°C (444 mmHg)]; IR (neat) 2150, 1420, 1220, 1160, 1130 cm^{-1}; MS, m/z 175 (M^+). Phenyl azide,[14] *p*-toluenesulfonyl azide,[15] and benzoyl azide,[16] were prepared by the methods reported in the literature. 2-Nitroso-2-methylpropane[17] and nitrosobenzene[18] were also synthesized according to literature methods.

ESR Measurements. A solution of 20 mg of azide and 5 mg of 2-nitroso-2-methylpropane (or nitrosobenzene), in 2.0 mL of benzene in an ESR tube, was degassed and then placed in a JEOL JES-PE-3X ESR spectrometer. Strong ESR signals were observed at room temperature.

Identification of Gaseous Products by GC-Mass Spectrometry. To a degassed solution of 18 mg of 2-nitroso-2-methylpropane in 2.0 mL of benzene was added 18 mg of trifluoromethanesulfonyl azide by a microsyringe, and the solution was allowed to stand for 3 h at room temperature. The gasous product evolved was collected by a microsyringe and analyzed by GC-mass spectrometry using a JEOL JMS-DX 300 mass spectrometer. Two major peaks were observed by GLC (1-m column packed with silicone OV-1 on Chromosorb W); one product with shorter retention time peak (2 min) and m/z 44 (M^+) was determined to be nitrous oxide and the other product with longer retention time peak (3 min) and m/z 64 (M^+) was determined to be sulfur dioxide.

Registry No. 1, 2406-25-9; 2, 27695-72-3; 7, 3229-61-6; 8, 52168-44-2; 9, 35822-90-3; 10, 712-51-6; 11, 42467-30-1; 12, 3229-38-7; 16, 94042-44-1; $CF_3SO_2N_3$, 3855-45-6; PhN_3, 622-37-7; $TosN_3$, 941-55-9; $PhCON_3$, 582-61-6; *t*-BuNO, 917-95-3; PhNO, 586-96-9.

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Mechanistic Studies in the Deoxygenation of Pyridine *N*-Oxide: A New 1,2 Elimination

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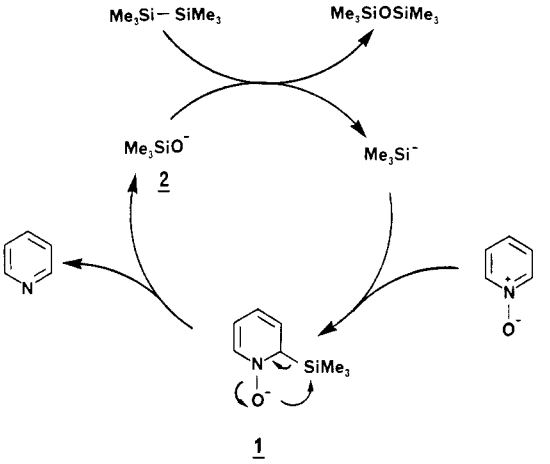
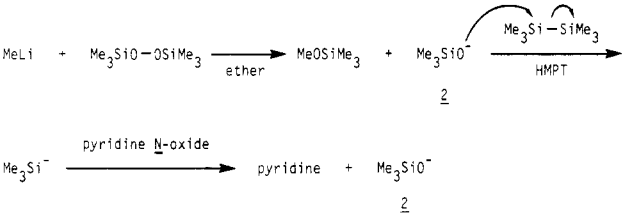
Hexamethyldisilane, an isologue of hydrogen, possesses unique capabilities as a reagent for functional group transformations. It has been used extensively not only to prepare the trimethylsilyl anion[1] but also as a reducing agent[2] and as a source of halotrimethylsilanes.[3] Very recently, hexamethyldisilane was employed as a "counterattacking" reagent in a disproportionation reaction.[4]

We are interested in the mechanism of the reduction of pyridine *N*-oxides to pyridines with hexamethyldisilane. Although hexamethyldisilane does not react with pyridine *N*-oxide under pyrolytic conditions,[5] a successful conversion of the latter compound to pyridine in the presence of a catalytic amount of tetra-*n*-butylammonium fluoride (TBAF) in tetrahydrofuran (THF) has been reported by Vorbrüggen and Krolikiewicz.[6] We have also achieved this reduction, under different conditions ((trimethylsilyl)-lithium in hexamethylphosphoric triamide (HMPT)). Our data suggest a mechanism for the reaction in HMPT that is different from that proposed by the above authors for their reaction in THF. Our mechanism involves 1,2 elimination in a substrate containing an α-(trimethylsilyl) *N*-oxide moiety. Our findings are as follows.

