of *m*-chloroperbenzoic acid (83.0%, 78.8 mg, 0.379 mmol) in 3 mL of $CHCl_3$ was pipetted into a stirred solution of 4-methoxy-4′-nitro-2,2′-bipyridyl (**24**, 21.9 mg, 0.0947 mmol) in 3 mL of $CHCl_3$ at 0 °C. The reaction was allowed to stir at room temperature for 45 h. The solution was placed on a 5.0-g basic alumina column and eluted with 250 mL of $CHCl_3$, 100 mL of 19:1 $CHCl_3$:MeOH, and 50 mL of 9:1 $CHCl_3$:MeOH. The combined filtrates were evaporated, providing 24.6 mg of solid. This was placed on a 500-μm silica gel prep plate with $CHCl_3$ and developed with 9:1 $CHCl_3$:MeOH. Three UV-active bands were seen and were removed with 19:1 $CHCl_3$:MeOH. The top band yielded 1.6 mg (0.0069 mmol) of 4-methoxy-4′-nitro-2,2′-bipyridyl (**24**), mp 135 °C. The middle band gave 16.0 mg (0.0647 mmol) of 4-methoxy-4′-nitro-2,2′-bipyridyl *N*-oxide (**22**, 68.3% conversion of **24** or 73.3% based on recovered **24**), mp 177–178 °C. The bottom band gave 0.1 mg (0.0004 mmol) of 4-methoxy-4′-nitro-2,2′-bipyridyl *N,N′*-dioxide (**19**, 0.4% conversion of **24** or 0.4% based on recovered **24**), mp 225–230 °C (mp of the dioxide prepared from **3** was 236 °C, mixed mp 225–230 °C; IR and TLC properties also identical).

4-Methoxy-4′-nitro-2,2′-bipyridyl (24). Phosphorus trichloride (0.200 mL, 2.29 mmol) was syringed into a stirred solution of 4-methoxy-4′-nitro-2,2′-bipyridyl *N*-oxide (**22**, 100 mg, 0.405 mmol) in 7 mL of $CHCl_3$. Within a few seconds the yellow color of the solution had disappeared. The reaction was refluxed for 4.25 h and allowed to stand at room temperature overnight. The reaction was worked up with use of the procedure described in the preparation of **10** providing 92.5 mg of 4-methoxy-4′-nitro-2,2′-bipyridyl (**24**): mp 136 °C (98.9% yield); ^1H NMR ($CDCl_3$) δ 3.97 (s, OCH_3), 6.94 (dd, H_5), 8.03 (dd, $H_{5'}$), 8.04 (d, H_3), 8.57 (d, H_6), 8.95 (dd, $H_{6'}$), 9.17 (dd, $H_{3'}$) [$J_{3,5}$ = 2.5, $J_{5,6}$ = 5.7, $J_{3',5'}$ = 2.2, $J_{3',6'}$ = 0.6, $J_{5',6'}$ = 5.3 Hz]; UV (95% EtOH) λ_{max} (ε) 217 nm (36 600), 246 (sh, 15 500), 313 (3700); IR (KBr) 6.53, 7.38 μm. Anal. (sample recrystallized from CH_2Cl_2:hexanes, mp 138 °C). Calcd for $C_{11}H_9N_3O_3$: C, 57.14; H, 3.92; N, 18.18. Found: C, 56.91; H, 3.97; N, 17.94.

4-Methoxy-4′-nitro-2,2′-bipyridyl (24). A solution of *m*-chloroperbenzoic acid (83.0%, 37.9 mg, 0.182 mmol) in 3 mL of $CHCl_3$ was added over 10 min to a stirred solution of 4-methoxy-4′-nitro-2,2′-bipyridyl *N*-oxide (**22**, 30.0 mg, 0.121 mmol) in 3 mL of $CHCl_3$ at 0 °C. The reaction was allowed to stir at room temperature for 38 hours, partially concentrated at room temperature, placed on a 2.0-g basic alumina column, and eluted with 24 mL of $CHCl_3$. This was evaporated to provide 25.8 mg of solid, which was placed on a 500-μm silica gel prep plate with $CHCl_3$ and developed with ethyl acetate. Only two UV-active bands were present. The bottom band was removed with 1:19 MeOH:$CHCl_3$ and provided upon evaporation 18.7 mg of 4-methoxy-4′-nitro-2,2′-bipyridyl *N*-oxide (**22**). Further elution of the original alumina column with 75 mL of $CHCl_3$ gave 3.0 mg more of the monooxide, and thus 21.7 mg (0.0878 mmol) was obtained in all. The top band of the prep plate was removed with $CHCl_3$ and gave 4.2 mg (0.018 mmol) of 4-methoxy-4′-nitro-2,2′-bipyridyl (**24**), mp 136 °C (15% conversion of **22** or 54% based on recovered **22**).

4-Methoxy-4′-nitro-2,2′-bipyridyl (24). A solution of 4-methoxy-4′-nitro-2,2′-bipyridyl *N,N′*-dioxide (**19**, 4.1 mg, 0.016 mmol) and PCl_3 (0.044 mL, 0.50 mmol) in 1.7 mL of $CHCl_3$ was refluxed for 21 h. The reaction was thrown on 7 g of ice and worked up by using the procedure described in the preparation of **10**, providing 3.4 mg of 4-methoxy-4′-nitro-2,2′-bipyridyl (**24**, 94%), mp 112–115 °C (mp of **24** prepared from **22** was 136 °C, mixed mp 129–135 °C; IR and TLC properties of the two samples were identical).

Photooxygenations. Photooxygenations were carried out by using a setup similar to that described on page 179 of ref 3b. A 650-W DWY lamp was used at 90 V. The reaction solution was maintained at approximately room temperature via a continuous flow of tap water in the condenser on the outside of the reaction vessel. Dry oxygen (passed through anhydrous $CaCl_2$) was introduced into the reaction solution via a syringe needle at a flow rate of 25–35 mL/min. Concentration of sensitizer used was between 10^{-3} and 10^{-4} M. Solvent volume was 7–8 mL. Solvent that evaporated during long runs was replaced. Reagent grade MeOH and dry (distilled from CaH_2) CH_2Cl_2 were used as solvents; 50–100 mg of substrate was used.

