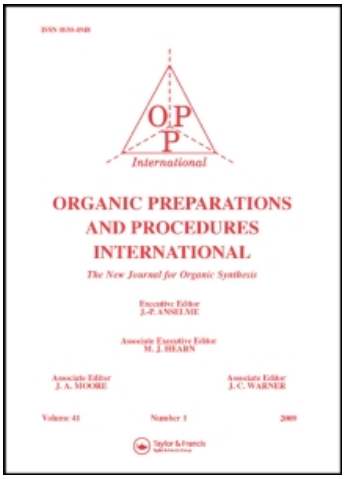

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PREPARATION OF TETRAMETHYLPIPERIDINE-1-OXOAMMONIUM SALTS AND THEIR USE AS OXIDANTS IN ORGANIC CHEMISTRY. A REVIEW

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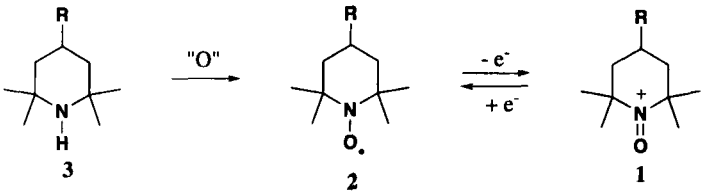
INTRODUCTION

The discovery of 2,2,6,6-tetramethylpiperidine-based oxoammonium salts in 1965 by Golubev *et al.*[1] has led to the synthesis of a number of oxoammonium-based oxidizing agents with diverse properties. However, many of the oxoammonium salts or their precursors are either not commercially available or are expensive. Reports of their preparation are spread over 40 years of literature. This review is a compilation of the most often cited and most practical procedures for their syntheses. A large body of work detailing the use of oxoammonium salts as catalytic and stoichiometric oxidants in preparative organic chemistry also accumulated over the past four decades. The review of their use, however, will focus on the literature from 1990 to date, excluding the patent literature, as a number of excellent earlier reviews on select aspects of this chemistry are available.[2-6] The goal of this review is to allow organic chemists to prepare and study oxoammonium salts, irrespective of their list prices or commercial availability.

Oxoammonium salts **1** are derived from nitroxide free radicals **2** by a one-electron oxidation (*Scheme 1*). Nitroxides are generally prepared by oxidation of the corresponding amine 2,2,6,6-tetramethylpiperidine derivatives (**3**). The α-methyl groups are crucial for the stabilization of the oxoammonium salts. A number of 4-substituted tetramethylpiperidine derivatives were used for the synthesis of oxoammonium salts, combined with several counter ions. In



3 **2** **1**

Scheme 1

Chapter I, the synthesis of a variety of oxoammonium salts and some of their physical and chemical properties are summarized.

Oxoammonium salts are potent but selective oxidants. They can either be prepared *in situ* from a nitroxide by reaction with a secondary oxidant, thus making the nitroxide a catalyst, or they can be used as stoichiometric oxidants. In Chapters II and III, both aspects are discussed respectively.

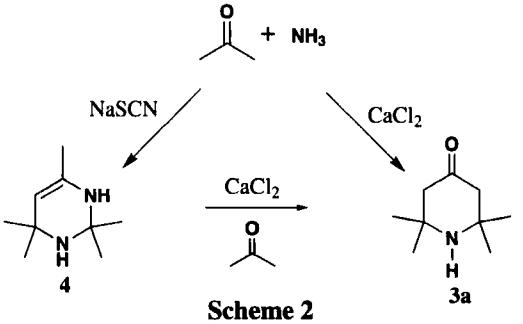
All procedures reported here were taken from the literature cited. However, instead of a *verbatim* reproduction of the procedures, they were formatted to maintain a consistent style, while the gist of their contents was preserved. The naming of nitroxides varies in the literature. They have become known as *N*-oxyl, iminoxyl, nitroxyl, or nitroxides radicals. Likewise, the naming of oxoammonium salts is inconsistent in the literature. They have been referred to as oxoaminium, oxonium, or oximinium salts. However, we will use only the names nitroxide and oxoammonium salt, irrespective of how a compound might be named in the primary literature. For the sake of brevity, only select physical data will be presented in the Experimental Section. For a full list of physical data, the reader is referred to the literature cited.

I. PREPARATION OF OXOAMMONIUM SALTS

The preparation of 2,2,6,6-tetramethylpiperidine-based oxoammonium salts can be divided into three distinct steps, discussed separately in subsequent chapters: (1) The synthesis of the piperidine derivative. (2) Oxidation of the amine to the corresponding stable nitroxide, 2,2,6,6-tetramethylpiperidine-*N*–oxide (TEMPO). (3) Conversion of the nitroxide radical to the oxoammonium salt.

1. Syntheses of 2,2,6,6-Tetramethylpiperidines

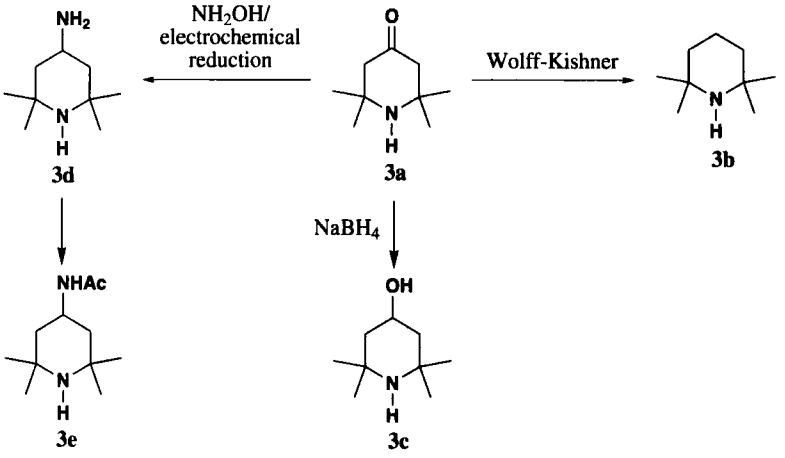
The most useful starting material for the preparation of 2,2,6,6-tetramethylpiperidine-1-oxammonium salts is 2,2,6,6-tetramethylpiperidine-4-one or triacetonamine (**3a**). It can be prepared on a large scale from readily available materials and is commercially available (*Scheme 2*). A number of procedures are available,[7-10] many of which have only been covered in the patent literature. Some procedures are easily reproducible and use inexpensive and available



Scheme 2

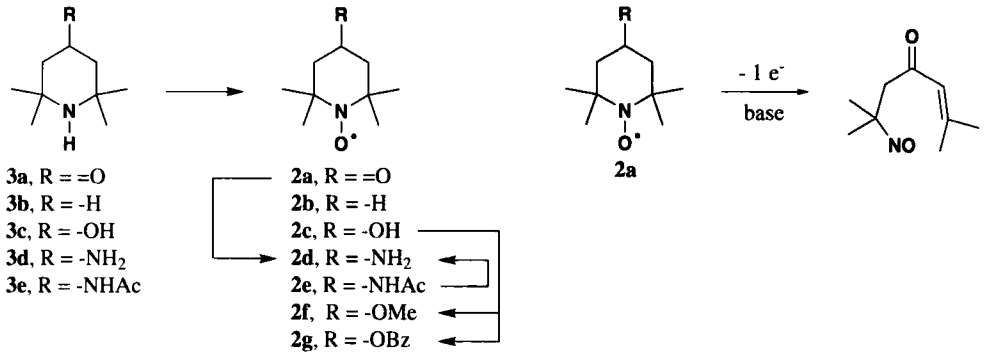
catalysts. For example, reaction of acetone, ammonia, and calcium chloride over a period of several days produces triacetonamine (**3a**). A number of complementary procedures are available but we will detail only the procedure by Sosnovski and Konieczny.[8] Alternatively, the preparation of acetonine (**4**)[11] can precede its conversion to **3a**.[12]

Triacetonamine (**3a**) is a versatile starting material not only because it can be prepared on a large scale but because it is susceptible to conversion to a number of derivatives (*Scheme 3*).



Scheme 3

Reduction under Wolff-Kishner conditions generates piperidine **3b**,[13] while sodium borohydride reduction forms the 4-hydroxy derivative **3c**.[14] Only one cumbersome electrochemical process was described for the direct conversion of **3a** to the 4-amino derivative **3d**.[15,16] In contrast, the analogous transformations of nitroxides **2a** and **2e** to the corresponding amine **2d** are well described (*Scheme 4*).[17,18] Fortunately, however, amine **3d** is commercially available and it is inexpensive due to its large-scale use in the polymer field. Acetylation of **3d** produces the widely used *N*-acetyl derivative **3e**.[19]



Scheme 4

2. Syntheses of 2,2,6,6-Tetramethylpiperidine-based Nitroxides

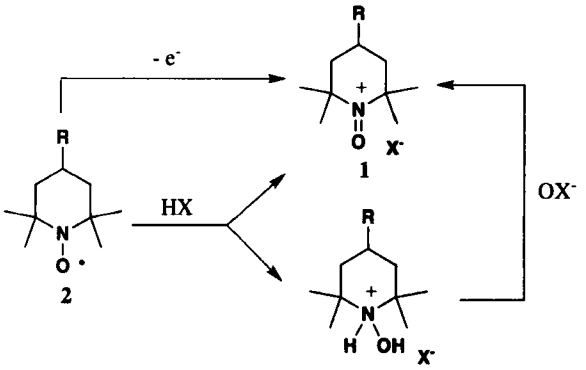
The conversion of the 2,2,6,6-tetramethylpiperidine (**3b**) to its corresponding nitroxide was first described by Lebelev *et al.*[20] The oxidation generally involves the use of hydrogen peroxide and a tungsten-based catalyst such as sodium tungstate or phosphotungstic acid. This oxidation reaction tolerates the presence of a number of substituents on the piperidine ring, notably, the presence of a 4-hydroxy group (*Scheme 4*). Alkylation or benzoylation of **2c**, respectively, generates the widely used derivatives **2f** and **2g**, respectively. Next to their use as intermediates in the synthesis of oxoammonium salts, the 2,2,6,6-tetramethylpiperidine-based nitroxides are stable radicals which have found use in many applications such as radical trapping or spin labeling. The electron-spin resonance (ESR) spectra of these nitroxides are well defined, indicating the presence of an unpaired electron.[21,22] Due to their paramagnetic character, however, NMR spectra are difficult to obtain.[23] Their crystal structures show that the piperidine ring adopts a chair conformation with the exception of the 4-oxo-TEMPO in which the piperidine ring adopts a boat conformation.[24,25] The average N-O bond distances are 1.28-1.30 Å.

While all the nitroxides listed in *Scheme 4* are stable, their physical properties and chemical stability are substituent-dependent. For instance, parent TEMPO (**2b**) has a low melting point, is volatile and readily sublimes, which may pose practical problems in its use. The 4-oxo- and the 4-hydroxy-derivatives **2a** and **2c** rearrange to a nitroso compound upon oxidation under basic conditions (*Scheme 4*).[26] The reduction of **2a** to form, by way of the imine, the 4-amino derivative **2d** was described.[17] However, the utility of the 4-amino along with the 4-hydroxy derivative **2c** as oxidation catalysts are of limited use as they are susceptible to oxidative degradation. These derivatives serve primarily as intermediates in the synthesis of polymer bound nitroxides. The 4-hydroxy-substituted nitroxide **2c** can be methylated and benzoylated.[27,28] The 4-methoxy derivative **2f** is somewhat more stable but is still characterized by a low melting point and high volatility. The 4-acetamido derivative **2e** is probably the most robust derivative of this series. Its synthesis can be achieved in large scale (up to 250 g batches were described). Its crystallinity allows also its purification by recrystallization from water or EtOAc.[19]

3. Syntheses of 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Salts

The oxoammonium salts are derived from the nitroxides by a one-electron oxidation (*Scheme 1*). Suitable chemical oxidants for this conversion are, for instance, halogens or hypohalites. The use of an anode in an electrochemical setup as oxidant is reviewed in Chapter II.7. The counter ion of the oxoammonium salt is generally derived from the oxidant.