Scheme I



Scheme II



Addition of pyridine *N*-oxide (1.0 equiv) to hexamethyldisilane (1.1 equiv) plus a catalytic amount (0.05 equiv) of (trimethylsilyl)lithium[1b] in HMPT at 0 °C, followed by warming to room temperature and stirring for 24 h gave a dark purple solution. After aqueous workup and purification, pyridine was obtained in 82% yield along with hexamethyldisiloxane. In a second experiment, pyridine *N*-oxide was added to excess (trimethylsilyl)-lithium in HMPT at 0 °C and the mixture was stirred at room temperature for 8 h. Pyridine was isolated in 86% yield. These results provide two pieces of mechanistic information: (1) The first reaction can only occur through a catalytic cycle. (2) The second reaction apparently involves spontaneous decomposition of α-trimethylsilyl *N*-oxide 1, formed by addition of trimethylsilyl anion (Me_3Si^-) to pyridine *N*-oxide, to give pyridine and trimethylsiloxide ion (2). This can be inferred because no electrophilic silylating reagent was left in the reaction mixture when pyridine *N*-oxide was added. A mechanism that accounts for these findings is shown in Scheme I.

Completion of the cycle in Scheme I requires regeneration of trimethylsilyl anion from hexamethyldisilane and trimethylsiloxide ion (2). The feasibility of this step was proven by the following experiment. Reaction of MeLi (1.2 equiv) with bis(trimethylsilyl) peroxide[7] (1.2 equiv) in ether

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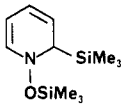
at room temperature for 1 h gave methyl trimethylsilyl ether and the desired lithium trimethylsiloxide.[8] Addition of hexamethyldisilane (1.2 equiv) in HMPT and stirring for another 1 h, followed by injection of pyridine *N*-oxide (1.0 equiv) in HMPT, afforded pyridine in 89% yield after 8 h (Scheme II). Since hexamethyldisilane does not react with pyridine *N*-oxide alone,[5] generation of Me_3Si^- from trimethylsiloxide (2) and hexamethyldisilane is the only pathway that can account for the formation of pyridine under these conditions.[9] This experiment also reveals a route to (trimethylsilyl)lithium.

Our procedure differs from that reported by Vorbrüggen et al. in the choice of base used to initiate the reaction (MeLi vs. TBAF) and in the choice of solvent (HMPT vs. THF). The mechanisms proposed by the two groups have in common the 1,2 addition of Me_3Si^- to pyridine *N*–oxide to give the key intermediate 1. However, the two mechanisms differ in the way that pyridine is generated from 1. Our experiments indicate that once the *N*-oxide 1 is formed in HMPT, it can directly provide pyridine without reacting with additional reagents. The oxide (O^-) on the epimerizable nitrogen center in 1 can achieve a *cis* relationship with the silicon atom at the α position. Decomposition of 1 by a new 1,2 elimination, presumed to be *syn* because of its similarity to the Peterson olefination,[10] then provides the imine moiety of pyridine. This reaction is also analogous to a reaction reported by Krüger et al.,[11] involving 1,2 elimination of an α-(bis(trimethylsilyl)-amino)alkoxide to form *N*-(trimethylsilyl)diphenylcarbimide.

The mechanism that has been suggested[6] for the reaction between pyridine *N*-oxide and hexamethyldisilane in the presence of TBAF involves silylation of 1 with fluorotrimethylsilane to give a disilylated intermediate (3) and

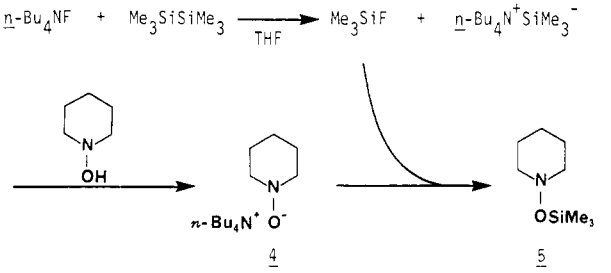


3

fluoride ion. In the procedure reported for this reaction, the amounts of hexamethyldisilane and TBAF initially present are 1.2 and 0.05 equiv, respectively. As fluorotrimethylsilane comes from the reaction of these two reagents, it can only exist in the amount of 0.05 equiv at any instant. We question whether, during the formation of 3, 1 selectively reacts with this small amount of fluorotrimethylsilane instead of reacting with excess hexamethyldisilane.[12] Note also that the intramolecular 1,2 elimination of 1 evidenced by our experiments offers an entropically more favorable route to pyridine.