1,1′-Bicyclohexenyl. 1,1′-Bicyclohexenyl[27] was found to be more conveniently prepared by using the following procedure.[28]

1-Chlorocyclohexene[29] (800 mg, 6.86 mmol) and lithium (150 mg, 21.6 mmol) were stirred together in 25 mL of dry diethyl ether under nitrogen for 18 h at room temperature and then refluxed for 2.5 h. Stirring was stopped, particulate matter allowed to settle, and the ether solution transferred via canula into another flask maintained under a nitrogen atmosphere. The stirred solution was cooled to −65 °C, cuprous iodide (1.31 g, 6.88 mmol) added, and the reaction allowed to warm to 5 °C over 40 min (after 5 min a black solid suspension began to form). An ice bath was placed around the reaction flask, and dry oxygen was then rapidly bubbled into the reaction for 15 min. The reaction contents were then washed with 10% aqueous ammonium hydroxide and the ether layer dried (K_2CO_3) and evaporated to 390 mg. This was placed on an 8-g silica gel column, eluted with 60 mL of hexane, evaporated to 190 mg, and then distilled bulb to bulb (1.0 mmHg, oven temperature 80–110 °C) to provide 167 mg (30%) of 1,1′-bicyclohexenyl.

Acknowledgment. This work was supported by the National Institutes of Health Grant GM 04229 (principal investigator R.B.W.). D.W. thanks Professor Y. Kishi for helpful suggestions concerning the writing of this paper.

(27) Greidinger, D. S.; Ginsburg, D. *J. Org. Chem.* **1957**, *22*, 1406. Isabelle, M. E.; Lake, D. H.; Wightman, R. H. *Can J. Chem.* **1977**, *55*, 3268.

(28) For examples of the oxidative coupling of alkenylcopper(I) reagents, see: Banks, R. B.; Walborsky, H. M. *J. Am. Chem. Soc.* **1976**, *98*, 3732. Posner, G. H. *Org. React.* **1975**, *22*, 253.

(29) Preparation of 1-chlorocyclohexene and cyclohex-1-enyllithium described: Braude, E. A.; Coles, J. A. *J. Chem. Soc.* **1950**, 2014.

Preparation of Primary Amines and 2-Azetidinones via *N*-Trimethylsilyl Imines

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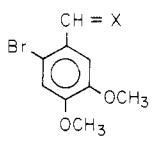
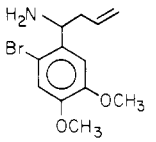
Nonenolizable aldehydes react with lithium bis(trimethylsilyl)amide at ambient temperatures to afford solutions of *N*-trimethylsilyl aldimines. Treatment of these solutions with Grignard reagents or alkyllithiums followed by an aqueous workup gives primary amines in moderate to excellent yields. Treatment of *N*-trimethylsilyl aldimines with ester enolates provides an expedient route to 1-unsubstituted 2-azetidinones.

During the course of executing a total synthesis of the Lythraceae alkaloid vertaline, a need arose to convert benzaldehyde **1** to homoallylic amine **3**. Several conventional procedures for accomplishing this task were ex-

0022-3263/83/1948-0289$01.50/0



1 X = O
2 X = NSiMe$_3$



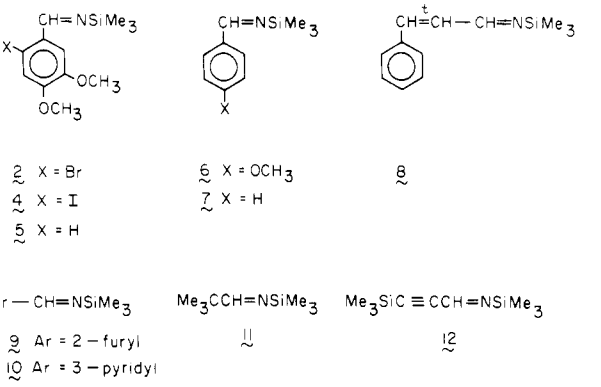
3

plored, but problems were always encountered.[1] We eventually found that sequential treatment of **1** with lithium bis(trimethylsilyl)amide and allylmagnesium bromide gave the desired amine **3** in a 97% yield, presumably via the intermediacy of *N*-trimethylsilyl imine **2**.[2] To our knowledge, this was the first example of a reaction between an *N*-trimethylsilyl imine and an organometallic compound. Since this appeared to be a potentially useful method for preparing certain primary amines, we examined the scope and limitations of this procedure. The details of this study are presented herein.[3,4]

All of the *N*-trimethylsilyl imines used in this study were prepared by a modification of a procedure developed by Wannagat and Rochow.[5,6] Thus, treatment of aldehydes with a slight excess of lithium bis(trimethylsilyl)amide in tetrahydrofuran afforded solutions of *N*-trimethylsilyl imines, presumably in the presence of lithium trimethylsiloxide. The *N*-trimethylsilyl imines prepared in this manner are shown in Chart I. Most of the *N*-trimethylsilyl imines were not purified or characterized. Thus the intermediacy of imines **2**, **4**–**6**, **8**, and **11** was merely presumed on the basis of the products obtained upon treatment of the tetrahydrofuran solutions with organometallic reagents. On several occasions, however, pure *N*-trimethylsilyl imines were isolated by direct distillation from the reaction mixture. For example, imines **7**, **9**, and **10** were isolated in yields of 89%, 30%, and 14%, respectively.[7] The major limitation of this method is that only nonenolizable *N*-trimethylsilyl imines can be prepared efficiently (vide infra).

The *N*-trimethylsilyl imines shown in Chart I were allowed to react with a variety of Grignard reagents and alkyllithiums (Table I) by either of two procedures. Purified *N*-trimethylsilyl imines were treated with organometallics (method A), or tetrahydrofuran solutions of the imines, prepared as described above, were treated directly