An alternative way to prepare oxoammonium salts **1** is by an acid-catalyzed disproportionation of nitroxides **2** (*Scheme 5*). The use of tetrafluoroboric acid or perchloric acid led to a 1:1 mixture of the oxoammonium salt **1** and the corresponding hydroxylammonium salt **5**.[29] Either the two salts are isolated, and the hydroxylamine oxidized separately to the oxoammonium salt, or the hydroxylammonium derivative can be oxidized *in situ* by hypohalites to produce



Scheme 5

oxoammonium salts in good yields. Depending on the oxidation procedure, this may give rise to some ambiguity of the composition of the oxoammonium salt. For instance, using bromine as oxidant, the resulting salt may be a bromide, tribromide, or a mixture thereof.[30] The procedures provided herein provide products of definite composition.

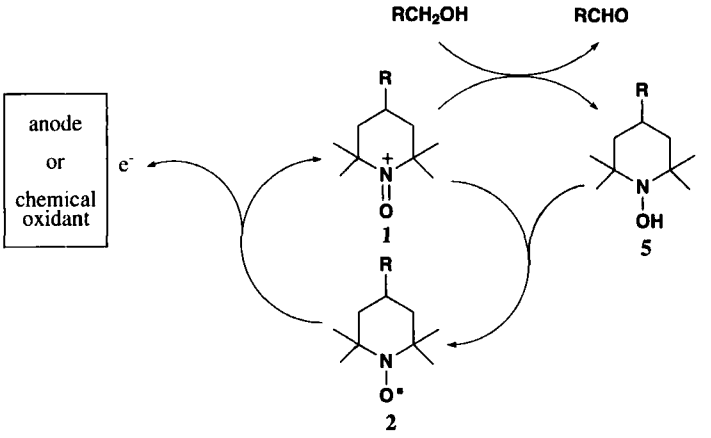
The physical and chemical properties of oxoammonium salts are dependent upon counterions. This is mainly due to their varying hygroscopic character and light sensitivity, which imparts varying shelf-lives to these derivatives. While the bromide, tribromide and chloride salts are quite hygroscopic, the tetrafluoroborate salts are not. In particular, the 4-acetamido derivatives, as their tetrafluoroborate salts, are characterized by high crystallinity and stability.

Note of Caution: The perchlorate salts of many oxoammonium derivatives are also well known but due to their latent ability to detonate, their use cannot be recommended.[31] They will, therefore, not be reviewed here. The chemical reactivities of the perchlorate and tetrafluoroborate are, in our experience, nearly identical. At least one of the oxoammonium chlorides reportedly also decomposed explosively.[32] Thus, we recommend that the general precautions taken for other strong oxidants be exercized when oxoammonium salts are used.

II. OXOAMMONIUM SALTS AS CATALYTIC OXIDANTS

Oxoammonium salts are strong and selective two-electron oxidants. Upon oxidation of a substrate such as a primary alcohol to the corresponding aldehyde, they are reduced to a hydroxylamine **5** (*Scheme 6*). This hydroxylamine conproportionates with one other equiv of oxoammonium salt **1** to yield two equiv of nitroxide **2**. If this nitroxide is oxidized electrochemically or chemically, the oxoammonium reagent is regenerated. This reaction sequence is the basis for the use of nitroxides (or oxoammonium salts) as catalytic oxidants. These reactions are reviewed here. Reactions involving the use of oxoammonium salts as stoichiometric oxidants are reviewed in Chapter III.

The use of nitroxides (or oxoammonium salts) as catalytic oxidants requires the use of a co-oxidant (also referred to as the secondary oxidant). The secondary oxidant can be as diverse



Scheme 6

as an anode,[33,34] household bleach,[35] *t*-butyl hypochlorite,[36] oxone,[37,38] elemental bromine, chlorine,[39] iodine,[40] *meta*-chloroperbenzoic acid,[41] *N*–chlorosuccinimide,[42,43] *N*–bromosuccinimide, sodium bromite[44,45] or chlorite,[46] enzymes (laccase),[47] heavy metal supported polymers (polymer-bound diacetoxybromite),[48] hypervalent iodine,[49,50] potassium ferricyanide,[51] and copper(II) salts,[52,53] periodic acid,[54] polyoxometalate,[55] ceric ammonium nitrate,[56] and select precious metals in combination with oxygen.[57,58] Some of the oxidants are used with co-catalysts such as bromide ion. The reactions were performed in mono- and biphasic systems, in ionic liquids,[59] and under sonication conditions.[60] The reactions can be performed under tight pH and temperature control. Two excellent papers on the mechanistic considerations of these reactions have been published by Semmelhack *et al.*[61] and Kishioka *et al.*[62]

1. Oxidation of Alcohols to Aldehydes and Ketones

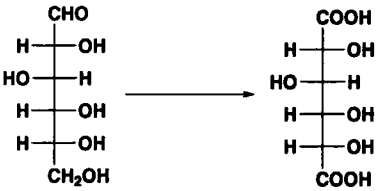
The most investigated oxidation reaction using oxoammonium salts in catalytic oxidations is the conversion of alcohols to aldehydes and ketones. These reactions have been described using a large variety of co-oxidants and using aqueous, organic or biphasic systems. Remarkably, the oxidation reactions are very specific, high yielding, and the reaction conditions are mild enough to tolerate a range of sensitive protective groups (*e.g.* TBDMS, THP, MOM, Boc, Cbz, isopropylidene and acetyl groups).[6]

General Oxidation Procedure Under Monophasic Conditions:[6] To a solution of the alcohol (1 equiv) in the chosen solvent (CH_2Cl_2, CH_3CN or H_2O) is added nitroxide **2** (0.01 equiv) and the co-oxidant (from the list above, but matching the solubility of the co-oxidant with the solvent used; 1.1 equiv per oxidizable function). The mixture is stirred at R.T., and monitored by TLC. Upon completion, the reaction is quenched (addition of EtOH, aqueous $NaHSO_3$, as appropriate); the organic layer (if present) is separated and washed with brine and H_2O; and the solvent is removed under reduced pressure. The residue is purified by column chromatography, or distillation.

General Oxidation Procedure Under Biphasic Conditions:[6,63] Under biphasic conditions, when, for example, using the combination of CH_2Cl_2/oxone or CH_2Cl_2/*meta*-chloroperbenzoic acid systems, phase-transfer catalysts such as Bu_4NBr are added to the reaction mixture.

2. Oxidation of Primary Alcohols to Carboxylic Acids

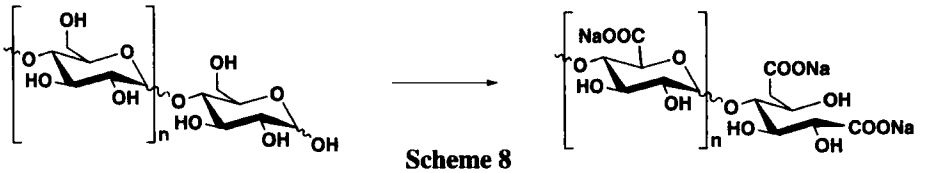
The mandatory presence of a secondary oxidant in the catalytic oxidations has the disadvantage that the substrates may be susceptible to undesired and nonselective degradation reactions. On the other hand, the catalytic oxidation can be combined with non-catalytic oxidations. For instance, the selective oxoammonium oxidation of primary alcohols in carbohydrates generates the corresponding aldehydes, and the oxidation of the aldehyde moiety by the secondary oxidant generates the carboxylates (*Scheme 7*). Thus, two selective and high yielding oxidation steps can be combined to convert reducing hexoses to the corresponding aldaric acids in an aqueous system.[39,64] Neither reaction oxidizes secondary alcohols.



Scheme 7

Typical Oxidation Procedure. Oxidation of Glucose to Glucaric Acid.-[64] D-Glucose (3.00 g, 16.6 mmol), 4-acetamido-TEMPO (**1e**) (0.04 g, 0.013 mmol), and NaBr (0.40 g, 3.36 mmol) in H_2O (50 mL) were cooled in an ice bath to 0-5°C, and the pH was adjusted to 11.5 with a NaOH solution (2 M). NaOCl (77 mL of 5.25% NaOCl, 3.3 equiv) was then added slowly (2 mL every 2 minutes for the first 25 mL, then 5 mL every 20 minutes for the rest). By means of an automatic titration system, the pH was kept between 11.4 and 11.6 with a NaOH solution (2 M). The end of the reaction was detected by a negative potassium iodide-starch paper test and occurred about one hour after the last bleach had been added. The reaction mixture (about 150 mL) was concentrated under vacuum (0.1 mmHg) to about 30 mL, and 100 mL of 95% EtOH was added to precipitate a mixture of disodium D-glucarate and some inorganic salts. The supernatant liquid was decanted and the gummy precipitate was dissolved in H_2O (30 mL) and precipitated with EtOH (100 mL). The resulting gum, after decantation of the supernatant, was washed with a mixture of EtOH-H_2O (4:1) to give crude disodium D-glucarate (3.9 g, 95% crude yield) after drying at 50°C under reduced pressure.

Oxidation of Polysaccharides.- Likewise, the catalytic oxidations have proven very useful in the conversion of high-molecular-weight polysaccharides (such as starch and pullulan) to polyuronic acids (*Scheme 8*).[65-68] Starch was selectively oxidized to polyglucuronates with a selectivity and yield of at least 95%, and a C-6 conversion rate of 98%. The oxidation of polysaccharides has been best achieved in high pH regimes to limit depolymerization.



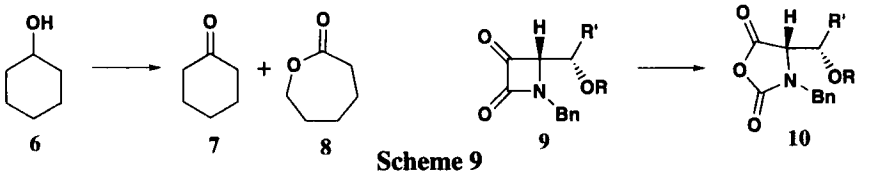
Scheme 8

3. Oxoammonium Salts in Baeyer-Villiger-Type Reactions

Oxoammonium salts, generated *in situ* with *m*-CPBA as co-oxidant, can be used for the conversion of cyclohexanol (**6**) to cyclohexanone (**7**) and the Baeyer-Villiger product ε-caprolactone (**8**).[69] The initial oxidation of the secondary alcohol to a ketone mediated by the oxoammonium salt is followed by a Baeyer-Villiger type oxygen insertion induced by the co-oxidant. Since cyclohexanone is particularly susceptible to a Baeyer-Villiger reaction, this reaction sequence may not be general. However, it again highlights how the co-oxidant can be chosen such as to induce reactions in addition to the generation of oxoammonium salts from nitroxides.