Although fluoride ion catalyzed reactions are well-known,[13] the role of fluorotrimethylsilane in some of these reactions is still uncertain.[14] We have employed *N*-hydroxypiperidine as a model with the hope of providing some information on the role of fluorotrimethylsilane in the fluoride ion catalyzed deoxygenation of pyridine *N*-oxide (Scheme III). Excess TBAF was dried and treated with hexamethyldisilane (1.3 equiv) in THF (in order to generate fluorotrimethylsilane and trimethylsilyl anion[6,15]). *N*-Hydroxypiperidine (1.0 equiv) was injected (presumably generating the corresponding *N*-oxide 4, paired with the same counterion (n-Bu_4N^+) as 1 in Vorbrüggen's procedure). Only 1.4% of trimethylsilyl ether 5 was detected after 3 h![16] This result casts some doubt on the efficiency of silylation of 1 with fluorotrimethylsilane. This silylation is a step in the mechanism proposed by Vorbrüggen for the high yield formation of pyridine in a short period of time.

Scheme III



4 5

In summary, our findings suggest the involvement of a new 1,2 elimination of α-trimethylsilyl *N*-oxide 1 in the deoxygenation of pyridine *N*-oxide to pyridine with hexamethyldisilane and a catalytic amount of MeLi in HMPT. However, we cannot rule out the formation of pyridine by decomposition of 3, which may be generated from 1 and hexamethyldisilane. In addition, the observation that trimethylsilyl anion can be generated from trimethylsiloxide ion and hexamethyldisilane in HMPT suggests that further applications of hexamethyldisilane as a counter-attacking reagent should be investigated.

Experimental Section

All reactions were carried out under an atmosphere of argon or nitrogen. All chemicals were available from Aldrich, unless otherwise noted. Solvents were dried by using standard procedures and distilled immediately before use. GC analyses were performed on a Hewlett-Packard 5794A instrument equipped with a 12.5-m cross-linked methylsilicone gum capillary column (0.2-mm i.d.). Analytical TLC precoated plates were purchased from Analtech, Inc. (Silica Gel GHLF). Dry column chromatography was performed on 63–200 μm silica gel (*E.* Merck #7734).

Deoxygenation of Pyridine *N*-Oxide. (a) To a solution of hexamethyldisilane (0.42 g, 2.9 mmol) in HMPT (2.0 mL) was added methyllithium (1.4 M in ether, 2.0 mL, 2.8 mmol) at 0 °C. After the solution was stirred for 20 min, pyridine *N*-oxide (0.190 g, 2.00 mmol) in HMPT (0.95 mL) was added and the color changed to purple brown. The mixture was stirred at room temperature for 8 h and was quenched with water. The solution was extracted three times with fresh ether, and the combined ether layers were washed once with a saturated ammonium chloride solution and three times with water. After the ether solution was dried (K_2CO_3) and degassed, the solvent was carefully removed to give a yellow oil with the strong odor of pyridine. Dry column chromatography on silica gel using 1% ethylamine in methylene chloride as eluent provided pyridine (0.136 g, 86%), identical by

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(16) Under the same conditions, injection of chlorotrimethylsilane provided 5 in 39% yield. This indicates that *N*-hydroxypiperidine is an appropriate model for the silylation of 1.

NMR, IR, GC, and TLC to an authentic sample.

(b) By a similar procedure, hexamethyldisilane (1.72 g, 11.8 mmol), methyllithium (1.4 M in ether, 0.40 mL, 0.56 mmol), and pyridine *N*-oxide (1.02 g, 10.7 mmol) were reacted in HMPT (15.0 mL). After being stirred for 24 h, the mixture was worked up and chromatographed as described above. Short-path distillation of the major fraction gave pyridine (0.694 g, 82%).

(c) Methyllithium (1.4 M in ether, 1.8 mL, 2.5 mmol) was added slowly to a solution of bis(trimethylsilyl) peroxide[7] (0.453 g, 2.54 mmol) in ether (1.0 mL) at 0 °C. After the mixture was stirred for 1 h, hexamethyldisilane (0.370 g, 2.53 mmol) and HMPT (2.0 mL) were added at 0 °C. The solution was stirred for an additional hour, and pyridine *N*-oxide (0.201 g, 2.11 mmol) in HMPT (1.0 mL) was injected. The solution was stirred at room temperature for 8 h and was quenched as described above. It was worked up and chromatographed as in a. Pyridine (0.148 g, 89%) was obtained.