Chart I



2 X = Br
4 X = I
5 X = H

6 X = OCH$_3$
7 X = H

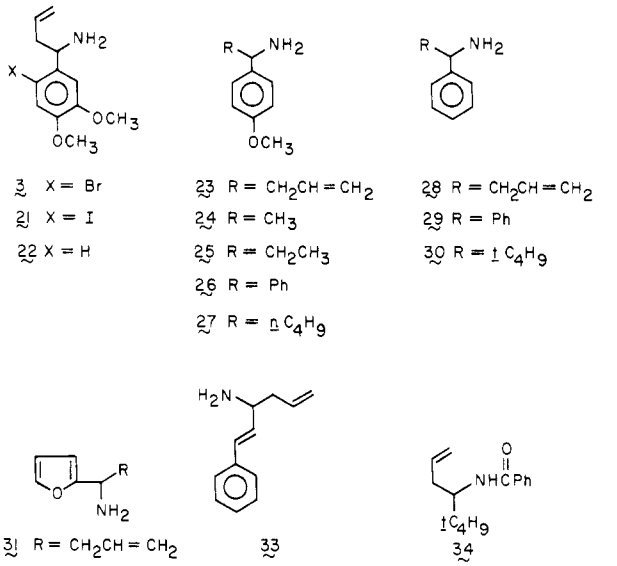
8

Ar—CH=NSiMe$_3$
9 Ar = 2-furyl
10 Ar = 3-pyridyl

Me$_3$CCH=NSiMe$_3$
11

Me$_3$SiC≡CCH=NSiMe$_3$
12

Chart II



3 X = Br
21 X = I
22 X = H

23 R = CH$_2$CH=CH$_2$
24 R = CH$_3$
25 R = CH$_2$CH$_3$
26 R = Ph
27 R = *n*-C$_4$H$_9$

28 R = CH$_2$CH=CH$_2$
29 R = Ph
30 R = *t*-C$_4$H$_9$

31 R = CH$_2$CH=CH$_2$
32 R = Ph

33

34

with organometallic reagents (method B). The results of these studies are shown in Table I and Chart II. From these results, it is clear that *N*-trimethylsilyl imines react with a variety of organometallic compounds to afford moderate to good yields of primary amines after an aqueous workup. The conditions which must be used depend on the structure of the organometallic reagent. For example, allylmagnesium bromide (**13**) affords high yields of amines under very mild conditions (entries 1–8) while other Grignard reagents (**14**–**18**) require longer reaction times (entries 9–14). In one case, an alkyllithium reagent also required less vigorous conditions than the analogous Grignard reagent (see entries 13 and 16).

The stoichiometry of the reaction generally required the use of equimolar amounts of the *N*-trimethylsilyl imine and organometallic reagents. In some cases, however, slightly higher yields were obtained when 2 equiv of organometallic reagent was used. In this regard, it is noteworthy that *phenyltrimethylsilane was detected as a product in the reaction of phenylmagnesium bromide with N-(trimethylsilyl)benzaldimine* (entry 10).[8] Thus *attack of the organometallic reagent on silicon may sometimes compete with addition to the azomethine group.*

During the course of these studies, several other noteworthy experiments were performed. As noted earlier, the

(1) In one abortive effort we found that treatment of 3,4-dimethoxybenzaldoxime or its *O*-methyl ether with allylmagnesium bromide gave high yields of *N*-(hepta-1,6-dien-4-yl)-3,4-dimethoxyaniline. Although the analogous derivatives of **1** were not tried, the following report suggests that rearrangement would be a persistent problem with this approach: Lyle, R. E.; Troscianiec, H. J. *J. Org. Chem.* **1955**, *20*, 1757. For other problems see ref 2.

(2) For a description of this reaction and its use in a total synthesis of *dl*-vertaline see: Hart, D. J.; Kanai, K. *J. Org. Chem.* **1982**, *47*, 1555.

(3) This work is taken in part from the M.S. Thesis of D.G.T., The Ohio State University, 1982.

(4) For a related approach to the synthesis of primary amines see: Davis, F. A.; Mancinelli, P. A. *J. Org. Chem.* **1977**, *42*, 398.

(5) Krüger, C.; Rochow, E. G.; Wannagat, U. *Chem. Ber.* **1963**, *96*, 2132.

(6) Several other methods for preparing *N*-trimethylsilyl imines have been reported: Sundermeyer, W.; Lidy, W. *Chem. Ber.* **1976**, *109*, 1491. Chan, L.-H.; Rochow, E. G. *J. Organomet. Chem.* **1967**, *9*, 231. The Sundermeyer method, which involves the reaction between *N*-(trimethylsilyl)phosphinimines and carbonyl compounds, appears to be restricted to electron-deficient carbonyl compounds with the phosphinimines used to date. For example, treatment of aldehyde **1** with *N*-(trimethylsilyl)triphenylphosphinimine afforded no reaction. The Rochow method involves treatment of nitriles with alkyllithium reagents followed by quenching with chlorotrimethylsilane. This provides a route to *N*-trimethylsilyl imines of enolizable carbonyl compounds. These authors note that enolizable *N*-trimethylsilyl imines exist in tautomeric equilibrium with sizable amounts of enamines.

(7) The yields of **9** and **10** were not maximized. It is conceivable that the use of distillation pressures lower than those described in the Experimental Section would improve the yields.

(8) The phenyltrimethylsilane exhibited ^{1}H NMR and mass spectra as well as gas chromatographic behavior identical with those of an authentic sample purchased from Petrarch Systems, Inc.

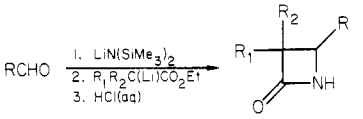
Table I. Reactions of *N*-Trimethylsilyl Imines with Organometallic Reagents

$$RCH{=}NSiMe_3 \xrightarrow[2.\ H_2O]{1.\ R'MgBr\ or\ R'Li} RCH(NH_2)R'$$

entry	*N*-trimethylsilyl imine	organometallic	product	time (method)[e]	yield,[i] %
1	2	$CH_2{=}CHCH_2MgBr$ (13)[a]	3	30 min (B)[f]	97
2	4	13[a]	21[c]	30 min (B)[f]	77
3	5	13[a]	22	60 min (B)[f]	97
4	6	13[a]	23	2 min (B)[f]	76
5	7	13[a]	28	30 min (A)[f]	59
6	8	13[a]	33	10 min (B)[f]	87
7	9	13[a]	31	10 min (B)[f]	80
8	11	13[a]	34[d]	24 h (B)[g]	23
9	6	PhMgBr (14)[b]	26	44 h (B)[g]	56
10	7	14[a]	29	40 h (A)[g]	36
11	9	14[b]	32	16 h (B)[g]	57
12	6	EtMgBr (15)[b]	25	24 h (B)[g]	53
13	7	*t*-BuMgBr (16)[b]	30	18 h (A)[g]	66
14	6	MeMgBr (17)[b]	24	24 h (B)[g]	75
15	6	*n*-BuLi (18)[a]	27	5 h (B)[f]	53
16	7	*t*-BuLi (19)[a]	30	2 h (A)[h]	87
17	6	MeLi (20)[a]	24	7 h (B)[f]	30