Oxidation Procedure for Baeyer-Villiger-Type Reaction.-[69] A 100-mL flask was charged with a solution of the alcohol (10 mmol), TEMPO **2b** (0.1 mmol), and Bu_4NBr (0.2 mmol) in CH_2Cl_2 (25 mL) and cooled to 0°C. A solution of *m*-CPBA (12 mmol) in CH_2Cl_2 (20 mL) was added dropwise over a period of 15 minutes. The color turned bright orange upon addition of *m*-CPBA. The mixture was stirred at 0°C for 10 minutes and at 23°C for 30 minutes, by which time the orange color had faded away. The reaction mixture was quenched by the addition of NaOH (1 M, 20 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (2 x 20 mL), dried (Na_2SO_4), filtered, and concentrated, and the residue was chromatographed on silica gel (CH_2Cl_2).

The role of the oxoammonium salt in the Baeyer-Villiger-type reaction is not clear. However, nitroxides used in combination with the co-oxidant bleach convert α-keto-β–lactams **9** to anhydride **10** in high yields (*Scheme 9*).[70]



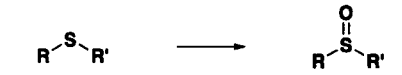
Scheme 9

General Preparation of Threonine N-Carboxyanhydrides from α-Hydroxy β-Lactams.-[70] To a magnetically stirred solution of 3-hydroxyazetidin-2-one (3 mmol) in CH_2Cl_2 (15 mL) were added TEMPO (**2b**) (6 mg, 0.03 mmol) and a solution of KBr (36 mg, 0.3 mmol) in H_2O (0.15 mL) at room temperature. The solution was cooled to -5-0°C (ice-salt bath) and NaOCl (available $Cl_2 \geq 4\%$, 30 mL) buffered at pH 6.9 (1.8 g of $NaHCO_3$ for 84 mL of a 0.25 M buffer solution phosphate) was added, keeping the temperature of the reaction mixture between 10 and 15°C.

The mixture was stirred for a further 10 minutes. Workup afforded the corresponding amino acid N-carboxy anhydrides.

4. Oxidations of Sulfides to Sulfoxides

Sulfides can be converted to sulfoxides using catalytic amounts of nitroxides, in conjunction with a secondary oxidant (*Scheme 10*). Sulfides are oxidized very rapidly, allowing the oxidation of sulfides to take place in the presence of primary and secondary alcohols.[71,72]

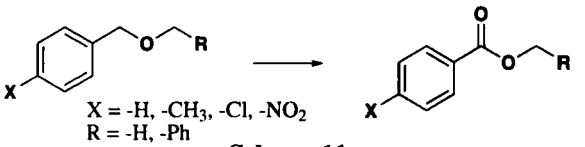


Scheme 10

General Procedure for the Preparation of Sulfoxides from Sulfides.-[71] To a solution of sulfide (3 mmol) in CH_2Cl_2 (8 mL) were added TEMPO (**2b**) (4.5 mg, 1 mol%) and a saturated aqueous $NaHCO_3$ (5 mL) containing KBr (30 mg, 10 mol%) and Bu_4NCl (40 mg, 5 mol%). To this cooled (0°C) and well-stirred mixture, a solution of NaOCl (1.95 M, 2 mL, 3.9 mmol, 30% excess), saturated $NaHCO_3$ solution (3 mL) and brine (6 mL) was added dropwise over 45 minutes. The mixture was stirred for 1 h at 0°C, then 20 minutes at 20°C, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined extracts were washed with saturated $NaHCO_3$ solution (10 mL), brine (10 mL) and dried over anhydrous Na_2SO_4. The evaporated crude product was analyzed (GC) and purified by distillation, crystallization or chromatography on silica gel.

5. Oxidation of Benzyl Ethers to Benzoates

A mild method to converts benzyl ethers to benzoate esters uses oxoammonium salts under catalytic conditions (*Scheme 11*).[73] Side-products are benzaldehyde, and benzoic acid. No formates were observed in the oxidation of benzyl methyl ethers, highlighting the selectivity of the oxidation. The yields of oxidations to benzoates varied between 62 to 76%.



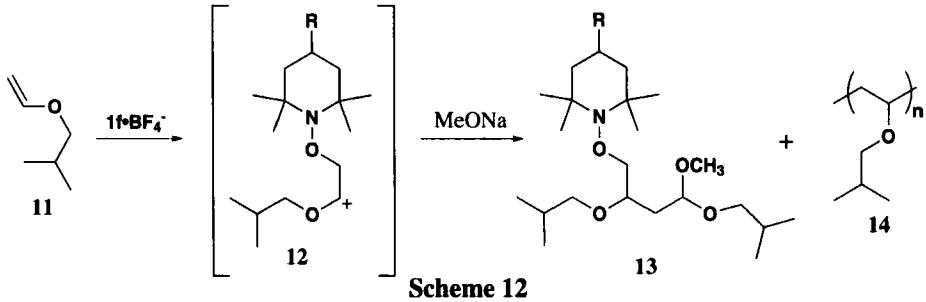
Scheme 11

Oxidation of Benzyl Ethers to Benzoate Esters.-[73] Dibenzyl ether (4 mmol) and 4-methoxy-TEMPO (**2f**) (22 mg, 0.12 mmol) were dissolved in CCl_4 (13 mL) and combined with an aqueous solution of KBr (1.2 M, 1 mL). $NaHSO_4$ (5 mmol) was added to adjust the pH value below 8.0 during the reaction. After reaction mixture had been cooled to 0-5°C, NaOCl (0.86 M,

24 mL, 20.6 mmol) was added dropwise over a period of 2.5 h, and the reaction was stirred for further 10 minutes. The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 x 10 mL). The organic phases were combined, washed with cold water, and dried over $MgSO_4$. After evaporation of the solvent, the residue was analyzed by NMR spectroscopy, GC-MS, and purified by either distillation or column chromatography.

6. Cationic Vinyl Polymerization Catalyzed by Oxoammonium Salts

Oxoammonium salts can also be initiators for the cationic polymerization of vinyl monomers.[74] The most successful oxoammonium salts are those having counter-ion of low nucleophilicity such as, perchlorate, tetrafluoroborate, and hexafluoroantimonate. Polymerization is induced by the addition of the oxoammonium salt to the electron-rich vinyl double bond such isobutyl vinyl ether (IBVE) (**11**) to provide species **12** (*Scheme 12*). After quenching of the reaction with MeONa, ether **13** was isolated, although the main product was poly-IBVE (**14**).



Scheme 12

General Procedure for the Cationic Vinyl Polymerization Catalyzed by Oxoammonium Salts.-[74] The polymerization was carried out between 0°C and ambient temperature under a dry N_2 atmosphere in a baked flask with a three-way neck stopcock. To a solution of a vinyl monomer in CH_2Cl_2 was added a CH_2Cl_2 solution of the oxoammonium salt **1f**. The mixture was vigorously stirred and kept at room temperature for 5 h. The polymerization was quenched by addition of NH_4OH/MeOH. The quenched mixture was washed with water, evaporated under reduced pressure, and dried *in vacuo* to give the product polymer. Conversion of the vinyl monomer was measured by gas chromatography of the crude reaction mixture. The resulting polymer **14** had degrees of polymerization between 5000-8000, and polydispersities of 2.4-3.1.

7. Electro-catalytic Oxidations

One of the best secondary oxidants is the anode of an electrochemical cell. Such electro-synthetic systems combine the highly specific oxidations of oxoammonium salts with general and inexpensive electrochemistry.

The susceptibility of nitroxides toward oxidations is generally investigated by electrochemistry. A reversible oxidation wave is indicative of the formation of an oxoammonium salt.[5,75] An irreversible oxidation wave indicates that the oxoammonium salt is rapidly decom-

posing, implying that that particular nitroxide is not a suitable catalyst. The usefulness of electrocatalytic oxidations was demonstrated by Semmelhack and co-workers for the oxidation of alcohols to aldehydes or ketones, and the oxidation of amines to carbonyl compounds and nitriles.[33,34,53] Using TEMPO (**2b**) as the catalysts, the reactions were carried out at +0.33 V (vs. Ag/Ag^+) on a platinum gauze electrode in acetonitrile or acetonitrile-water mixtures, with $LiClO_4$ as the electrolyte. For the oxidations of alcohols, the addition of one equiv of 2,6-lutidine proved neccessary. Enantioselective oxidations of racemic alcohols using sparteine as a chiral auxilliary was reported,[76] although the findings have been challenged.[77] The electro-catalytic oxidation of a series of alkyl glycosides and diglycosides to compounds in which the primary alcohol is oxidized to a carboxylic acid has also been reported.[78-80] It is of interest that the secondary alcohol groups of the sugars are not oxidized.

The ideal arrangement for electro-catalytic oxidations would consist of an electrode coated with the nitroxide catalyst, and such a system has been devised by Osa, Kashiwagi, and coworkers. The system has been used for the oxidation of alcohols,[81,82] thiols,[83] amines,[84] and in phenol coupling reactions.[85] The enantioselective oxidations of alcohols and amines was also claimed using an electrode coated with a chiral nitroxide.[84,86]

III. OXOAMMONIUM SALTS AS STOICHIOMETRIC OXIDANTS

As stoichiometric oxidants, oxoammonium salts represent a family of non-heavy metal-based oxidation reagents. Since they are colored, many reactions can be monitored colorimetrically. The reactions show counter-ion-dependent rates and specificities, and the reactions in acid and basic media differ in their outcomes and selectivities.

1. Oxidation of Alcohols

By far the best studied reaction using oxoammonium salts as oxidants is the oxidation of alcohols.[19,87-90] In general, the reaction is highly specific for the oxidation of primary alcohols to the corresponding aldehydes. The oxidants are characterized by high functional group specificity under a given set of conditions. The specificity is often the result of vastly differing reaction rates of the various functional groups, requiring a careful control of the oxidant stoichiometry and reaction times. For instance, primary alcohols are selectively oxidized to the aldehydes by **1e•BF_4^-** in the presence of secondary alcohols because secondary aliphatic alcohols are very slowly oxidized. Benzyl and allyl alcohols are rapidly oxidized. Phenolic benzyl alcohols can be oxidized without protection of the phenol although, as *Scheme 19* demonstrates, phenols are also susceptible to oxoammonium-induced phenol couplings. Oxoammonium salts do not induce isomerization of allylic alcohols. The reactions do not, however, take place readily when the alcohol carries a β–oxygen or β–electron-withdrawing groups. The oxidations can be carried out under acidic (with or without silica gel catalysis) or basic conditions (pyridine), depending on the lability of the substituents present on the alcohol. Further, the oxidations are generally high yielding, allowing the use of the crude aldehyde in further steps without purification and the development of tandem reactions (*Scheme 21*).

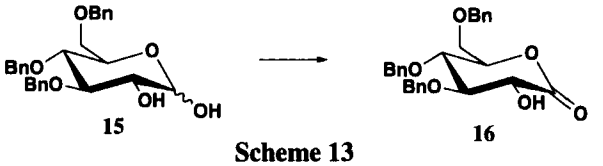
General Alcohol Oxidation Procedure.- The alcohol (10 mmol) was dissolved in CH_2Cl_2 (50–150 mL), and about twice the weight of the alcohol in silica gel was added. A slight excess (1.05 equiv) of oxoammonium salt **1** was added, and the brightly colored slurry was stirred until it became colorless. For allyl and benzyl alcohols, this only required a few minutes. Aliphatic alcohols took several hours. The slurry was then filtered, and the precipitate was washed several times with CH_2Cl_2. The filtrates and washings were evaporated under vacuum to constant weight, and the crude product was examined by GC or TLC and by ^1H and ^{13}C NMR. If necessary, the material was dissolved in CH_2Cl_2 and further purified by passing it through about 10 g of silica gel, using CH_2Cl_2 as eluent.

