°C [pure by TLC (silica, 1:4 EtOAc/petroleum ether)].

Acknowledgment. Support of this work by the National Institutes of Health (Grant CA 17631) is gratefully acknowledged. We thank Professors B. Franck[7] and L. A. Mitscher for exchange of information and Dr. A. Bonati for a gift of emodin.

Registry No. 1, 518-82-1; 3, 481-74-3.

Reaction of 1-Nitroso-1,2,3,4-tetrahydropyridine with Mineral Acids

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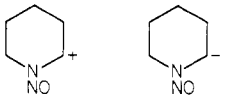
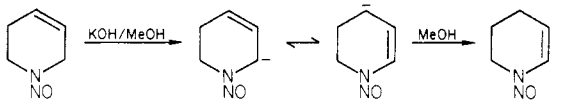
It has been postulated[2-4] that the presence of a nitroso group on an amino nitrogen allows for the stabilization of either a carbanion or a carbocation at the α-position. This



imparts to the amine the ability to accept a wide variety of substituents at the α-position that could not be introduced by conventional methods.

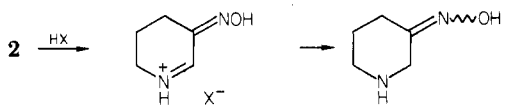
The base-catalyzed conversion of 1-nitroso-1,2,3,6-tetrahydropyridine (1) to 1-nitroso-1,2,3,4-tetrahydropyridine (2),[8] as described in detail by Michejda and co-



1 3 2

workers,[4,5] is thought to proceed in nearly quantitative yield by the initial removal of the α-allylic hydrogen to form resonance stabilized carbanion **3**. Protonation at the terminal carbon gives thermodynamically more stable **2**.

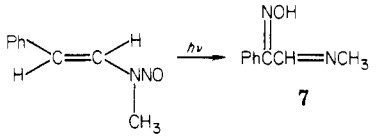
The reaction of the 1-nitroso-1,2,3,4-tetrahydropyridine (**2**) with acid was studied to determine if the double bond would protonate regiospecifically to give the α-carbocation. Reaction of **2** with trifluoroacetic acid caused the precipitation of a solid with the properties of a salt. The NMR spectrum of the solid showed an isolated vinyl proton with no α-proton coupling. This could only result from a 3,4,5,6-tetrahydro-3-pyridone derivative. The remainder of the NMR spectrum was consistent with the structure of 3-oximino-3,4,5,6-tetrahydropyridinium trifluoroacetate (**4a**). A similar reaction was observed with hydrogen



4a, X = CF_3COO^-
b, X = Cl^- **5**

chloride to give the chloride salt **4b**. These salts were reduced by sodium borohydride to 3-piperidone oxime (**5**), confirming the ring skeleton. A mixture of *Z* and *E* isomers was obtained, with the *E* isomer formed in excess.

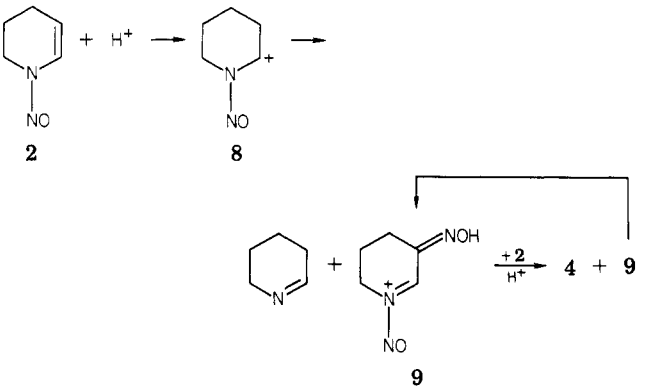
This reaction has a structural analogy in the observation by Seebach and Enders[6] that the reaction of methyl-*p*-styrylnitrosamine (**6**) under "radical producing" conditions formed an oxime (**7**) or its hydrochloride.



6 **7**

Concurrent with our studies, Michejda and co-workers[7] confirmed the finding of Seebach and Enders[6] that radical conditions caused the rearrangement of **2** to the oxime in the absence of oxygen, or 5-nitro-1,2,3,4-tetrahydropyridine if oxygen is present. These reactions appear to occur through radical intermediates.