[a] One equivalent of organometallic was used. [b] Two equivalents of organometallic were used. [c] An 8% yield of 22 was also isolated. [d] The crude amine was converted to the benzamide for the purpose of isolation. [e] Method A: pure *N*-trimethylsilyl imine was treated with the appropriate organometallic reagent. Method B: the *N*-trimethylsilyl imine was generated in situ from lithium bis(trimethylsilyl)amide and the appropriate aldehyde followed by addition of the organometallic reagent to the resulting mixture. [f] The reaction was run in tetrahydrofuran at room temperature. [g] The reaction was run in tetrahydrofuran under reflux. [h] The reaction was run in tetrahydrofuran at −70 to 0 °C. [i] The yields were not optimized.

Table II. Synthesis of β-Lactams via *N*-Trimethylsilyl Imines



entry	*N*-trimethylsilyl imine	ester[a]	product	time, h (method)[b]	yield,[c] %
1	7	37	40	3 (A)	71
2	7	37	40	2 (B)	72
3	7	38	43 + 46 (41:17)[d]	40 (B)	58
4	7	39	44 + 47 (48:5)[e]	2.5 (B)	53
5	8	37	41	4 (B)	69
6	12	37	42	15 (B)	79
7	12	38	45 + 48 (54:20)[f]	18 (B)	74

[a] Equamolar amounts of imine (aldehyde) and ester were used. [b] Method A: pure *N*-trimethylsilyl imine was added to the ester enolate in tetrahydrofuran. Method B: the *N*-trimethylsilyl imine was generated from lithium bis(trimethylsilyl)amide and the appropriate aldehyde in tetrahydrofuran, and the solution was added to the ester enolate; the enolates and imines were mixed at −70 °C, warmed to room temperature, and stirred for the noted time period. [c] Total yield of 2-azetidinones after purification. [d] Stereochemical assignment based on NOE studies. Irradiation of the C(3) methyl group in 43 and 46 gave 2% and 14% enhancement of the H_4 signals, respectively. [e] Stereochemical assignment based on H_3–H_4 coupling constants. [f] Stereochemical assignment based on NOE studies. Irradiation of the C(3) methyl group in 45 and 48 gave 1.5% and 16.5% enhancement of the H_4 signals, respectively.

method of *N*-trimethylsilyl imine preparation used here is limited to nonenolizable carbonyl compounds.[5] In fact, we did find that sequential treatment of *n*-octanal (35)

$$\underset{\mathbf{35}}{n\text{-}C_7H_{15}CHO} \xrightarrow[2.\ CH_2{=}CHCH_2MgBr]{1.\ LiN(SiMe_3)_2} \underset{\mathbf{36}}{n\text{-}C_7H_{15}CH(NH_2)CH_2CH{=}CH_2}$$

with lithium bis(trimethylsilyl)amide and allylmagnesium bromide gave a 10% yield of homoallylic amine **36**. Therefore in this case, addition of the amide to the carbonyl group competes with enolization.[9] Furthermore, if an expedient route to enolizable *N*-trimethylsilyl imines can be developed, this result provides hope that they may be well behaved upon treatment with organometallic compounds.[10]

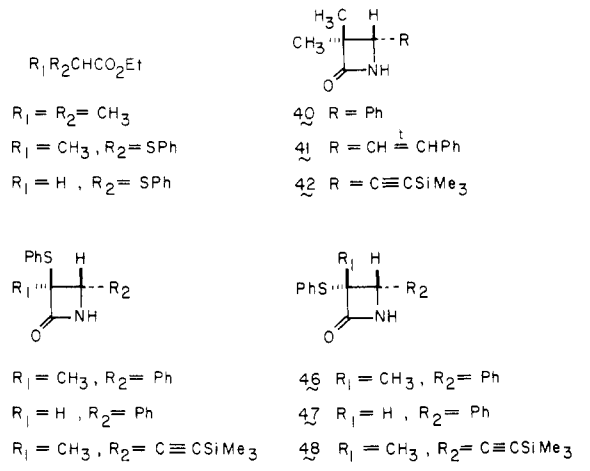
Other nucleophiles will add to the azomethine moiety of *N*-trimethylsilyl imines. For example, sequential treatment of *p*-methoxybenzaldehyde with lithium bis(trimethylsilyl)amide and lithium aluminum hydride in tetrahydrofuran afforded *p*-methoxybenzylamine in an 87% yield.

We also examined the use of *N*-trimethylsilyl imines in the synthesis of 1-unsubstituted 2-azetidinones. Thus *N*-trimethylsilyl imines were treated with ester enolates (Chart III) to afford good yields of the β-lactams docu-

(9) For a recent example of an amide base which appears to undergo selective carbonyl addition to an enolizable aldehyde see: Comins, D. L.; Brown, J. D. *Tetrahedron Lett.* **1981**, *22*, 4213.

(10) Thus far our attempts to prepare enolizable *N*-triethylsilyl imines from triethylsilylamine (Sommer, L. H.; Kerr, G. T.; Whitmore, F. C. *J. Am. Chem. Soc.* **1946**, *70*, 434) and carbonyl compounds has been unsuccessful.

Chart III



mented in Table II and Chart III. Although this approach to β-lactam synthesis has been previously reported,[11,12] *this variant is unique in that the products lack alkyl or aryl substitution at nitrogen.* It is this aspect of the reaction which may render it useful in the synthesis of pharmacologically interesting β-lactams.[13] Entry 7, in particular, demonstrates that this method is amenable to the introduction of potentially useful substitution patterns at C(3) and C(4) of the azetidinone moiety.

In summary, we have found that solutions of *N*-trimethylsilyl imines which might be difficult to isolate can be used directly in reactions with a variety of nucleophiles. The methods presented herein provide rapid access to certain primary amines and N-unsubstituted 2-azetidinones. The utility of this chemistry has been demonstrated during the course of a synthesis of the macrocylic alkaloid vertaline.[2]

Experimental Section

All melting points were taken with a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H nuclear magnetic resonance spectra were recorded on a Varian Associates EM-390 or EM-360 spectrometer and are reported in parts per million from internal tetramethylsilane on the δ scale. Data are reported as follows: chemical shift [muliplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants, integration, interpretation]. Infrared spectra were taken with a Perkin-Elmer 457 instrument. Mass spectra were recorded on an AEI MS9 instrument. Samples on which exact masses were measured exhibited no significant peaks at *m/e* values greater than that of the parent. Elemental analyses were carried out by Micro Analysis, Inc., Wilmington, DE.