Alternatively to the addition of silica gel, the reaction can be performed in CH_2Cl_2 containing pyridine (2 equiv) and of oxoammonium salt (2 equiv), see also below.

2. Oxidation of Hemiacetals and Oxidative Esterification of Alcohols

a) Oxidation of Hemiacetals

When the oxidation reaction is carried out under basic conditions, hemiacetals are rapidly and selectively oxidized to form esters or lactones in the presence of unprotected secondary alcohols, circumventing the use of protecting groups (*Scheme 13*).[91] Nonetheless, the oxidation procedure is tolerant toward a number of protecting groups, among them silyl, benzyl and acetal groups.

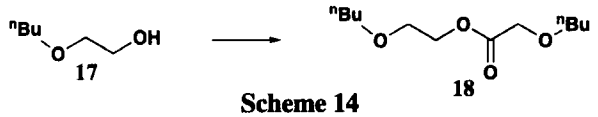


Scheme 13

Typical Procedure for the Oxidation of Hemiacetals.-[91] The substrate **15** (2 mmol) was dissolved in CH_2Cl_2 (20 mL) and pyridine (2.05 equiv) was added, followed by **1e•BF$_4^-$** (2.05 equiv). The mixture was stirred overnight, filtered to remove the precipitated pyridinium tetrafluoroborate, and evaporated to dryness under reduced pressure. The residue was suspended in dry Et_2O. Filtration of the suspension yields most of the recovered nitroxide **2e**. The filtrate was concentrated and passed over a short (~5 x 1 cm) column of silica gel. Using Et_2O as eluent, the product eluted ahead of the orange nitroxide band in all cases investigated. Evaporation of the main fraction yielded the product **16** in high to quantitative yields.

b) Oxidative Esterifications of Alcohols

The rapid oxidation of primary alcohols and hemiacetals can be combined in oxidative ester coupling reactions in which a primary alcohol is oxidized to the corresponding aldehyde which reacts with excess alcohol to form a hemiacetal which, in turn, is oxidized to form the ester or lactone (*Scheme 14*).



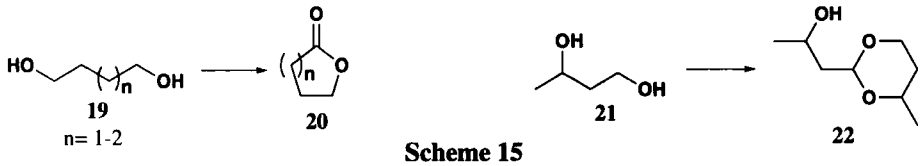
Scheme 14

The inhibition of the oxoammonium oxidation of alcohols containing a β–oxygen such as **17** (or nitrogen, sulfur or an electron-withdrawing group such as trifluoromethyl, cyano, carbonyl, etc.)[92,93] is an advantage in the oxidative esterification. The rate of oxidation of the alcohol is relatively slow compared to the rate at which the hemiacetal is formed. The subsequent relative rapid oxidation of the hemiacetal gives rise to the ester **18**. The oxidation conditions are tolerant toward acetals, epoxides and allyl groups.

General Procedure for the Oxidative Esterification of Alcohols.-[94] 2-Butoxyethanol (**17**), (0.616 g, 5.22 mmmol) was dissolved in dry CH_2Cl_2 (5 mL) and **1e•BF$_4^-$** (3.758 g, 12.5 mmol) was added. Pyridine (0.99 g, 12.5 mmol) was dissolved in CH_2Cl_2 (5 mL) and added dropwise over about 5 minutes to the salt-alcohol mixture. The mixture turned red/orange, and pyridinium-tetarafluoroborate precipitated as a white solid. After 3 h, the solution was filtered, and the filtrate was evaporated to dryness. The dried filtrate containing a mixture of products and nitroxide **2e** was stirred with Et_2O (2 x 15 mL). The Et_2O/nitroxide slurry was filtered to recover most of the solid nitroxide **2e**. The solution was dried over Na_2SO_4 and passed through silica gel (5 g) using Et_2O as eluent. The ether solution was evaporated to dryness to give ester **18** in 94% yield. The material was pure by GC and NMR.

c) Oxidation of Diols

Oxoammonium oxidations of diols **19** with four or five carbons generates the cyclized lactones **20** while 1,2-diols or 1,3-diols **21** generate cyclic hemiacetals and acetals such as **22** (*Scheme 15*).[95] However, under these conditions, no four or seven membered ring are observed for 1,3- and 1,6-diols. If a symmetrical 1,2-diol is oxidized with one equivalent of oxidant, only one α-hydroxy ketone is generated. If two equivalents of oxidant are used, the vicinal diketone is obtained. Diol cleavage products are not observed in neither cases.



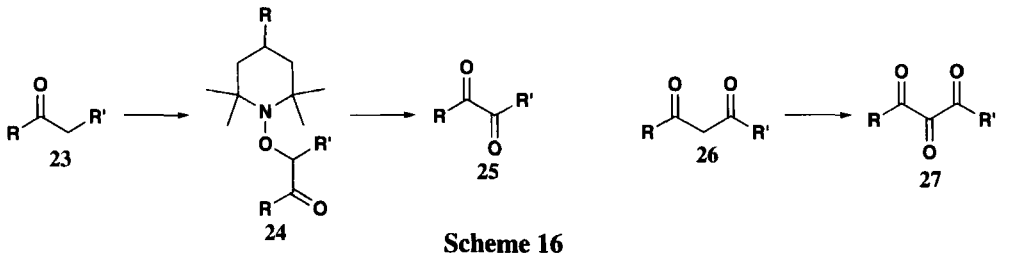
Scheme 15

Oxidation of 1,4-Butanediol with 1f•Cl$^-$.- To a solution of 1,4-butanediol (2.05 g, 22.7 mmol) in CH_2Cl_2 (200 mL) was added **2f•Cl**$^-$ (10.6 g, 47.8 mmol) under Argon and at R.T. After the reaction was over, the solution was washed with H_2O (200 mL) and dried over anhyd Na_2SO_4. The solvent was evaporated *in vacuo*. The residue was distilled under reduced pressure to give butyrolactone (1.59 g, 81% yield).

3. Oxidation of Activated Methylene Groups

a) α-Oxyfunctionalization of Ketones

Selective oxyfunctionalization of enolizable ketones **23** with 1 equiv oxoammonium salts can be achieved under standard conditions (CH_3CN) in high yields, thus making it a reagent of choice for the synthesis of *vic*-diketones **25** (*Scheme 16*).[96,97] The intermediate in this reaction is the α-(2,2,6,6-tetramethyl-piperidinyloxy)ketone **24** which can be isolated. This product is decomposed in the presence of *p*-TsOH to give the corresponding *vic*-diketones **25**.[97] It is interesting to note that unsymmetrical ketones afford mostly one regioisomer. The reaction is counter-ion dependent.[98] Oxoammonium Br^- or Br_3^- salts are nucleophilic enough to be able to substitute the *N*-oxypiperidine adduct **24** to form the corresponding α-bromoketones.



Scheme 16

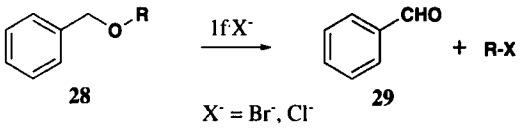
Standard Procedure for the Oxidation of Enolizable Ketones. Synthesis of 24.- A mixture of an enolizable ketone (3 mmol) and **1f•Cl**$^-$ (3.6 mmol) in dry CH_3CN (20 mL) was stirred at R.T. under Ar. The reaction was monitored by TLC. When the starting material was consumed, the reaction mixture was poured into H_2O and neutralized with aqueous $NaHCO_3$ (5%) and then extracted with $CHCl_3$ (100 mL). The organic layer was washed with H_2O, dried and evaporated. The reaction products were obtained by column chromatography on silica gel using EtOAc/petroleum ether as eluent.

Conversion of α-(2,2,6,6-Tetramethyl-4-methoxypiperidinyloxy)ketone (24) to 1,2-Diketone (25).- A mixture of the α–(2,2,6,6-tetramethyl-4-methoxypiperidinyloxy)ketone **24** (1 mmol) and *p*-TsOH (1 mmol) in CH_3CN (10 mL) was stirred and refluxed under Ar for several h. The reaction was monitored by TLC. When the reaction was completed, the reaction mixture was poured into H_2O and extracted with $CHCl_3$ (50 mL). The organic layer was washed with H_2O, dried and evaporated. The reaction products were separated by column chromatography on silica gel using EtOAc/petroleum ether.

Oxidation of 1,3-Diketones to 1,2,3-Triketones.- Oxoammonium salts such as **1•BF**$_4^-$ or **1•Cl**$^-$ reacted with 1,3-diketones **26** under standard conditions generates 1,2,3-triketones **27** in good yields (*Scheme 16*).[99]

b) Oxidative Removal of Benzyl Groups

A special case of the oxyfunctionalization of activated methylene groups is the oxidation of benzyl groups.[100] Benzyloxy groups are removed slowly by oxoammonium salts, generating benzaldehyde (**29**) and the corresponding alkyl halide (*Scheme 17*).

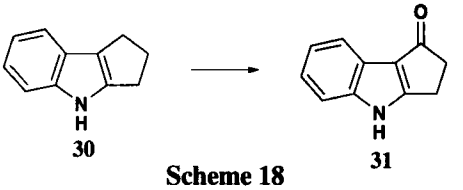


Scheme 17

Various benzyl ethers **28** were oxidized by Miyazawa *et al.* using standard conditions (CH_2Cl_2, R.T.).[100] Benzyl methyl ether was oxidized with 2 equiv of the oxoammonium **2f•Br**$^-$ to provide benzaldehyde (**29**) quantitatively. Dibenzyl ether was also oxidized by oxoammonium bromide to give benzaldehyde and benzyl bromide. When 3 equiv of water were added to the reaction mixture of dibenzyl ether and **2f•Br**$^-$, two equiv of benzaldehyde were obtained. These results suggest that a benzyl cation forms as an intermediate. Thus, the oxoammonium salts are excellent reagents to simultaneously deprotect benzyl ethers and to oxidize the deprotected alcohol to the corresponding aldehyde. Note that the equivalent reaction under catalytic oxidation conditions produces the benzoates (*Scheme 11*).

c) Oxidation of 1,2,3,4-Tetrahydrocyclopentane[b]indole (30)

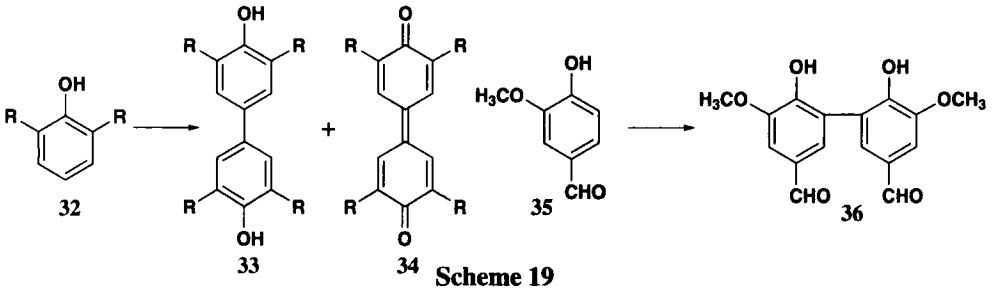
Reaction of oxoammonium salt **1•BF**$_4^-$ with tetrahydrocyclopentane[b]indole (**30**) in a CH_3CN/H_2O mixtures oxidize the β-carbon substituents on the indole system to ketone **31** in 60% yield.[101] No other examples of this reaction type have been reported.



