-resolution mass spectra were measured by the time-of-flight (TOF) method. NMR spectra of the oxidation products were measured at 400 MHz with 5 mm of molecular sieves 4 Å in the tube to dry the sample. When noted, equiv refers to the molar equivalents.

Chemicals. Although the oxoammonium salt **1b** is commercially available, our material was prepared from 4-amino-2,2,6,6-tetramethylpiperidine on multimole scale using our published protocol.^{6,77} It was recrystallized from water and

dried under vacuum at 80 °C.^{6,77} All other chemicals were commercial samples used without purification. DCM, pyridine, and 2,6-lutidine were dried over molecular sieves 4 Å. Commercial dry Et₂O was used without treatment.

Comparative Oxidations of 2-Butoxyethanol (6) with Various Pyridine Bases (Table 1). Oxoammonium salt **1b** (0.75 g, 2.5 mmol, 2.5 equiv), activated molecular sieves 4 Å (0.5 g), and pyridine base (2.3 mmol, 2.3 equiv) were added to 40 mL of DCM and stirred for 30 min. 2-Butoxyethanol (**6**) (0.118 g, 1 mmol, 1 equiv) was added dropwise, and the mixture was stirred for 3 h, during which time it turned from yellow to red, and some of the tetrafluoroborate salt of the protonated base precipitated. Five drops of methanol were added to the reaction vessel to complete the reaction, and the mixture was filtered and evaporated to dryness. The solids were triturated with dry Et₂O (50 mL), and the Et₂O solution was passed over a column of silica gel (5 × 1 cm). The red–orange nitroxide moved very slowly through the column. Elution was continued until the red band neared the bottom of the column, and the eluate was analyzed by GC on a 10 m × 0.53 mm OV-1 capillary column. The results were corrected by comparison with known compounds, and the results are given in Table 1.

Partial Oxidations of a Mixture of 2-Butoxyethanol (6) and 1-Nonanol (9) in the Presence of Pyridine (4) and Separately with 2,6-Lutidine (5), (Scheme 4 and Figure 1). A mixture of 2-butoxyethanol (**6**) (0.236 g, 2 mmol) and 1-nonanol (**9**) (0.289 g, 2 mmol) were dissolved in 100 mL of DCM, and enough oxoammonium salt **1b** (1.20 g, 4 mmol) and base, either pyridine (**4**) (0.316 g, 4 mmol) or 2,6-lutidine (**5**) (0.429 g, 4 mmol), to oxidize just one molar equivalent of alcohol. After 4 h, the reaction mixture was concentrated under vacuum to about 10 mL, and 50 mL of dry Et₂O was added to precipitate pyridinium or lutidinium tetrafluoroborate and most of the nitroxide **2b**. The GC/MS scans are given in Figure 1a for the oxidations in the presence of 2,6-lutidine and in Figure 1b for pyridine. Some nitroxide remained in the Et₂O solution and appears at 11.8 min in Figure 1a–c.

The experiment was repeated for pyridine but with enough oxidant **1b** (2.41 g, 8 mmol) and pyridine (**4**) (0.633 g, 8 mmol) to complete the oxidation. The mixture was worked up the same way, and the results are shown in Figure 1c.

All of the products of the oxidations were on hand for corroboration of the peaks except for the unsymmetrical esters **11** and **12**. One ester, 1-nonyl 2-butoxyacetate (**11**) has not been previously reported. The other ester, 2-butoxyethyl nonanoate (**12**) is known, but no spectral data have been reported for it.

1-Nonyl 2-Butoxyacetate (11). 2-Butoxyacetic acid (1.75 g, 13.2 mmol, 1.32 equiv) and 1-nonanol (**9**) (1.44 g, 10 mmol, 1 equiv) were dissolved in 100 mL of benzene containing 1 g of Amberlyst 15 (dry), and the mixture was heated to reflux within a flask equipped with a Dean–Stark trap until no more water collected (14 h). The Amberlyst 15 was removed by filtration, and the filtrate was evaporated to dryness under vacuum. The crude ester was distilled in a Kugelrohr to give **11** as a clear, colorless oil (2.57 g, 100%). ¹H NMR (CDCl₃, 400 MHz) δ 0.83–0.95 (m, 6 H), 1.18–1.45 (m, 14 H), 1.55–1.68 (m, 4 H), 3.52 (t, *J* = 6.60 Hz, 2 H), 4.05 (s, 2 H), 4.14 (t, *J* = 6.85 Hz, 2 H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 14.1, 14.3, 19.4, 22.9, 26.1, 28.9, 29.5, 29.7, 31.9, 32.1, 65.2, 68.6, 71.9, 171.0; HRMS (DART) calcd for C₁₅H₃₁O₃, [M + H⁺] 259.2273, found 259.2276.