All reactions were carried out under a blanket of either nitrogen or argon. Column chromatography was performed over EM Laboratories silica gel (70–230 mesh) or LoBar columns (medium pressure).

Lithium bis(trimethylsilyl)amide was prepared by the following standard procedure. To a solution of 1,1,1,3,3,3-hexamethyldisilazane (1.04 equiv) in tetrahydrofuran (1–2 mL mmol^{-1}) cooled in an ice–water bath was added a hexane solution of *n*-butyllithium (1.0 equiv) via syringe. The cold bath was removed, and the mixture was stirred at room temperature for 15–30 min prior to use.

Procedures for the preparation of selected *N*-trimethylsilyl imines, primary amines, and β-lactams are provided below. The other compounds shown in Tables I and II were prepared by using analogous procedures (see Tables I and II for conditions). Compounds **3**,[2] **21**,[2] **24**,[14] **26**,[15] **28**,[16] **29**,[17] **30**,[18] and **32**[19] have been previously reported. The spectral data (^{1}H NMR, IR, mass spectra) collected on samples of these compounds, prepared as described herein, were consistent with the assigned structures. Data characterizing new compounds not reported previously also appears below.

Preparation of *N*-Trimethylsilyl Imines: *N*-(Trimethylsilyl)benzaldimine[5] (7). To 23.0 mL (0.11 mol) of 1,1,1,3,3,3-hexamethyldisilazane was added 64.5 mL (0.10 mmol) of a 1.55 M hexane solution of *n*-butyllithium over a 5-min period. Solvent was removed in vacuo until a white precipitate appeared. The resulting slurry was cooled in an ice bath, and 10.6 g (0.1 mol) of benzaldehyde was added over a 10-min period. Direct fractional distillation of the resulting solution gave 15.8 g (89%) of imine **7** as a pale yellow liquid: bp 45 °C (0.15 mm); IR (neat) 2960, 2800, 1650, 1250 cm^{-1}; NMR ($CDCl_3$) δ 0.27 (s, 9 H, $SiMe_3$), 7.3 (m, 3 H, Ar H), 7.7 (m, 2 H, Ar H), 8.9 (s, 1 H, CH=N); mass spectrum, *m/e* (relative intensity) 177 (52), 163 (21), 162 (100), 147 (48), 105 (43), 104 (54), 73 (91), 59 (87); exact mass calcd for $C_{10}H_{15}NSi$ *m/e* 177.0973, found *m/e* 177.0979.

***N*-(Trimethylsilyl)furan-2-carboxaldimine (9):** bp 42 °C (0.2 mm); IR (neat) 3120, 2950, 1625, 1575, 1475, 1250 cm^{-1}; NMR ($CDCl_3$) δ 0.27 (s, 9 H, $SiMe_3$), 6.4 (dd, J = 5, 2 Hz, 1 H, H_4), 6.7 (d, J = 5 Hz, 1 H, H_3), 7.5 (br s, 1 H, H_5) 8.66 (s, 1 H, CH=N); mass spectrum, *m/e* (relative intensity) 167 (65), 152 (100); exact mass calcd for $C_8H_{13}NOSi$ *m/e* 167.0766, found *m/e* 167.0770.

***N*-(Trimethylsilyl)pyridine-3-carboxaldimine (10):** bp 90 °C (0.1 mm); IR (neat) 2950, 1659, 1587, 1573, 1250 cm^{-1}; NMR ($CDCl_3$) δ 0.2 (s, 9 H, $SiMe_3$), 7.2 (dd, J = 8, 5 Hz, 1 H, H_5), 8.1 (dt, J = 8, 2 Hz, 1 H, H_4), 8.6 (dd, J = 5, 2 Hz, 1 H, H_6), 8.8 (d, J = 2 Hz, 1 H, H_2), 8.9 (s, 1 H, CH=N); mass spectrum, *m/e* (relative intensity) 178 (17), 146 (100); exact mass calcd for $C_9H_{14}N_2Si$ *m/e* 178.0926, found *m/e* 178.0932.

One-Pot Preparation of Primary Amines from Aldehydes: 4-Amino-4-(3,4-dimethoxyphenyl)-1-butene (22). To a stirred solution of 5 g (30 mmol) of 3,4-dimethoxybenzaldehyde in 10 mL of tetrahydrofuran was added a solution of lithium bis(trimethylsilyl)amide [prepared from 23.2 mL (36 mmol) of a 1.55 M hexane solution of *n*-butyllithium and 8.2 mL (39.0 mmol) of 1,1,1,3,3,3-hexamethyldisilazane in 10 mL of tetrahydrofuran] with cooling in an ice–water bath. To the resulting solution containing *N*-trimethylsilyl imine **5** was added 61 mL (36 mmol) of a 0.59 M solution of ethereal allylmagnesium bromide. The mixture was stirred at room temperature for 30 min, poured into 200 mL of saturated aqueous ammonium chloride, and extracted with three 30-mL portions of dichloromethane. The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residual yellow oil was chromatographed over 200 g of silica gel (eluted with chloroform–methanol–aqueous ammonium hydroxide, 250:10:1) to give a solid which was recrystallized from ether–hexane to afford 5.92 g (95%) of amine **22** as a white solid: mp 56–57 °C; IR (CCl_4) 3390, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.56 (s, 2 H, NH_2), 2.37 (m, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 3.90 (m, 1 H, CHN), 3.91 (s, 3 H, OCH_3), 5.01–5.20 (m, 2 H, $=CH_2$), 5.53–6.00 (m, 1 H, =CH), 6.73–6.93 (m, 3 H, Ar H); mass spectrum, *m/e* (relative intensity) 207 (13), 166 (100); exact mass calcd for $C_{12}H_{17}NO_2$ *m/e* 207.1259, found *m/e* 207.1264. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27. Found: C, 69.23; H, 8.06.