Scheme 18

4. Oxidative Coupling Reactions

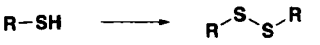
Oxoammonium salts, using standard reaction conditions, will induce oxidative phenol coupling reactions (*Scheme 19*).[102-104] *o*-Disubstituted phenols **32** give the *p*-coupled phenols **33**



Scheme 19

and the corresponding *p*-quinones **34**. When *o*-unsubstituted phenols such as vanillin (**35**) are oxidized, the oxidative coupling occurs to give the *o,o*-coupling product **36**. The reactivity of oxoammonium salts, thus, follows that of other oxidants inducing phenol couplings.

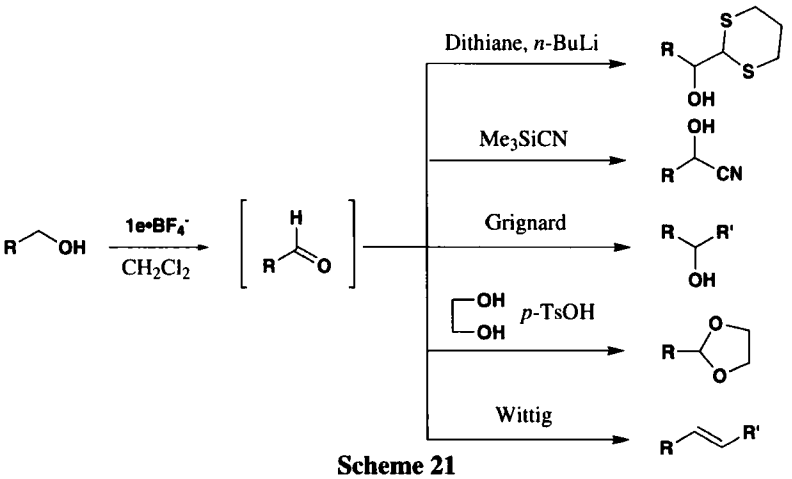
The use of stoichiometric amounts of oxoammonium salts oxidatively couple thiols to disulfides (*Scheme 20*). This reaction using standard conditions is rapid. The oxoammonium salt is decolorized within a few seconds upon mixing with the thiols at R.T. No further oxidation products are observed when the reaction stoichiometry is controlled.[105]



Scheme 20

5. Tandem Reactions

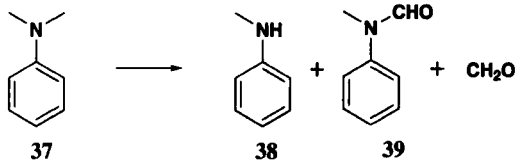
Of all of the functional classes in organic chemistry, the most difficult to isolate and work with are aldehydes. They are easily oxidized in air, they undergo various condensations, and, when small, are quite volatile. Thus, it is convenient to forgo their isolations and use them in a subsequent reaction. Since the stoichiometric reactions of oxoammonium salts are essentially quantitative in CH_2Cl_2, these reactions lend themselves to tandem reactions. This is especially appropriate since excess oxidant and its reduced product can be completely removed from the reaction solvent by a simple filtration through a silica gel pad. When CH_2Cl_2 is a suitable solvent for the subsequent reaction, the reaction can be carried out directly in the oxidation solvent. If the reaction must be carried out in another solvent, methylene chloride can be removed, or partially removed, and replaced with the new solvent. When appropriate, the solvents and salt should be carefully dried. Some of these reactions that have been carried out at the University of Connecticut[106] are summarized in *Scheme 21*. The "R" groups can be quite complex. Yields for the two steps vary between 75 and 95%.



Scheme 21

6. Miscellaneous Oxidation Reactions

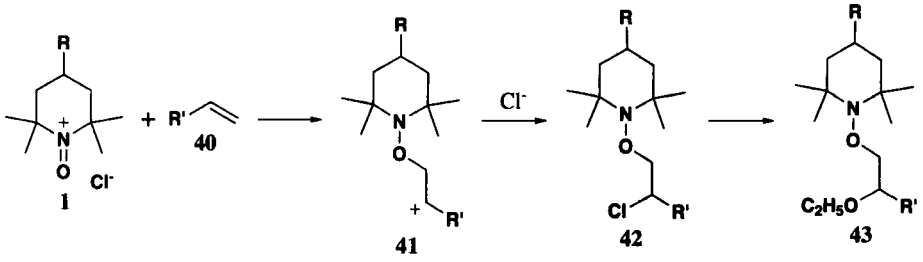
Oxidation of Amines.- Oxoammonium salts react rapidly with amines. For instance, in CH_2Cl_2, reaction of two equiv oxoammonium salts with one equiv of a tertiary amines such as *N,N*-dimethylaniline **37** produces the mono-dealkylated product **38** and the *N*-formyl reaction product **39** (*Scheme 22*).[107,108] The generality and utility of this reaction is not known.



37 38 39

Scheme 22

1,2-Addition of Oxoammonium Salts to Electron-rich Olefins.- 1,2-Addition of oxoammonium salts to electron-rich olefins such as vinyl ethers **40**, enamines and trialkyl-alkenes takes place in high yields (*Scheme 23*).[109] In case of the absence of a nucleophilic counter anion, the resulting cationic product **41** is can be used for cationic polymerizations (*Scheme 12*).[74] In case of a nucleophilic anion such as Br^- or Cl^-, the 1,2-addition product **42** is formed and can be isolated. Alcoholysis of this product gives rise to the formation of **43**. However, removal of the piperidine-1-oxy functionality generally requires relatively harsh conditions (THF/H_2O/acetic acid/heat).



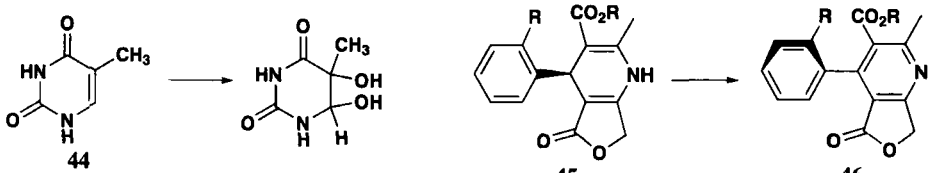
1 40 41 42 43

Scheme 23

General Procedure of the Electrophilic 1,2-Addition of Oxoammonium Salts to Electron-rich Olefins.-[109] To a solution of isobutyl vinyl ether (0.18 mmol) in $CDCl_3$ (0.5 mL) in a flask was added **1f•Cl**$^-$ (0.2. mmol) at R.T. The ^{1}H NMR spectrum of the mixture measured just after the addition suggested the formation of the 1,2-adduct **42** (R' = -*i*-Bu). Reaction of the adduct with EtOH/EtONa (2 equiv) at 5°C produces compound **43**.

Dihydroxylation of Thymine (44).-[110] Oxoammonium salts can also be used for the selective dihydroxylation as shown in the case of thymine (**44**) (*Scheme 24*; the stereochemistry of the diol moiety was not assigned). This reaction is unique as oxoammonium salts are not known to generally dihydroxylate olefins. However, the perceivable reaction mechanism – electrophilic addition to the activated double bond, hydrolysis of the intermediate with water – is consistent with the reactivity of oxoammonium salts (*Scheme 24*). The optimal conditions for the dihydrox-

ylation of thymine were determined to be in aqueous solution at pH 7.0 and 15 h reaction time using **2b**, as its bromide salt.



Scheme 24

Stereoselective Oxidation of 4-Aryl-1,4-dihydropyridines.-[111] 4-Aryl-1,4-dihydropyridines **45** exist in two diastereomeric atropisomers. The oxidation of **45** using **1e•BF_4^-**, using standard oxidation conditions (CH_3CN) furnished stereoselectively the 4–arylpyridine derivative **46** (ee = 93-97%). This is in contrast to other oxidants which show the formation of the isomeric product or not a large degree of stereoselectivity at all.

Other Reactions of Oxoammonium Salts.- The reaction of oxoammonium salts with Grignard compounds, dibenzyl mercury, stannanes, phosphines,[107] and other reagents has been reviewed.[5]

IV. SELECTED PREPARATIONS

1. Syntheses of 2,2,6,6-Tetramethylpiperidines

*a) Triacetonamine (**3a**).*-[8] Into a well-stirred mixture of acetone (1000 g, 17.3 mol, reagent grade) and anhydrous $CaCl_2$ (400 g, 4-20 mesh) was introduced anhydrous NH_3 (140 g, 8.2 mol) over a period of 3 days at ambient temperature. All precautions were taken to exclude moisture from the system. No more than 2.0 mol of NH_3 were introduced on the second and third day in four approximately equal portions. The temperature of the reaction mixture was not allowed to exceed 46°C. Following the final addition, stirring was discontinued, and the thickened reaction mixture was left to stand undisturbed at 23-25°C for 4 days. The apparatus was then set up for distillation. The stirred reaction mixture was distilled at 35°C under reduced pressure (100 mmHg). The unreacted acetone (310 g, 31%) was collected in two traps chilled by *i*PrOH/Dry Ice baths. An aqueous NaOH (500 mL of H_2O containing 100 g of NaOH) was added to the remaining cake and the mixture was stirred well. The resulting oil was decanted, and the remaining aqueous slurry was extracted with Et_2O (5 x 200 mL). The oil and ether extracts were combined and dried over $MgSO_4$. After removal of the drying agent, the solvent was evaporated *in vacuo* (12 mmHg) to afford 644 g of crude **3a**. The purity of **3a** as determined by GC was 85% (30% yield, based on consumed acetone). Pure **3a** can be obtained by solidification in CCl_4. Thus, crude **3a** (644 g) was mixed with an equal volume of CCl_4 and stored at 0°C overnight. The resulting solid was collected by filtration and dried at 10 mmHg to constant weight. In this manner, pure **3a** was obtained as a colorless solid (210 g, 11% yield, based on consumed acetone), mp. 34-36°C; bp. 50-56°C/1 mmHg; $n_D^{20} = 1.4630$.

b) Acetonine (4).-[11] Gaseous NH_3 was slowly bubbled, over 5 h, into a solution of NH_4SCN (0.33 g, 4.3 mmol) in acetone (60 mL, 1.03 mol, reagent grade). During the first hour, the solution was cooled in an ice bath; afterward it was kept at room temperature. The solution was then stirred for several hours during which samples of the mixture were analyzed by GC. After 5 h, the colorless solution was flushed with N_2 and was extracted with aqueous NaOH (50%, 30 mL). The layers were separated, and the organic phase was passed through a filter paper. The solution was concentrated *in vacuo* below 35°C to yield a viscous liquid which was placed in the freezer at –15°C overnight. The mass solidified as white crystals (43 g, 70%), mp. 42-44°C, $n_D^{20} = 1.4561$.

c) Triacetonamine (3a) from Acetonine (4).-[12] Acetonine (15.4 g), $CaCl_2 \cdot 2H_2O$ (14.7 g), H_2O (1.8 g), and acetone (5 g) were mixed in a round bottom flask equipped with reflux condenser, and cooled in an ice-bath. The mixture was stirred and kept at 50°C for 22 h. After cooling, NaOH (50%, 30 mL) was added, and the layers were separated. The organic layer was dried over K_2CO_3 and distilled under reduce pressure. Triacetonamine was collected as an oil (9.5 g, 61.3% yield), bp. 95-99°C/10mmHg.