2-Butoxyethyl Nonanoate (12).^{78,79} Compound **12** was prepared by heating a mixture of nonanoyl chloride (1.76 g, 10 mmol, 1 equiv) and 2-butoxyethanol (**6**) (1.77 g, 15 mmol, 1.5 equiv) to 100 °C for 15 h. The mixture was dissolved in 50 mL of DCM and filtered through a 4.5 × 2 cm pad of silica gel to remove excess 2-butoxyethanol (**6**), giving **12** as a clear, colorless oil (2.25 g, 87%). ¹H NMR (CDCl₃, 400 MHz) δ 0.84–0.96 (m, 6 H), 1.19–1.43 (m, 12 H), 1.51–1.68 (m, 4 H), 2.33 (t, *J* = 7.58 Hz, 2 H), 3.46 (t, *J* = 6.60 Hz, 2 H), 3.61 (apparent triplet, *J* = 5.10 Hz, 2 H), 4.21 (apparent triplet, *J* = 4.90 Hz, 2 H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 14.1, 14.3, 19.5, 22.9, 25.2, 29.4, 29.4, 29.5, 31.9, 32.1, 34.5, 63.7, 68.8, 71.4, 174.1 ppm; HRMS (DART) calcd for C₁₅H₃₁O₃, [M + H⁺] 259.2273, found 259.2237.

Oxidation of Hexanal to Isopropyl Hexanoate with Oxoammonium Salt in the Presence of Pyridine (4), eq 1. A slurry of **1b** (3.74 g, 12.5 mmol, 2.5 equiv), pyridine (**4**) (1.60 g, 20.2 mmol, 4.04 equiv), and 4 Å molecular sieves (0.50 g, 0.1 g/mL of solvent) in 5 mL of DCM was stirred at rt, and a mixture of hexanal (0.500 g, 5.00 mmol, 1 equiv) and 2-propanol (0.371 g, 6.17 mmol, 1.23 equiv) in 1 mL of DCM was added through a syringe pump over 30 min. After stirring for 30 min, the resulting orange slurry was filtered, and the residual white precipitate was washed with DCM. The filtrate was reduced to dryness under vacuum. The orange residue was triturated with 40 mL of dry Et₂O, filtered and washed again with two 10-mL portions of Et₂O. The combined ethereal solution and washings were reduced to approximately 5 mL under vacuum and filtered through a pad of silica gel on a 5 cm × 1 cm column using Et₂O as the eluant. The eluate, which was collected until the orange color reached the bottom of the column, was washed with 10% aq. HCl (4 × 10 mL), deionized water (2 × 10 mL), dried with Na₂SO₄, and concentrated to yield isopropyl hexanoate (0.402 g, 51%). The compound was found to be pure by GC and GC/MS and was identified by comparison of its GC retention time and mass spectrum to that of an authentic sample.

Oxidation of Benzaldehyde with Oxoammonium Salt in the Presence of Pyridine and *tert*-Butyl Alcohol, eq 2. A slurry of **1b** (3.78 g, 12.3 mmol, 2.43 equiv), pyridine (**4**) (1.33 g, 16.8 mmol, 3.33 equiv), and *tert*-butyl alcohol (0.893 g, 12.0 mmol, 2.38 equiv) in 30 mL of DCM was stirred at rt. To this slurry, was added benzaldehyde (0.536 g, 5.05 mmol, 1 equiv) in 4 mL of DCM dropwise over 30 min. After stirring overnight, the resulting orange slurry was filtered, and the white precipitate was washed with DCM. The filtrate was reduced to dryness under vacuum, and the orange residue was triturated with 30 mL of absolute EtOH. The solid was isolated by filtration and washed with EtOH to yield **15** (0.437 g, 46%). This compound was identified by comparison of its mp and ¹H NMR to that of an authentic sample, prepared as described below. The filtrate was evaporated to dryness under vacuum by rotary evaporation, triturated with 30 mL of dry Et₂O, and filtered to remove the nitroxide (**2b**). The ethereal solution was reduced to approximately 5 mL and chromatographed on a 5 cm × 1 cm column of silica gel using Et₂O as the eluant. The eluate, which was collected until the orange color reached the bottom of the column, was reduced to dryness under vacuum by rotary evaporation. Analysis of the residue by GC/MS on a 25 m × 0.2 mm × 0.33 μm HP-5 capillary column indicated that it consisted of a mixture of *tert*-butyl benzoate and benzoic acid. The compounds were identified by comparison of their

GC retention time and mass spectra to those of the authentic samples.