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4-Amino-4-(*p*-methoxyphenyl)-1-butene (23): IR (neat) 3360, 3280 cm^{-1}; NMR ($CDCl_3$) δ 1.55 (s, 2 H, NH_2), 2.3 (m, 2 H, CH_2), 3.7 (s, 3 H, OCH_3), 3.85 (t, J = 6 Hz, 1 H, CHN), 5.1 (m, 2 H, $=CH_2$), 5.6 (m, 1 H, =CH), 6.8 (d, J = 9 Hz, 2 H, Ar H), 7.2 (d, J = 9 Hz, 2 H, Ar H); mass spectrum, m/e (relative intensity) 177 (1), 134 (100), 107 (28).

1-(*p*-Methoxyphenyl)propylamine (25): IR (neat) 3450 cm^{-1}; NMR ($CDCl_3$) δ 0.7 (t, J = 6 Hz, 3 H, CH_3), 1.5 (s, 2 H, NH_2), 1.55 (m, 2 H, CH_2), 3.7 (s with underlying m, 4 H, CH_3O and ArCHN), 6.8 (d, J = 9 Hz, 2 H, Ar H), 7.2 (d, J = 9 Hz, 2 H, Ar H); mass spectrum, m/e (relative intensity) 165 (2), 137 (5), 136 (100); exact mass calcd for $C_{10}H_{15}NO$ m/e 165.1153, found m/e 165.1158.

1-(*p*-Methoxyphenyl)pentylamine (27): bp 100 °C (0.15 mm); IR (neat) 3350 cm^{-1}; NMR ($CDCl_3$) δ 0.8 (t, J = 7 Hz, 3 H, CH_3), 1.2 (m, 4 H, CH_2), 1.6 (m, 2 H, CH_2), 2.2 (s, 2 H, NH_2), 3.7 (s with underlying m, 4 H, CH_3O and ArCHN), 6.8 (d, J = 9 Hz, 2 H, Ar H), 7.25 (d, J = 9 Hz, 2 H, Ar H); mass spectrum, m/e (relative intensity) 193 (1.5), 136 (100); exact mass calcd for $C_{12}H_{19}NO$ m/e 193.1466, found m/e 193.1472.

4-(2-Furyl)-4-amino-1-butene (31): IR (neat) 3360, 3280 cm^{-1}; NMR ($CDCl_3$) δ 1.85 (s, 2 H, NH_2), 2.4 (m, 2 H, CH_2), 3.9 (t, J = 6 Hz, 1 H, CHN), 5.1 (m, 2 H, $=CH_2$), 5.7 (m, 1 H, =CH), 6.2 (m, 2 H, Ar H), 7.33 (br s, 1 H, Ar H); mass spectrum, m/e (relative intensity) 137 (1), 96 (100), 41 (5).

(*E*)-3-Amino-1-phenyl-1,5-hexadiene (33): IR (neat) 3370, 3290 cm^{-1}; NMR ($CDCl_3$) δ 2.3 (t, J = 7 Hz, 2 H, CH_2), 2.45 (s, 2 H, NH_2), 3.5 (q, J = 7 Hz, 1 H, CHN), 4.9–5.25 (m, 2 H, $=CH_2$), 5.5–6.0 (m, 1 H, =CH), 6.15 (dd, J = 15, 7 Hz, 1 H, =CH), 6.5 (d, J = 15 Hz, 1 H, Ar CH=), 7.3 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 173 (1), 132 (100), 91 (8), 77 (65).

***N*-(5,5-Dimethylhex-1-en-4-yl)benzamide (34)**: mp 164–165 °C; IR ($CHCl_3$) 3440, 1655 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (s, 9 H, CH_3), 1.9–2.7 (m, 2 H, CH_2), 4.15 (td, J = 10, 4 Hz, 1 H, CHN), 5.1 (m, 2 H, $=CH_2$), 5.6–6.1 (m, 2 H, =CH and NH), 7.6 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 231 (18), 216 (18), 149 (100), 105 (27); exact mass calcd for $C_{15}H_{21}NO$ m/e 231.1623, found m/e 231.1629. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15. Found: C, 77.62; H, 9.03.

4-Amino-1-undecene (36): IR (neat) 3360 cm^{-1}; NMR ($CDCl_3$) δ 0.85 (t, 3 H, CH_3), 1.33 (m, 12 H, CH_2), 1.75 (s, 2 H, NH_2), 1.7–2.4 (m, 2 H, $=CCH_2$), 2.8 (m, 1 H, CHN), 5.1 (m, 2 H, $=CH_2$), 5.5–6.0 (m, 1 H, =CH); mass spectrum, m/e (relative intensity) 169 (1), 128 (57), 85 (67), 83 (100).

Preparation of 2-Azetidinones from Aldehydes and Esters: *rel*-(3*S*,4*S*)-3-Methyl-3-thiophenoxy-4-[(trimethylsilyl)ethynyl]-2-azetidinone (45) and *rel*-(3*R*,4*S*)-3-Methyl-3-thiophenoxy-4-[(trimethylsilyl)ethynyl]-2-azetidinone (48). To 207 mg (1.24 mmol) of 1,1,1,3,3,3-hexamethyldisilazane in 1.5 mL of dry tetrahydrofuran was added 0.8 mL (1.24 mmol) of 1.55 M n-butyllithium in hexane at 0 °C. The mixture was stirred at 0 °C for 10 min and added dropwise to a solution of 144 mg (1.14 mmol) of (trimethylsilyl)propargylaldehyde[20] in 1.0 mL of tetrahydrofuran at −70 °C over a period of 5 min. The resulting solution of trimethylsilyl imine **12** was used directly in the following reaction.