The formation of **4** from **2** under the strongly acid conditions we used probably results from the protonation of **2** at the 3-position to give the α-carbocation **8**. This intermediate would act as a nitrosation reagent for an unprotonated molecule of **2** to form the oxime **4**.



2 **8** **9**

Experimental Section

Preparation of 1-Nitroso-1,2,3,4-tetrahydropyridine (2). The title compound was prepared by the base-catalyzed isomerization of 1-nitroso-1,2,3,6-tetrahydropyridine (1), as described by Michejda and Kupper.[4,5]

Reaction of 2 with Trifluoroacetic Acid To Form 4a. A solution of 1.0 g (9 mmol) of 1-nitroso-1,2,3,4-tetrahydropyridine (**2**) in 6 mL of chloroform was treated with 0.7 mL (9 mmol) of trifluoroacetic acid in 6 mL of $CHCl_3$ at 0 °C. The ice bath was removed after 5 min, and within 0.5–1 h a precipitate formed. The solid was removed by filtration to give 1.7 g, 7.6 mmol (85%), of 3-oximino-3,4,5,6-tetrahydropyridinium trifluoroacetate (**4a**). Two recrystallizations of the solid from acetonitrile provided an analytical sample of **4a**; mp ~100 °C dec; IR (mull) 2850 cm^{-1} (NH), 1665 cm^{-1} (COO); UV (MeOH) λ_{max} 257 nm (ϵ 1.3 × 10^4); NMR (acetone-d_6 δ [multiplicity, integration (assignment)] 2.1 [quin, 2 (C-5)], 2.9 [t, 2 (C-4)], 5.0 [d of t, 2 (C-6)], 8.6 [t (*J* =

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(8) The 1-nitrosotetrahydropyridines described in this paper have been shown to be potent carcinogens in animals, and extreme precautions should be observed in working with these compounds.

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1.8), C-2)], 11 [s, 2 ($^+$NH, OH)].

Anal. Calcd for $C_7H_9F_3N_2O_3$: C, 37.18; H, 4.01. Found: C, 37.39; H, 4.04.

Reaction of 2 with Hydrochloric Acid and Reduction of 4b to 5. An excess of dry hydrogen chloride gas was bubbled through a solution of 1.1 g (10 mmol) of 1-nitroso-1,2,3,4-tetrahydropyridine (**2**) in 30 mL of chloroform at 0 °C. The solid that formed was collected by filtration to give 0.7 g (4.8 mmol) (48%) of 3-oximino-3,4,5,6-tetrahydropyridinium chloride (**4b**); mp 155–159 °C dec. The spectral properties were nearly identical with those of **4a**.

The rearrangement product **4b** (1.15 g, 7.7 mmol) in 40 mL of MeOH was added to an excess of sodium borohydride in 30 mL methanol at 0 °C. After being stirred for 2 h, the reaction mixture was concentrated under reduced pressure. The residue was triturated with acetone, and the acetone solution was treated with anhydrous hydrogen chloride for 5 min. The solid that formed was removed by filtration to give a quantitative yield of solid, which on recrystallization from ethanol gives the 3-piperidone oxime hydrochloride (**5**), as a mixture of *Z* and *E* isomers: mp 115–145 °C dec; NMR (D_2O) δ [multiplicity, integration (assignment)] 2.4 [m, 2 (C-5)], 3.1 [t, 2 (C-4)], 3.8 [t, (C-6)], 4.1 and 4.4 [s, 2 (C-2 in *Z* and *E* isomer)]. (The signal at δ 4.4 is only 33% of that at 4.1.)

Anal. Calcd for $C_5H_{11}ClN_2O$: C, 39.88; H, 7.34. Found: C, 39.85; H, 7.36.

Acknowledgment. We express our appreciation for partial support of this research by a grant from the National Institutes of Environmental Health Sciences (1-R01-ESO-1975), and V.E.G. acknowledges appointment as a Mary Blanche Taxis Cancer Research Scholar.

Registry No. **2**, 70501-82-5; **4a**, 86834-59-5; **4b**, 86834-60-8; (*Z*)-**5**·HCl, 86834-61-9; (*E*)-**5**·HCl, 86834-62-0; trifluoroacetic acid, 76-05-1; hydrogen chloride, 7647-01-0.