α -Benzoyloxybenzylpyridinium Tetrafluoroborate (15), eq 3. A slurry of **1b** (1.5 g, 5.00 mmol, 1 equiv), pyridine (**4**) (0.456 g, 5.76 mmol, 1.15 equiv), and benzaldehyde (0.825 g, 7.77 mmol, 1.55 equiv) in 20 mL of DCM was stirred at rt overnight. The resulting red slurry was then filtered, and the white precipitate was washed with DCM. The combined filtrate and washings were reduced to dryness under vacuum. The orange residue was triturated with 40 mL of absolute EtOH and filtered. The precipitate was dried to yield **15** (0.782 g, 83%), identical in all respects to the **15** isolated in eq 2. ^1H NMR (CDCl_3 , 400 MHz) δ 7.41–7.53 (m, 5 H), 7.57–7.65 (m, 1 H), 7.75–7.84 (m, 2 H), 8.06–8.14 (m, 4 H), 8.17 (s, 1 H), 8.50 (t, J = 7.83 Hz, 1 H), 9.24 (d, J = 6.11 Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 77.5, 90.5, 127.1, 127.1, 129.3, 129.4, 130.2, 130.8, 131.9, 132.3, 135.3, 143.0, 148.3, 164.3 ppm; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{16}\text{NO}_2^+$, $[\text{M} - \text{BF}_4^-]$, 290.1181, found, 290.1190.

α -Benzoyloxybenzylpyridinium chloride (19), eq 4, Scheme 5. The title compound was prepared following the procedure of French and Adams.⁴⁰ A mixture of benzoyl chloride (4.90 g, 34.9 mmol, 1 equiv) and pyridine (**4**) (2.80 g, 35.4 mmol, 1.01 equiv) was allowed to stand overnight at rt. After this time, benzaldehyde (3.70 g, 34.9 mmol, 1 equiv) was added (CAUTION! Reaction is exothermic!). The white solid that formed rapidly was dissolved in 30 mL of absolute EtOH and precipitated by the addition of 400 mL of dry Et₂O. The mixture was filtered to yield **19** as a white solid (8.60 g, 76%), mp 188–191 °C [lit. mp 192 °C]; ^1H NMR (CDCl_3 , 400 MHz) δ 7.36–7.47 (m, 5 H), 7.54–7.63 (m, 1 H), 7.99–8.12 (m, 4 H), 8.28 (t, J = 7.09 Hz, 2 H), 8.59 (t, J = 7.82 Hz, 1 H), 9.19 (s, 1 H), 10.12 (d, J = 5.87 Hz, 2 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 77.5, 89.4, 127.2, 127.4, 129.2, 129.9, 130.6, 131.4, 133.2, 133.2, 135.0, 143.7, 147.6, 164.1 ppm; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{16}\text{NO}_2^+$, $[\text{M} - \text{BF}_4^-]$, 290.1181, found, 290.1172.

α -Benzoyloxybenzylpyridinium tetrafluoroborate (15), eq 5, Scheme 5 by Exchange of Ions. A solution of **19** (3.91 g, 12.0 mmol, 1 equiv) and NaBF_4 (1.33 g, 12.2 mmol, 1.02 equiv) in 60 mL of deionized water was stirred for 30 min at rt, and the solution was filtered to yield **15** as a white solid (2.67 g, 58%), mp 109–112 °C. This sample of **15** was identical in all respects from that prepared as described in eq 3.