To 128 mg (1.28 mmol) of diisopropylamine in 1.5 mL of tetrahydrofuran was added 0.82 mL (1.26 mmol) of 1.55 M n-butyllithium in hexane at 0 °C. The solution was cooled to −70 °C followed by the addition of 237 mg (1.13 mmol) of ethyl α-thiophenoxypropionate[21] (**38**) in 1.0 mL of tetrahydrofuran over a 5-min period. The solution was stirred at −70 °C for 60 min followed by addition of the solution of trimethylsilyl imine **12** via cannula at a rate such that the temperature did not exceed −60 °C. The mixture was stirred at −70 °C for 60 min, allowed to warm to room temperature, and stirred for an additional 18 h. The solution was diluted with 100 mL of ether and washed sequentially with 50 mL of 1.5 M aqueous hydrochloric acid and 50 mL of water. The combined aqueous washes were extracted with 50 mL of dichloromethane. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residual brown oil (280 mg) was chromatographed over 40 g of silica gel (eluted with ethyl acetate–hexane, 1:7 gradually increased to 1:3) to give 176 mg (54%) of azetidinone **45**: mp 104.5–106 °C; IR (CH_2Cl_2) 3400, 1780 cm^{-1}; NMR ($CDCl_3$) δ 0.20 (s, 9 H, $SiCH_3$), 1.60 (s, 3 H, CH_3), 4.10 (s, 1 H, CH), 6.33 (br s, 1 H, NH), 7.25–7.70 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 289 (13), 288 (12), 274 (5), 246 (23), 231 (26), 215 (9), 164 (100), 136 (11), 121 (20), 110 (12), 105 (79), 97 (7), 83 (7), 77 (7), 73 (11), 59 (24); exact mass calcd for $C_{15}H_{19}NOSSi$ m/e 289.0956, found m/e 289.0964. Continued elution gave 66 mg (20%) of azetidinone **48**: mp 109–110.5 °C; IR (CH_2Cl_2) 3400, 1780 cm^{-1}; NMR ($CDCl_3$) δ 0.20 (s, 9 H, $SiCH_3$), 1.50 (s, 3 H, CH_3), 4.23 (s, 1 H, CH), 6.67 (br s, 1 H, NH), 7.25–7.80 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 289 (12), 288 (10), 274 (14), 246 (20), 231 (25), 215 (9), 177 (5), 164 (100), 149 (19), 136 (12), 121 (28), 110 (46), 105 (98), 77 (17), 73 (21); exact mass calcd for $C_{15}H_{19}NOSSi$ m/e 289.0956, found m/e 289.0964.

3,3-Dimethyl-4-(β-styryl)-2-azetidinone (41). To a stirred solution of 1.19 g (11.9 mmol) of diisopropylamine in 20 mL of tetrahydrofuran cooled to −70 °C was added 7.7 mL (11.9 mmol) of 1.55 M n-butyllithium in hexane. The solution was stirred for 10 min followed by addition of 1.16 g (10.0 mmol) of ethyl isobutyrate (**37**) in 20 mL of tetrahydrofuran at a rate such that the internal temperature did not exceed −70 °C. To the resulting solution of ester enolate was added a solution of *N*-(trimethylsilyl)cinnamaldimine [**8**; prepared by the addition of 1.32 g (10 mmol) of cinnamaldehyde to a solution of 10 mmol of lithium bis(trimethylsilyl)amide in 18 mL of tetrahydrofuran–hexane at 25 °C] at a rate that kept the internal temperature at −70 °C. The resulting mixture was allowed to stir while the cold bath expired followed by additional 4 h at room temperature. The solution was diluted with 20 mL of ether and washed with three 20-mL portions of 1.0 M aqueous hydrochloric acid, 25 mL of saturated aqueous sodium bicarbonate, and 20 mL of brine. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residual solid was recrystallized from hexane to give 1.38 g (69%) of azetidinone **41** as a white solid: mp 102–104 °C; IR ($CHCl_3$) 3409, 1770 cm^{-1}; NMR ($CDCl_3$) δ 1.1 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 3.9 (d, J = 7 Hz, 1 H, CHN), 6.1 (dd, J = 16, 7 Hz, 1 H, =CH), 6.50 (d, J = 16 Hz, 1 H, PhCH=), 6.60 (s, 1 H, NH), 7.3 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 201 (48), 158 (18), 143 (41), 132 (100), 130 (51), 70 (60), 42 (26); exact mass calcd for $C_{13}H_{15}NO$ m/e 201.1153, found m/e 201.1158. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.31; H, 7.46.

3,3-Dimethyl-4-phenyl-2-azetidinone (40): mp 103–104.5 °C (lit.[22] mp 104–105 °C); IR ($CHCl_3$) 3415, 1760 cm^{-1}; NMR ($CDCl_3$) δ 0.7 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 4.4 (s, 1 H, CHN), 6.85 (br s, 1 H, NH), 7.2 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 175 (63), 132 (65), 117 (75), 106 (100), 51 (55); exact mass calcd for $C_{11}H_{13}NO$ m/e 175.0997, found m/e 175.1001. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48. Found: C, 75.44; H, 7.69.

3,3-Dimethyl-4-[(trimethylsilyl)ethynyl]-2-azetidinone (42): mp 57–58 °C; IR (CH_2Cl_2) 3400, 1775 cm^{-1}; NMR ($CDCl_3$) δ 0.20 (s, 9 H, $SiCH_3$), 1.32 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 3.97 (s, 1 H, CHN), 6.50 (br s, 1 H, NH); mass spectrum, m/e (relative intensity) 195 (1), 180 (3), 152 (42), 137 (100), 126 (16), 110 (10), 97 (6), 83 (11), 70 (27); exact mass calcd for $C_9H_{17}NOSi$ m/e 195.1079, found m/e 195.1084.

***rel*-(3*S*,4*S*)-3-Methyl-4-phenyl-3-thiophenoxy-2-azetidinone (43)**: mp 106–107 °C; IR (CH_2Cl_2) 3400, 1775 cm^{-1}; NMR ($CDCl_3$) δ 1.67 (s, 3 H, CH_3), 4.67 (s, 1 H, CHN), 6.95–7.47 (m, 11 H, ar H and NH); mass spectrum, m/e (relative intensity) 269 (30), 226 (18), 211 (4), 164 (95), 121 (34), 115 (34), 110 (5), 105 (100), 91 (30), 77 (41); exact mass calcd for $C_{16}H_{15}NOS$ m/e 269.0874, found m/e 269.0881.