Triacetonamine can also be synthesized by mixing acetonine (50 g), $ZnCl_2$ (24 g), H_2O (24 mL) at R.T. for 5 h. The work-up was identical as above, the yield of the triacetonamine was 35%.

d) 2,2,6,6-Tetramethylpiperidine (4b) by Wolff-Kishner Reduction of Triacetonamine (4a).-[13] Compound **4a** (77 g, 0.49 mol), aqueous hydrazine (85%, 75 mL), KOH (70 g, 1.25 mol), and triethylene glycol (475 g, 3.28 moles) were mixed in a flask fitted with a Dean-Stark trap. The mixture was maintained at 135°C for 2 h, after which the temperature was raised to 195°C while H_2O and product (upper layer) were constantly withdrawn from the Dean-Stark trap. Product **4b** was purified by distillation to yield 48.8 g (70%) of a colorless liquid, bp. 151-152°C/750 mmHg, $n_D^{20} = 1.4455$.

e) 4-Hydroxy-2,2,6,6-tetramethylpiperidine (3c) by Reduction of 4a.-[14] To a solution of compound **3a** (7.75 g, 0.05 moles) in EtOH (95%, 26 mL), were added $NaBH_4$ (0.95 g, 0.025 mol); and the mixture was stirred for 4 h at R.T. The flask was occasionally immersed in a cold water bath to prevent boiling. The solvent was removed on a rotary evaporator, and the residue was triturated with H_2O (20 mL). After standing for 2 days, the H_2O was removed on the rotary evaporator, and the remaining powder was extracted with ligroin (bp. 90-97°C) in a Soxhlet extractor. The extract was concentration to ~65 mL and cooled. The crystals which separated, were collected, washed with petroleum ether (bp. 30–60°C), and dried to afford pale yellow crystals (7.87 g, 97% yield), mp. 128-131°C.

*f) 4-Acetamido-2,2,6,6-tetramethylpiperidine (**3e**) from 4-Amino-2,2,6,6-tetramethylpiperidine (**3d**).*-[19] Compound **3d** (220 g, 1.42 mol) was dissolved in Et_2O (800 mL) in a 3 L Erlenmeyer flask equipped with a very large magnetic stirring bar. The mixture was cooled in an ice bath, and with vigorous stirring, freshly opened acetic anhydride (445 g, 4.36 mol) in Et_2O (200 mL) was added slowly over ~1 hour. Some heat was given off in the early stages, and there is a tendency for the product to clump together. The clumps can be broken up with a glass rod so that the final product is a free-flowing slurry. After addition of the an-hydride, the slurry was stirred for 3 hours, the solid was collected and washed with dry Et_2O to yield after drying in a hood to constant weight, 360 g (99% yield) of 4-acetylamino-2,2,6,6-tetramethylpiperidinium acetate, mp. 205°C. Free base **3e** does not need to be isolated for the oxidation to the nitroxide (see below). The free base can, however, be obtained by basification with Na_2CO_3 and extraction with Et_2O to give 4-acetylamino-2,2,6,6-tetramethylpiperidine (**3e**), mp. 118-120°C; bp. 161-163/6-7 mmHg.

2. Syntheses of 2,2,6,6-Tetramethylpiperidine-Based Nitroxides

*a) 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO, **2b**) by Oxidation of **3b**.*-[112] Compound **3b** (1.0 g, bp. 153.5-154°C, freshly distilled from solid KOH), H_2O (10 g), aqueous H_2O_2 (30%, 2.0 g) and phosphotungstic acid [24 WO_3•2 H_3PO_4•48 H_2O (0.01 g)] were stirred for 2-3 days. The resulting mixture was extracted with Et_2O (3 x 10 mL). The organic phase was washed with H_2SO_4 (6 x 1 mL, 0.5 M) to remove unreacted **3b**, and then with H_2O. The organic phase was dried over $CaSO_4$, and the solvent was removed at 25°C by rotary evaporation. The residue was purified by sublimation (twice) to give pure **2b** (~50% yield), mp. 39.3-39.8°C, bp. 60°C/10 mmHg. IR and UV spectral data are available.[22]

*b) 4-Oxo-TEMPO (**2a**) by Oxidation of **3a**.*-[114] A mixture of **3a** (2.0 g, 10.4 mmol) in distilled H_2O (25 mL), aqueous H_2O_2 (30%, 1.3 mL, 41.7 mmol) and $NaWO_4$ (0.08 g, 0.25 mmol) were vigorously stirred at R.T. for 2 h. The solution was then saturated with K_2CO_3 and the mixture was extracted with Et_2O (5 x 20 mL) until the organic layer became colorless. The combined ethereal extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was crystallized from a mixture of cyclohexane and benzene to give low melting, orange, crystalline solid (1.73 g, 98%), mp. 36°C. IR and UV spectral data were reported by Banerjee *et al.*[113]

*c) 4-Hydroxy-TEMPO (**2c**) by Oxidation of **3c**.*-[115] To compound **3c** (1.0 g) in H_2O (8 mL) were added phosphotungstic acid (24 WO_3•2 H_3PO_4•48H_2O, 10 mg) and H_2O_2 (30%, 2 mL). The solution was stirred vigorously at R.T. for 2 days. The orange solution was saturated with NaCl and extracted with Et_2O (3 x 20 mL). The organic phase was dried over K_2CO_3, filtered, and evaporated. The orange residue was chromatographed on a silica gel column (approx. 20 g) using $CHCl_3$ as mobile phase. The average yield of **2c** is 500 mg (50%), mp. 69-71°C. IR[22] and UV[116] spectral data are available.

d) 4-Methoxy-TEMPO (2f) Prepared by Methylation of **2c**.-[27] To a stirred solution of **2c** (17.2 g, 100 mmol) in anhydrous DMF (150 mL) was added NaH (3.6 g, 150 mmol). While this suspension was stirred under N_2, CH_3I (9.34 mL, 150 mmol), dissolved in DMF (34 mL), was added dropwise to the solution at 0°C. The reaction mixture was allowed to stir at R.T. for 5 hours. After removal of the precipitated NaI and excess NaH by filtration, Et_2O (500 mL) was added. The resulting extract was washed with H_2O, and the organic layer was dried over anhydrous $MgSO_4$. The ethereal solution was concentrated *in vacuo* to give a viscous red liquid. *n*-Hexane was added, and the mixture stored a –20°C. A total of 16.5 g of red needle crystals of **2f** were obtained (89% yield), mp. 35-36°C. IR and UV spectral data are available.[22]

e) 4-Benzoyloxy-TEMPO (2g) by Reaction of **2c** *with Benzoyl Chloride*.-[28] Under stirring and cooling in ice, benzoyl chloride (3.8 mL) was added to a solution of **2c** (5.2 g) in anhydrous pyridine (20 mL). The reaction mixture was allowed to stir at R.T. After 20 h, it was poured with vigorous stirring into ice water (150 mL). The resulting precipitate was collected, washed with H_2O, dried, and recrystallized from MeOH (20 mL). The product **2g** (7.5 g, 90%), crystallized as bright red needles, mp. 105°C (sealed capillary); sublimation at 95°C.

f) 4-Amino-TEMPO (2d) by Imine Reduction of **2a**.-[17] To a solution of NH_4OAc (4.52 g, 58.8 mmol) in absolute MeOH (150 mL) at pH 7-8 was added **2a** (1.0 g, 58.8 mmol) and $NaBH_3CN$ (0.258 g, 41.0 mmol). The reaction was stirred at ambient temperature for 1 day, then filtered, and the solvent was removed *in vacuo*. The remaining oil was taken up in H_2O; the pH was lowered to 5-6 with 1 M HCl and the solution extracted with $CHCl_3$. The aqueous phase was made basic with NaOH, saturated with NaCl, and extracted with $CHCl_3$. The combined extracts were dried over anhydrous $MgSO_4$, evaporated to dryness, chromatographed on neutral Al_2O_3 and eluted with absolute EtOH, giving **2d** as a red solid, mp. 33-35°C, in 70% yield. IR and UV spectral data are available.[117]

g) 4-Acetamido-TEMPO (2e) by Oxidation of **3e**.-[19] 2,2,6,6-Tetramethylpiperidinium acetate (360 g, 1.41 mol) was dissolved in H_2O (2.5 L), and the solution was made basic with Na_2CO_3 (244 g, 2.3 mol), added in small portions. $NaWO_4$ (25.0 g, 0.075 mol) and EDTA (25 g, 0.060 mol) were added. To the slurry were added five successive portions of H_2O_2 (30%, 5 x 100 mL, ~4.4 mol) at ~3 h intervals. A small amount of heat was given off, and the mixture tended to foam. For this reason, a beaker or large mouth container is desirable. After 3 days of stirring, the orange precipitate was collected and was washed once with ice water. The washing and filtrate were concentrated *in vacuo* to about half of its volume, and a second crop of solid product, obtained on chilling, was collected. The two crops were combined to give up to 295.0 g of **2e** (yields varied from 90–98%). Nitroxide **2e** can be recrystallized from two parts of H_2O or EtOAc to afford analytically pure orange crystals, mp. 145-147°C.

h) 4-Amino-TEMPO (2d) by Saponification of 4-Acetamido-TEMPO (2e).-[18] Compound **2e** (11 g) was boiled in aqueous KOH (15%, 25 mL) for 12 h. The mixture was cooled, filtered, saturated with solid K_2CO_3, and extracted with Et_2O. The ethereal extract was dried over $MgSO_4$, and the ether was evaporated. The residue was distilled *in vacuo*, and the fraction boiling at 97-98°C (4 mmHg), was collected to yield **2d** (8 g, 73%) as red hygroscopic needles, mp. 34-35°C.

3. Syntheses of 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Salts

a) General Method for the Preparation of Oxoammonium Tribromides and Chlorides.-[30] A mixture of nitroxide **2** (0.05 mol) in CCl_4 (100-200 mL) was placed in a cylindrical reactor with a porous glass bottom and a cooling jacket. The solution was cooled to -20°C. A solution of Br_2 (0.08 mol) or Cl_2 (0.03 mole) in CCl_4 (50 mL), respectively, was added dropwise while stirring vigorously and with continuous bubbling of dry Ar from below. After 30 minutes, the precipitate was collected, washed with cold CCl_4, and dried *in vacuo*. All the operations were accomplished with the usual precautionary measure for the exclusion of moisture.