Preparative Oxidations; General Procedure. The alcohol (5 mmol, 1 equiv), and 2,6-lutidine (**5**) (1.17 g, 11 mmol, 2.2 equiv) were weighed into a flask and diluted to 100 mL with dry DCM. The oxoammonium salt **1b** (3.6 g, 12 mmol, 2.4 equiv) was added, and the mixture was stirred under nitrogen. The yellow suspension gradually turned pink and then red. In most cases, the reaction was complete after 4 h with the exception of the secondary alcohols, which took 48 h to completely oxidize. For several different alcohols, 0.5 mL samples were withdrawn, quenched with 2 mL of dry Et₂O, centrifuged, and injected into a GC/MS. Alternatively, NMR spectroscopy could be used to determine both the progress of the reaction and approximate yield (see below).

The reaction mixture was concentrated to about 5–10 mL of a viscous oil under vacuum. This oil was stirred, and 50 mL of dry Et₂O was slowly added. This precipitated about 65% of the theoretical mass balance of a mixture of nitroxide **2b** and 2,6-lutidine tetrafluoroborate as an orange powder. The suspension was allowed to settle, and the supernatant was poured onto a

column of 15 g of silica gel (43 \times 25 mm coarse, fritted funnel, wet-packed). The solid was washed with two more 50-mL portions of Et₂O which were added to the column. The nitroxide formed an orange band that moved very slowly through the column while the aldehyde or ketone product came out with the 150 mL of Et₂O as a clear, colorless solution. The Et₂O eluate was analyzed by GC/MS to show the purity of the product (suitable for tandem reactions); the Et₂O was evaporated to a constant weight to give an isolated yield; and the product was analyzed by ^1H and ^{13}C NMR.

The references for each known compound refer to published NMR data.

2-Butoxyacetaldehyde (20).⁸⁰ 2-Butoxyethanol (**6**) (0.590 g, 5 mmol, 1 equiv) was oxidized by the General Procedure to give **20** as a clear, colorless oil (0.566 g, 96%). ^1H NMR (CDCl_3 , 400 MHz) δ 0.93–0.99 (m, 3 H), 1.43 (dq, J = 14.98, 7.40 Hz, 2 H), 1.60–1.69 (m, 2 H), 3.56 (t, J = 6.60 Hz, 2 H), 4.08 (s, 2 H), 9.76 (s, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.0, 19.3, 31.8, 72.1, 76.5, 201.4 ppm.

2,2-Dimethyl-1,3-dioxolane-4-carboxaldehyde (21).⁸¹ 2,2-Dimethyl-1,3-dioxolane methanol (solketal) (0.660 g, 5 mmol, 1 equiv) was oxidized by the General Procedure to give **21** as a clear, colorless oil (0.574 g, 87%). ^1H NMR (CDCl_3 , 400 MHz) δ 1.41 (s, 3 H), 1.48 (s, 3 H), 4.07–4.12 (m, 1 H), 4.13–4.21 (m, 1 H), 4.38 (ddd, J = 7.21, 4.89, 1.83 Hz, 1 H), 9.71 (d, J = 1.71 Hz, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 25.4, 26.5, 65.8, 80.1, 111.6, 202.08 ppm.

Tetrahydro-2H-pyran-2-carbaldehyde (22).⁸² Tetrahydro-2H-pyran-2-methanol (0.580 g, 5 mmol, 1 equiv) was oxidized by the General Procedure to give **22** as a clear, white oil (0.479 g, 84%). ^1H NMR (CDCl_3 , 400 MHz) δ 1.38–1.66 (m, 4 H), 1.79–1.94 (m, 2 H), 3.53 (td, J = 10.80, 3.42 Hz, 1 H), 3.81 (dd, J = 11.00, 2.69 Hz, 1 H), 4.01–4.10 (m, 1 H), 9.61 (s, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 22.8, 25.8, 26.5, 68.4, 81.8, 202.1 ppm.

Acryloxyacetaldehyde (23). 2-Acryloxyethanol (0.58 g, 5 mmol, 1 equiv) was oxidized by the General Procedure to give **23** as a clear, colorless oil (0.399 g, 70%). ^1H NMR (CDCl_3 , 400 MHz) δ 4.72–4.78 (m, 2 H), 5.97 (d, J = 10.51 Hz, 1 H), 6.24 (dd, J = 17.24, 10.39 Hz, 1 H), 6.54 (d, J = 17.36 Hz, 1 H), 9.65 (s, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 68.9, 127.4, 132.9, 165.7, 196.0 ppm; HRMS (DART) calcd for $\text{C}_5\text{H}_7\text{O}_3^+$ $[\text{M} + \text{H}^+]$ 115.0395, found, 115.0416.