***rel*-(3*R*,4*S*)-3-Methyl-4-phenyl-3-thiophenoxy-2-azetidinone (46)**: mp 128–129 °C; IR (CH_2Cl_2) δ 3400, 1775 cm^{-1}; NMR ($CDCl_3$) δ 1.03 (s, 3 H, CH_3), 4.67 (s, 1 H, CHN), 6.46 (br s, 1 H, NH), 7.2–7.8 (m, 10 H, Ar H); mass spectrum, m/e (relative intensity) 269 (34), 226 (13), 211 (5), 193 (4), 164 (100), 137 (10),

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***rel*-(3*S*,4*S*)-4-Phenyl-3-thiophenoxy-2-azetidinone (44)**: mp 110.5–111.5 °C; IR (CH_2Cl_2) 3400, 1782 cm^{-1}; NMR ($CDCl_3$) δ 4.10 (d, J = 3 Hz, 1 H, CH), 4.47 (d, J = 3 Hz, 1 H, CH), 6.60 (br s, 1 H, NH), 7.20–7.65 (m, 10 H, Ar H); mass spectrum, m/e (relative intensity) 255 (15), 212 (47), 167 (12), 150 (15), 123 (38), 121 (41), 106 (100), 77 (38); exact mass calcd for $C_{15}H_{13}NOS$ m/e 255.0717, found m/e 255.0724.

***rel*-(3*R*,4*S*)-4-Phenyl-3-thiophenoxy-2-azetidinone (47)**: mp 126–126.5 °C; IR (CH_2Cl_2) 3400, 1775 cm^{-1}; NMR ($CDCl_3$) δ 4.77 (dd, J = 5, 1.5 Hz, 1 H, CHN), 5.03 (d, J = 5 Hz, 1 H, CHS), 6.55 (br s, 1 H, NH), 7.10–7.45 (m, 10 H, Ar H); mass spectrum, m/e (relative intensity) 255 (17), 212 (27), 150 (18), 123 (25), 121 (34), 106 (100), 77 (28); exact mass calcd for $C_{15}H_{13}NOS$ m/e 255.0717, found m/e 255.0724.

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Registry No. **2**, 83948-24-7; **3**, 83948-25-8; **4**, 83948-26-9; **5**, 83948-27-0; **6**, 64187-51-5; **7**, 17599-61-0; **8**, 83948-28-1; **9**, 83948-29-2; **10**, 83948-30-5; **11**, 61860-99-9; **12**, 83948-31-6; **13**, 1730-25-2; **14**, 100-58-3; **15**, 925-90-6; **16**, 2259-30-5; **17**, 75-16-1; **18**, 109-72-8; **19**, 594-19-4; **20**, 917-54-4; **21**, 83948-32-7; **22**, 83948-33-8; **23**, 83948-34-9; **24**, 6298-96-0; **25**, 83948-35-0; **26**, 2538-34-3; **27**, 83948-36-1; **28**, 4383-23-7; **29**, 91-00-9; **30**, 61501-04-0; **31**, 83948-37-2; **32**, 83948-38-3; **33**, 83948-39-4; **34**, 83948-40-7; **36**, 83948-41-8; **37**, 97-62-1; **38**, 20461-98-7; **39**, 7605-25-6; **40**, 7486-93-3; **41**, 83948-42-9; **42**, 83948-43-0; **43**, 83948-44-1; **44**, 83948-45-2; **45**, 83948-46-3; **46**, 83948-47-4; **47**, 83948-48-5; **48**, 83948-49-6; 1,1,1,3,3,3-hexamethyldisilazane, 999-97-3; benzaldehyde, 100-52-7; 3,4-dimethoxybenzaldehyde, 120-14-9; (trimethylsilyl)-propargylaldehyde, 2975-46-4; (*E*)-cinnamaldehyde, 14371-10-9; lithium bis(trimethylsilyl)amide, 4039-32-1.

Requisite Cation Complexation for the Reduction of 2,6-Pyrido-18-crown-6 *N*-Oxide and an Analogue by Potassium Tri-*sec*-butylborohydride. Evidence for a Single Electron Transfer Mechanism

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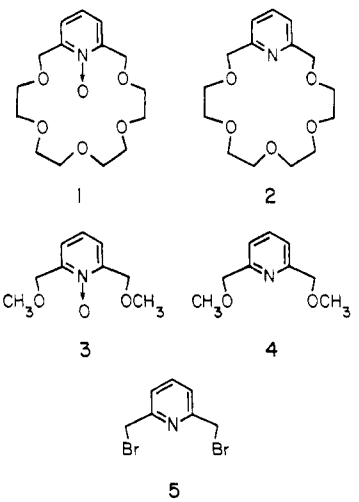
The reductions of 2,6-pyrido-18-crown-6 *N*-oxide (**1**) and a weakly complexing analogue (**3**) by potassium tri-*sec*-butylborohydride (K-Selectride) were studied. N-Oxides **1** and **3** are reduced to pyridines **2** and **4**, respectively, at equal rates with the reactions obeying competitive, consecutive second-order kinetics with $k_2/k_1 = \infty$. In a competitive reduction with limiting K-Selectride, only crown ether **1** is reduced while analogue **3** remains unreacted. The reduction of **1** in the presence of **3** follows simple second-order kinetics. Complexation of *N*-oxide substrate with a potassium cation is thought to be a prerequisite for these reductions. Evidence is presented supporting a single electron transfer (SET) as the rate-determining step of the reductions.

As a part of our continuing study of cationic transition-state stabilization,[2-4] we began an investigation of nucleophilic attack on the aromatic ring of 2,6-pyrido-18-crown-6 *N*-oxide (**1**).[5] Specifically, we chose to study the reduction of **1** to the corresponding pyridine crown ether (**2**)[6] by potassium tri-*sec*-butylborohydride (K-Selectride). In the course of this work, it became apparent that this reduction and that of 2,6-bis(methoxymethyl)-pyridine *N*-oxide (**3**) to 2,6-bis(methoxymethyl)pyridine (**4**) do not occur by the expected hydride transfer (polar) mechanism. Herein we report the results of our study and propose a mechanism for reduction of **1** and **3** by K-Selectride, involving single electron transfer (SET), followed by hydrogen atom transfer and elimination of HO^- to give the pyridine products (see Scheme II).

Crown ether **1** has been shown to be a good host for potassium cation complexation[5] (Table I). Corey–Pauling–Koltun (CPK) models suggest that a hexadentate cavity suitable for complexation of K^+ is formed when the *N*-oxide ring is held roughly perpendicular to the plane of the polyether ring. Complexation of an alkali-metal cation in a host such as **1** should increase the electron density at the *N*-oxide oxygen atom. Such polarization is expected to enhance the reactivity of the 4-position of the pyridine *N*-oxide toward nucleophiles.[7]



Pyridine *N*-oxide **3** is an electronic analogue of crown ether **1**, lacking the polyether ring necessary for strong cation complexation (Table I). The reactivities of **1** and

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