*b) 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Tribromide (**1b•Br_3^-**).*-[30] obtained in 99% yield according to the general procedure using **2b** and Br_2 as dark red prisms, mp. 88.5-89.5°C (dec.) by precipitation with cyclohexane from CH_3CN. IR and UV spectral data are available.[30]

*c) 4-Benzoyloxy-2,2,6,6-tetramethylpiperidine-1-oxoammonium Tribromide (**1g•Br_3^-**).*-[30] obtained in 94% yield according to the general procedure using **2g** and Br_2, as claret colored prisms, mp. 96-97°C (dec.) from EtOAc. IR and UV spectral data are available.[30]

*d) 4-Benzoyloxy-2,2,6,6-tetramethylpiperidine-1-oxoammonium Chloride (**1g•Cl^-**).*-[32] obtained in 90% yield according to the general procedure using **2g** and Cl_2, as fine orange crystals, mp. 86-88°C (dec.). IR and UV spectral data are available.[32]

*e) 4-Oxo-2,2,6,6-tetramethylpiperidine-1-oxoammonium Chloride (**1a•Cl^-**).*-[32] obtained (no yield provided) according to the general procedure using **2a** and Cl_2 as fine yellow crystals. It decomposes explosively at R.T.

*f) 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Chloride (**1b•Cl^-**).*-[108] Into a solution of **2b** (15.6 g, 0.1 mol) in CCl_4 (200 mL) at R.T., Cl_2 was bubbled until no further precipitate formed. The pumpkin-colored precipitate was collected and washed several times with fresh CCl_4. This material was transferred to a round-bottom flask and dried *in vacuo* overnight, to yield 17 g (90%) of **1b•Cl^-**, mp. 116-117°C (dec.). This product was analyzed for chloride by the Mohr procedure and found to have 0.985 chlorine/molecule. This hygroscopic material slowly bleaches when exposed to direct sunlight.

*g) 4-Methoxy-2,2,6,6-Tetramethylpiperidine-1-oxoammonium Chloride (**1f•Cl⁻**).*-[27] Cl_2 was bubbled into the stirred solution of **2f** (2.0 g, 10.7 mmol) in CCl_4 (100 mL). The orange precipitate was collected and washed with CCl_4 to provide 2.1 g of ***1f•Cl⁻*** (89%) as orange crystals, mp. 121-123°C. IR spectral data are available.[27]

*h) 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Bromide (**1b•Br⁻**).*-[110] A solution of Br_2 (5.0 mmol) in CCl_4 (10 mL) was added dropwise over 1 h to a CCl_4 solution (56 mL) of **2b** (10.0 mmol). The resulting mixture was stirred overnight. The reddish brown powder precipitated was collected, dissolved in MeOH, and then re-precipitated by addition of 10% v/v Et_2O/hexanes to give 13.2 g (56%) of **1b•Br⁻** as a red powder, mp. 76-78°C (dec.).

*i) 4-Methoxy-2,2,6,6-tetramethylpiperidine-1-oxoammonium Bromide (**1f•Br⁻**).*-[27] To a stirred solution of **2f** (3.37 g, 18.1 mmol) in *n*-hexane (100 mL) was added Br_2 dropwise (1.45 g, 9.1 mmol) in CCl_4 (20 mL) at R.T. A dark-red precipitate appeared from the red solution. The precipitate was collected and washed with CCl_4 to provide ***1f•Br⁻*** (4.04 g, 84% yield), mp. 206-207°C. IR spectral data are available.[27]

j) General Procedure for the Preparation of Oxoammonium Salts by the Acid-induced Disproportionation of Nitroxides.-[29] To a solution of nitroxide **2** (0.02 mol) in Et_2O (5-7 mL) or dioxane (1-2 mL), cooled at 10°C, were added aqueous HBF_4 (48%, 2 equiv). The resulting precipitate of the oxoammonium salt **1** was collected by filtration, washed and dried *in vacuo*. The yields provided are based on the theoretical yield of 50% of the disproportionation reaction. With the use of aqueous $HClO_4$ (72%, 1 equiv), this procedure affords the perchlorate salts of **1a**, **1h**, and **1g** in good yields.[29]

*k) 2,2,6,6-Tetramethylpiperidine-1-oxoammonium Tetrafluoroborate (**1b•BF_4^-**).*-[29] obtained in 72% yield, according to the general procedure using **2b** and HBF_4 in Et_2O as yellow prisms, mp. 162.5-163.5°C (dec.), from CH_3CN-CCl_4. IR and UV spectral data are available.[29]

*l) 4-Oxo-2,2,6,6-tetramethylpiperidine-1-oxoammonium Tetrafluoroborate (**1a•BF_4^-**).*-[29] obtained in 61% yield according to the general procedure using **2a** and HBF_4 in Et_2O as yellow prisms, mp. 116-117°C (dec.), from CH_3CN-CCl_4. IR and UV spectral data are available.[29]

*m) 4-Benzoyloxy-2,2,6,6-tetramethylpiperidine-1-oxoammonium Tetrafluoroborate (**1g•BF_4^-**).*-[29] obtained in 84% yield according to the general procedure using **2g** and HBF_4 in Et_2O as yellow prisms, mp. 130-132°C (dec.), from CH_3NO_2-Et_2O. IR and UV spectral data are available.[29]

n) 4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium Tetrafluoroborate (1e•BF_4^-).-[19] Compound **2e** (100 g, 0.469 mole) was stirred with H_2O (50 mL) and HBF_4 (48%, 90 g, 0.49 mole) was added over about 1 h. The mixture was placed in an ice bath, and commercial bleach (332.2 g, 5.25% NaOCl, 0.47 mole) was added over about 2 h. The mixture was stirred in an ice-bath for about 3 h and the bright yellow solid collected was pressed as dry as possible and was washed with ice water (2 x 50 mL) and CH_2Cl_2 (2 x 100 mL). The salt was dried at R.T. and in air to constant weight to give 90-95 g (about 65%) of **1e•BF_4^-**, mp. 190-195°C (dec.). The corresponding perchlorate salt may be obtained by using $HClO_4$.[19]

CONCLUSION

In conclusion, oxoammonium salts are versatile oxidants in organic chemistry. The mild, transition metal-free reaction conditions and the selectivity of the oxidations recommend this oxidant for wider use. Further, the option for tandem reactions will greatly increase the utility of this reagent. We hope this review will inspire organic chemists to test and further develop the scope of oxoammonium salts as oxidants.

REFERENCES

1. V. A. Golubev, E. G. Rozantsev, and M. B. Neiman, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1898 (Engl. Transl.) (**1965**); *Chem. Abstr.*, ***64***, 59770 (1966).

2. E. G. Rozantsev and V. D. Sholle, *Synthesis*, 190 (**1971**).

3. E. G. Rozantsev and V. D. Sholle, *Synthesis*, 401 (**1971**).

4. J. F. W. Keana, *Chem. Rev.*, **78**, 37 (1978).

5. J. M. Bobbitt and M. C. L. Flores, *Heterocycles*, **27**, 509 (1988).

6. A. E. J. de Nooy, A. C. Besemer, and H. van Bekkum, *Synthesis*, 1153 (**1996**).

7. F. Francis, *J. Chem. Soc.*, 2897 (**1927**).

8. G. Sosnovsky and M. Konieczny, *Synthesis*, 735 (**1976**).

9. G. Sosnovsky and M. Konieczny, *Z. Naturforsch.*, **32b**, 328 (1977).

10. G. Sosnovsky and M. Konieczny, *Z. Naturforsch.*, **32b**, 338 (1977).

11. Z. Ma, Q. Huang, and J. M. Bobbitt, *J. Org. Chem.*, **58**, 4837 (1993).

12. K. Murayama, S. Morimura, O. Amakasu, T. Toda, and E. Yamao, *Nippon Kagaku Zasshi*, **90**, 296 (1969); *Chem. Abstr.*, **70**, 114968 (1970).

13. N. J. Leonard and E. W. Nommensen, *J. Am. Chem. Soc.*, **71**, 2808 (1949).

14. W. B. Lutz, S. Lazarus, and R. I. Meltzer, *J. Org. Chem.*, **27**, 1695 (1962).

15. M. Dagonneau, E. S. Kagan, V. I. Mikhailov, E. G. Rozantsev, and V. D. Sholle, *Synthesis*, 895 (**1984**).

16. M. Y. Fioshin, I. A. Avrutskaya, I. I. Surov, and V. T. Novikov, *Collect. Czech. Chem. Commun.*, **52**, 182 (1987).

17. G. M. Rosen, *J. Med. Chem.*, **17**, 358 (1974).

18. E. G. Rozantsev and Y. V. Kokhanov, *Izv. Akad. Nauk USSR., Ser. Khim.*, 1422 (**1966**), *Chem. Abstr.*, **66**, 54758 (1967).

19. J. M. Bobbitt, *J. Org. Chem.*, **63**, 9367 (1998).

20. O. L. Lebedev and S. N. Kazarnovskii, *Zhur. Obshch. Khim.*, **30**, 1631 (1960); *Chem. Abstr.*, **55**, 7792 (1961).

21. E. G. Rozantsev and M. B. Neiman, *Tetrahedron*, **20**, 131 (1964).

22. R. Briere, H. Lemaire, and A. Rassat, *Bull. Soc. Chim. Fr.*, **32**, 3273 (1965).

23. W. Schilf, L. Stefaniak, J. Skolimwski, and G. A. Webb, *J. Mol. Struct.*, **407**, 1 (1997).

24. L. O. Atovmyan, V. A. Golubev, N. I. Golovina, and G. A. Klitskaya, *Izv. Akad. Nauk USSR., Ser. Khim.*, **16**, 92 (1975); *Chem. Abstr.*, **82**, 163631 (1975).

25. Z. Ciunik, *J. Mol. Struct.*, **412**, 27 (1997).

26. G. Moad, E. Rizzardo, and D. H. Solomon, *Tetrahedron Lett.*, **22**, 1165 (1981).

27. T. Miyazawa, T. Endo, S. Shiihashi, and M. Okawara, *J. Org. Chem.*, **50**, 1332 (1985).

28. E. G. Rozantsev, V. A. Golubev, and M. B. Neiman, *Izv. Akad. Nauk USSR., Ser. Khim.*, 379 (**1965**); *Chem. Abstr.*, **62**, 82415 (1965).

29. V. A. Golubev, R. I. Zhdanov, V. M. Gida, and E. G. Rozantsev, *Izv. Akad. Nauk USSR., Ser. Khim.*, **4**, 768 (1971); *Chem. Abstr.*, **75**, 63571 (1971).

30. R. I. Zhdanov, V. A. Golubev, and É. G. Rozantsev, *Izv. Akad. Nauk USSR., Ser. Khim.*, **1**, 188 (1970); *Chem. Abstr.*, **72**, 111227 (1970).

31. J. M. Bobbitt, *Chem. Eng. News*, **77**, 6 (1999).

32. V. A. Golubev, R. I. Zhadov, and E. G. Rozantsev, *Izv. Akad. Nauk USSR., Ser. Khim.*, **1**, 186 (1970); *Chem. Abstr.*, **72**, 111229 (1970).