1,2:3,4-Di-O-isopropylidene- α -galacto-hexodialdo-1,5-pyranose (24).⁸³ 1,2:3,4-di-O-isopropylidene- α -D-galactopyranose (1.300 g, 5 mmol, 1 equiv) was oxidized by the General Procedure to give **24** as a clear, colorless oil (1.258 g, 98%). ^1H NMR (CDCl_3 , 400 MHz) δ 1.30 (s, 3 H), 1.33 (s, 4 H), 1.42 (s, 3 H), 1.49 (s, 3 H), 4.17 (d, J = 1.96 Hz, 1 H), 4.37 (dd, J = 4.89, 2.45 Hz, 1 H), 4.55–4.66 (m, 3 H), 5.65 (d, J = 4.89 Hz, 1 H), 9.60 (s, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 24.5, 25.0, 26.0, 26.2, 70.6, 70.7, 72.0, 73.5, 96.5, 109.3, 110.3, 200.4 ppm.

1-Phenoxypropan-2-one (25).⁸⁴ 1-Phenoxy-2-propanol (0.760 g, 5 mmol, 1 equiv) was oxidized by the General Procedure with the following modification: the reaction time was increased to 48 h. Compound **25** was obtained as a clear, colorless oil (0.727 g, 97%). ^1H NMR (CDCl_3 , 400 MHz) δ 2.28 (s, 3 H), 4.53 (s, 2 H), 6.86–6.92 (m, 2 H), 7.00 (t, J = 7.34 Hz, 1 H), 7.27–7.34 (m, 2 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 26.9, 73.3, 114.8, 122.0, 130.0, 158.0, 206.2 ppm.

Analysis of Crude Reaction Mixtures in DCM by ^1H NMR.⁸⁵ The crude reaction mixtures consisted of an aldehyde

product, nitroxide **2b**, and 2,6-lutidine tetrafluoroborate (the proton peaks of the 2,6-lutidine tetrafluoroborate salt are shifted downfield from those of 2,6-lutidine; methyl groups from 2.5 to 2.8 ppm, C₃ and C₅ protons from 6.9 to 7.2 ppm, and C₄ from 7.4 to 8.3 ppm). The proton NMR spectra of the mixtures were measured using a preset, external irradiation at 5.34 ppm, the peak of DCM. However, the presence of nitroxide free radical **2b** complicated matters and shifted every peaks downfield (by the same amount).⁸⁶ The nitroxide radical itself could not be observed. Thus, the preirradiation had to be corrected by measuring one scan and correcting the irradiation to this position. The proton spectrum was then measured, and the spectrum was referenced to the residual DCM signal at 5.34 ppm. For the aldehyde products, the aldehyde proton was clearly seen. When the aldehyde proton was integrated and compared with the peak of the proton on C-4 of 2,6-lutidine (**5**), present in a known amount, it could be seen that an oxidation had indeed taken place, and the approximate yield of aldehyde could be calculated. The theoretical integral ratio for 100% conversion is 2.2. Spectra for each of the crude reaction mixtures in Table 2 are provided in the SI.

Relative Oxidation Reactivities of Various Alcohols in the Presence of 2,6-Lutidine (5**), Table 3.** The two alcohols (2 mmol, 1 equiv) being compared were diluted with 50 mL of DCM, and 2,6-lutidine (**5**) (0.428 g, 4 mmol, 2 equiv) was added. The oxoammonium salt **1b** (1.2 g, 4 mmol, 2 equiv) was added, and the mixture was stirred for 4 h at rt. The solution was filtered, and the supernatant was examined by NMR. When the two aldehydes were compared, the relative aldehyde peaks were integrated. Whereas, when a primary alcohol was compared to a secondary alcohol, the appropriate peaks of the products and reactants were integrated, and the relative reactivity was calculated.

■ ASSOCIATED CONTENT

■ Supporting Information

Proton NMR spectra of crude oxidation mixtures, GC/MS scans of partial oxidations in the presence of 4-picoline and 2,4,6-collidine, ether eluates of pure aldehydes, and ¹H and ¹³C NMR spectra for all products; GC/MS scans for all liquid compounds along with the observed fragmentation patterns; energies and Cartesian coordinates for all stationary points in Figure 4. 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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