***N*-Hydroxypiperidine Trimethylsilyl Ether (5).** Tetra-*n*-butylammonium fluoride was dried[15] and weighed (0.235 g). THF (5.0 mL) and hexamethyldisilane (0.132 g, 0.899 mmol) were added at −78 °C. The dry ice bath was removed, and the brown solution was stirred for 20 min after it had warmed to room temperature. *N*-Hydroxypiperidine (Alfa, 67.9 mg, 0.671 mmol) in THF (0.750 mL) was added at 0 °C to the above solution. The ice bath was removed, and the solution was stirred at room temperature for 3 h. The reaction mixture gave two spots on TLC (ethyl acetate as eluent): R_f 0.76 (faint, compound **5**); R_f 0.13 (dark, *N*-hydroxypiperidine). It was dissolved in ether and washed twice with a saturated solution of sodium bicarbonate, once with water, and once with brine. The ether solution was dried ($MgSO_4$), and the solvent was removed. GC analysis indicated that **5** was obtained in 1.4% yield and that 94% of the starting material *N*-hydroxypiperidine was recovered. Commercially available *N*-hydroxypiperidine and pure compound **5**,[17] prepared by reaction of *N*-hydroxypiperidine with chlorotrimethylsilane in triethylamine, were used as references.

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Registry No. **5**, 94070-51-6; MeLi, 917-54-4; pyridine *N*-oxide, 694-59-7; pyridine, 110-86-1; hexamethyldisilane, 1450-14-2; tetrabutylammonium fluoride, 429-41-4; *N*-hydroxypiperidine, 4801-58-5.

(17) Although compound **5** can be purified by flash column chromatography on silica gel, it hydrolyzes readily when left on silica gel for longer periods of time.

Anomeric Effect in Hydrogen Abstraction Reactions of Conformationally Fixed 2-Alkoxytetrahydropyrans

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One aspect of the anomeric effect[2] is the preference for abstraction of axial hydrogens over equatorial hydrogens in oxygen heterocycles. In our previous work,[3,4] we found that the cis isomers of 2-methoxy-4-methyltetrahydropyran (*cis*-**1**) and 2-methoxy-6-methyltetrahydropyran (*cis*-**2**) were more reactive than the trans isomers by factors of 8 and 10, respectively, toward photochemical hydrogen atom abstraction. This preference can be explained[3] in terms of the anomeric effect in that the more easily cleaved C–H bond is anti-periplanar to a nonbonding electron pair on the ring oxygen. The exocyclic methoxy group adds similarly to the reactivity of both isomers.

Table I. Relative Rates of Hydrogen Atom Abstraction

compd	K_{cis}/K_{trans}	uncertainty range
1[a]	8.0	6.6–9.4
2[b]	10.0	nd[c]
3	16.0	13–19
4	10.6	9.0–12.7
5	49	28–∞
6	36	24–70

[a] Reference 3. [b] Reference 4. [c] Not determined.

Beckwith and Easton[5] have found a similar stereoelectronic effect in reactions of 1,3-dioxanes, and Malatesta and Ingold[6] have studied a variety of cyclic, bicyclic, and tricyclic ethers. The latter authors could explain their rates in terms of similar overlap, and in rigid systems where such overlap was not possible, hydrogen abstraction was not observed, even in the presence of three neighboring oxygens. Descotes and co-workers found similar preferences in dimethoxytetrahydropyrans[7] and carbohydrate derivatives.[8] The structure[9] and theoretical aspects[10] of the resulting radicals have also been studied. Griller et al.[11] have found the same effect in amines.

Although the relative reactivities of cis and trans isomers of **1** and **2** demonstrate the preference for axial hydrogen abstraction, they may not give a quantitative measure of the effect because a single methyl group may not be enough to keep the compounds in a single conformation. Thus, the cis isomers might spend some of their time in the less reactive diaxial conformation, while the trans isomers might derive some of their reactivity from the minor alternative chair conformation. This paper describes our results on conformationally fixed 2-alkoxytetrahydropyrans.

Cis and trans isomers of 2-methoxy-*cis*-4,6-dimethyltetrahydropyran (**3**), 6-*tert*-butyl-2-methoxytetrahydropyran (**5**), and 2-isobutoxy-6-*tert*-butyltetrahydropyran (**6**) were available from a previous study.[12] 2-Ethoxy-*cis*-4,6-dimethyltetrahydropan (**4**) was prepared by alkoxy exchange from **3**. These compounds should be conformationally fixed[13] and provide a quantitative measure of

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