33. M. F. Semmelhack, C. S. Chou, and D. A. Cortes, *J. Am. Chem. Soc.*, **105**, 4492 (1983).

34. M. F. Semmelhack and C. R. Schmid, *J. Am. Chem. Soc.*, **105**, 6732 (1983).

35. P. L. Anelli, S. banfi, F. Montanari, and S. Quici, *J. Org. Chem.*, **54**, 2970 (1989).

36. F. Melvin, A. McMeill, P. J. F. Henderson, and R. B. Herbert, *Tetrahedron Lett.*, **40**, 1201 (1999).

37. C. Bolm, A. S. Magnus, and J. P. Hildebrand, *Chemistry Lett.*, **2**, 1173 (2000).

38. P. L. Bragd, A. C. Besemer, and H. Van Bekkum, *J. Mol. Catal., A* **170**, 35 (2001).

39. N. Merbouh, J. M. Bobbitt, and C. Brückner, *J. Carbohydr. Chem.*, **21**, 65 (2002).

40. R. A. Miller and R. S. Hoerrner, *Org. Lett.*, **5**, 285 (2003).

41. S. D. Rychnovsky and R. Vaidyanathan, *J. Org. Chem.*, **64**, 310 (1999).

42. J. Einhorn, C. Einhorn, F. Ratajczak, and J. L. Pierre, *J. Org. Chem.*, **61**, 7452 (1996).

43. S. Weik, G. Nicholson, G. Jung, and J. Rademann, *Angew. Chem., Int. Ed.*, **40**, 1436 (2001).

44. T. Inokuchi, S. Matsumoto, T. Nishiyama, and S. Torii, *J. Org. Chem.*, **55**, 462 (1990).

45. T. Inokuchi, P. Liu, and S. Torii, *Chemistry Lett.*, 1411 (**1994**).

46. M. Zhao, J. Li, E. Mano, Z. Song, D. M. Tsahen, E. J. J. Grabowski, and P. Reider, *J. Org. Chem.*, **64**, 2564 (1999).

47. M. Fabbrini, C. Galli, P. Gentili, and D. Macchitella, *Tetrahedron Lett.*, **42**, 7551 (2001).

48. G. Sourkouni-Argirusi and A. Kirshning, *Org. Lett.*, **2**, 3781 (2000).

49. A. de Mico, R. Margarita, L. Parlanti, A. Vesconi, and G. Piancatelli, *J. Org. Chem.*, **62**, 6974 (1997).

50. J. B. Epp and T. S. Widlanski, *J. Org. Chem.*, **64**, 293 (1999).

51. T. Miyazawa and T. Endo, *J. Mol. Catal.*, **31**, 217 (1985).

52. T. Miyazawa and T. Endo, *J. Mol. Catal.*, **32**, 357 (1985).

53. M. F. Semmelhack, C. R. Schmid, D. A. Cortes, and C. S. Chou, *J. Am. Chem. Soc.*, **106**, 3374 (1984).

54. S. S. Kim and K. Nehru, *Synlett*, 616 (**2002**).

55. R. Ben-Daniel, P. Alsters, and R. Neumann, *J. Org. Chem.*, **66**, 8650 (2001).

56. S. S. Kim and H. C. Jung, *Synthesis*, 2135 (**2003**).

57. A. Dijksman, I. W. C. E. Arends, and R. A. Sheldon, *Chem. Commun.*, 1591 (**1999**).

58. A. Cecchetto, F. Fontana, F. Minisci, and F. Recupero, *Tetrahedron Lett.*, **42**, 6651 (2001).

59. I. A. Ansari and R. Gree, *Org. Lett.*, **4**, 1507 (2002).

60. S. Lemoine, C. Thomazeau, D. Joannard, S. Trombotto, G. Descotes, A. Bouchu, and Y. Queneau, *Carbohydr. Res.*, **326**, 176 (2000).

61. M. F. Semmelhack, C. R. Schmid, and D. A. Cortes, *Tetrahedron Lett.*, **27**, 1119 (1986).

62. S. Kishioka, S. Ohki, T. Ohsaka, and K. Tokuda, *J. Electroanal. Chem.*, **452**, 179 (1998).

63. P. L. Anelli, F. Montanari, and S. Quici, *Org. Synth.*, **69**, 212 (1990).

64. N. Merbouh, J. F. Thaburet, M. Ibert, F. Marsais, and J. M. Bobbitt, *Carbohydr. Res.*, **336**, 75 (2001).

65. N. J. Davis and S. L. Flitsch, *Tetrahedron Lett.*, **34**, 1181 (1993).

66. A. E. J. de Nooy, A. C. Besemer, and H. van Bekkum, *Tetrahedron*, **51**, 8023 (1995).

67. A. E. J. de Nooy, A. C. Besemer, and H. van Bekkum, *Carbohydr. Res.*, **269**, 89 (1995).

68. J. F. Thaburet, N. Merbouh, M. Ibert, F. Marsais, and G. Queguiner, *Carbohydr. Res.*, **330**, 21 (2001).

69. J. A. Cella, J. A. Kelley, and E. F. Kenehan, *J. Org. Chem.*, **40**, 1860 (1975).

70. C. Palomo, J. M. Aizpurua, C. Cuevas, R. Urguechi, and A. Linden, *J. Org. Chem.*, **61**, 4400 (1996).

71. R. Siedlecka, J. Skarzewski, and J. Mlochowski, *Tetrahedron. Lett.*, **31**, 2177 (1990).

72. R. Siedlecka and J. Skarzewski, *Synthesis*, 401 (**1994**).

73. N. S. Cho and C. H. Park, *Bull. Korean Chem. Soc.*, **15**, 924 (1994); *Chem. Abstr.*, **122**, 105358 (1995).

74. E. Yoshida, K. Nakamura, T. Takata, and T. Endo, *J. Polym. Sci., Part A: Polym. Chem.*, **31**, 1505 (1993).

75. W. Summerman and U. Deffner, *Tetrahedron*, **31**, 593 (1975).

76. Y. Kashiwagi, Y. Yanagisawa, F. Kurashima, J. Anzai, T. Osa, and J. M. Bobbitt, *Chem. Commun.*, 2745 (**1996**).

77. E. M. Belgsir and H. J. Schäfer, *Chem. Commun.*, 435 (**1999**).

78. K. Schnatbaum and H. J. Schäfer, *Synthesis,* **5**, 864 (1999).

79. E. M. Belgsir and H. J. Schäfer, *Electrochem. Commun.,* **3**, 32 (2001).

80. M. Schämann and H. J. Schäfer, *Eur. J. Org. Chem.*, 351 (**2003**).

81. T. Osa, U. Akiba, I. Segawa, and J. M. Bobbitt, *Chemistry Lett.*, 1423 (**1988**).

82. T. Osa, Y. Kashiwagi, K. Mukai, A. Ohsawa, and J. M. Bobbitt, *Chemistry Lett.*, 75 (**1990**).

83. Y. Kashiwagi, A. Ohsawa, T. Osa, Z. Ma, and J. M. Bobbitt, *Chemistry Lett.*, 581 (**1991**).

84. Y. Kashiwagi, F. Kurashima, C. Kikuchi, J. i. Anzai, T. Osa, and J. M. Bobbitt, *Chem. Commun.*, 1983 (**1999**).

85. T. Osa, Y. Kashiwagi, Y. Yanagisawa, and J. M. Bobbitt, *Chem. Commun.*, 2535 (**1994**).

86. Y. Kashiwagi, F. Kurashima, S. Chiba, J. Anzai, T. Osa, and J. M. Bobbitt, *Chem. Commun.*, 114 (**2003**).

87. Z. Ma and J. M. Bobbitt, *J. Org. Chem.,* **56**, 6110 (1991).

88. C. A. Kernag, J. M. Bobbitt, and D. V. McGrath, *Tetrahedron Lett.,* **40**, 1635 (1999).

89. M. G. Banwell, M. P. Collis, M. F. Mackay, and S. L. Richards, *J. Chem. Soc., Perkin Trans., 1*, 1913 (**1993**).

90. M. G. Banwell, V. S. Bridges, J. R. Dupuche, S. L. Richards, and J. M. Walter, *J. Org. Chem.,* **59**, 6338 (1994).

91. N. Merbouh, J. M. Bobbitt, and C. Brückner, *Tetrahedron Lett.,* **42**, 8793 (2001).

92. M. Yamaguchi, T. Takata, and T. Endo, *Tetrahedron Lett.,* **29**, 5671 (1988).

93. M. Yamaguchi, T. Takata, and T. Endo, *J. Org. Chem.,* **55**, 1490 (1990).

94. N. Merbouh, J. M. Bobbitt, and C. Brückner, *manuscript in preparation.*

95. T. Miyazawa and T. Endo, *J. Org. Chem.,* **50**, 3930 (1985).

96. T. Ren, Y. C. Liu, and Q. X. Guo, *Bull. Chem. Soc. Jpn.,* **69**, 2935 (1996).

97. Y. C. Liu, T. Ren, and Q. X. Guo, *Chin. J. Chem.*, **14**, 252 (1996); *Chem. Abstr.*, **125**, 300543 (1996).

98. V. A. Golubev, R. I. Zhdanov, I. T. Protsishin, and E. G. Rozantsev, *Izv. Akad. Nauk USSR., Ser. Khim.*, **195**, 952 (1970); *Chem. Abstr.*, **74**, 76281 (1971).

99. V. A. Golubev and R. V. Miklyush, *Zh. Org. Khim.*, **8**, 1376 (1972).

100. T. Miyazawa and T. Endo, *Tetrahedron Lett.*, **27**, 3395 (1986).

101. J. M. Bobbitt, M. C. F. Guttermuth, Z. Ma, and H. Tang, *Heterocycles*, **30**, 1131 (1990).

102. J. M. Bobbitt and Z. Ma, *Heterocycles*, **33**, 641 (1992).

103. Y. B. Ding, l. Yang, Z. L. Liu, and Y. C. Liu, *J. Chem. Res., Synop.*, 328 (**1994**).

104. Y. C. Liu, W. Wang, and Q. X. Guo, *Chin. Chem. Lett.*, **7**, 790 (1996); *Chem. Abstr.*, **125**, 328197 (1996).

105. Z. Ma, *Ph.D Thesis*, University of Connecticut (1991).

106. R. So, M. J. Mealy, and J. M. Bobbitt, University of Connecticut, unpublished results.

107. D. H. Hunter, D. H. R. Barton, and W. J. Motherwell, *Tetrahedron Lett.*, **25**, 603 (1984).

108. D. H. Hunter, J. S. Racok, A. W. Rey, and Y. Z. Ponce, *J. Org. Chem.*, **53**, 1278 (1988).

109. T. Takata, Y. Tsujino, S. Nakanishi, K. Nakamura, E. Yoshida, and T. Endo, *Chemistry Lett.*, 937 (**1999**).

110. T. Kagiya, C. Komuro, K. Sakano, and S. Nishimoto, *Chemistry Lett.*, 365 (**1983**).

111. B. Koop, A. Straub, and H. J. Schäfer, *Tetrahedron: Asymmetry*, **12**, 341 (2001).

112. C. Harries, *Justus Liebigs Ann. Chem.*, **417**, 107 (1918).

113. T. Kawai, M. Jarjaoui, and R. L. Burwell Jr., *J. Am. Chem. Soc.*, **104**, 2951 (1982).

114. S. Banerjee and G. K. Trivedi, *Tetrahedron*, **48**, 9939 (1992).

115. A. J. Ozinskas and A. M. Bobst, *Helv. Chim. Acta*, **63**, 1407 (1980).

116. N. N. Quan and A. V. Guzzo, *J. Phys. Chem.*, **85**, 140 (1981).

117. V. A. Golubev, Y. E. Rashba, and A. N. Rozenberg, *Izv. Akad. Nauk USSR., Ser. Khim.*, **12**, 2442 (1982); *Chem. Abstr.*, **98**, 126015 (1983).

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