Persulfate/Silver Ion Decarboxylation of Carboxylic Acids. Preparation of Alkanes, Alkenes, and Alcohols

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The persulfate ion, $S_2O_8^{2-}$, is an inexpensive and easily handled oxidant that has seen little use in synthetic organic chemistry.[1] Its high reduction potential ($E°$ = 2.01 V, aqueous) makes persulfate a powerful oxidant; however, the high activation barrier (approximately 30 kcal/mol) to uncatalyzed homolytic decomposition renders persulfate less useful at reasonable temperatures. The actual reactive species, sulfate radical anion, $SO_4^{-}\cdot$, is also not very efficient at oxidizing many organic functional groups. Transition-metal catalysts greatly facilitate the decomposition of persulfate. They allow reactions at lower temperatures as well as produce higher oxidation state metal ions that are capable of performing unique oxidations themselves.

The persulfate/silver ion combination has been most widely used, and in particular, Anderson and Kochi have investigated the mechanism of carboxylic acid decarboxylation by this reagent pair.[2] Their work identified many of the mechanistic features of the decarboxylation of carboxylic acids with the persulfate/silver system; however, they consistently used a vast excess of carboxylic acid in the kinetic experiments. Thus the synthetic potential was not demonstrated. Other workers have used this same reagent pair to produce organic radicals for other purposes.[3] In this note we describe our results, which show that silver(II)-catalyzed decarboxylation is a synthetically useful reaction for producing alkanes, alkenes, or alcohols. Our choice of experimental conditions also gives either exclusively one product or a much simpler product mixture than observed previously.[2] Other decarboxylation methods such as *tert*-butyl perester decomposition,[4] copper/quinoline,[5] or lead tetraacetate[6] all have drawbacks such as the high temperature required or myriad of products produced. While our present method is not without flaw (vide infra) it is simple, fast (20-min reaction time), and proceeds predictably at moderate temperature (76 °C). The yields are modest, but still compare favorably with other known methods of decarboxylation.

Results and Discussion

Our silver(II) decarboxylations can be broken down into two types: (1) decarboxylation in a water/acetonitrile solvent combination which led to alkanes by hydrogen abstraction and (2) decarboxylation in the presence of a copper(II) cocatalyst which led to products from the corresponding carbonium ion. The hydrogen abstraction results are presented in Table I and were the result of the slow addition of 2 mol of sodium persulfate to 1 mol of the carboxylic acid and 2 mol % silver nitrate in refluxing 50% aqueous acetonitrile. Total reaction time required was 20 min. An excess of persulfate was found to be necessary to drive the reaction to even 50% completion. The excess persulfate is presumably consumed by oxidation of water.[1] Other water-miscible solvents capable of donating a hydrogen atom (THF, glyme, dioxane) were found to be unsuitable for this reaction as well as several two-phased systems. Table I also includes three entries that employed a stoichiometric amount of silver nitrate; however, this resulted in no substantial improvement over the catalytic silver reaction. By varying the percent of silver catalyst, we demonstrated that the catalyst could be satisfactorily reduced to a 2 mol % level.

The previously proposed mechanism (Scheme I) was

Scheme I

$$Ag(I) + S_2O_8^{2-} \rightarrow Ag(II) + SO_4^{-}\cdot + SO_4^{2-} \quad (1)$$

$$Ag(I) + SO_4^{-}\cdot \rightarrow Ag(II) + SO_4^{2-} \quad (2)$$

$$Ag(II) + RCO_2H \rightarrow Ag(I) + RCO_2\cdot + H^+ \quad (3)$$

$$RCO_2\cdot \rightarrow R\cdot + CO_2 \quad (4)$$

$$R\cdot + H\text{-solv} \rightarrow RH + \cdot solv \quad (5)$$

found to be consistent with all of our present results.[2] The reactivity of various carboxylic acids, as shown by the extent of conversion, roughly followed the expected order of radical stability (3° > 2° > 1°), although the difference in reactivity is small. Unreacted starting material exclusively constituted the acidic material recovered from the

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