121 (37), 115 (25), 110 (18), 105 (91), 91 (22); exact mass calcd for $C_{16}H_{15}NOS$ m/e 269.0874, found m/e 269.0881.

***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.

Acknowledgment. We thank Mr. Richard Weisenberger for recording mass spectra at The Ohio State University Chemical Instrument Center. Financial support from The National Institutes of Health (Grant No. GM 27647-02) is gratefully acknowledged.

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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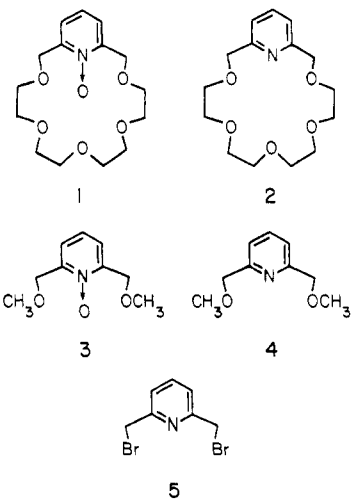
Received July 9, 1982

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

(1) Alfred P. Sloan Fellow, 1980–1982. Current address: Genentech, Inc., 460 Point San Bruno Blvd., South San Francisco, CA 94080.
(2) Rastetter, W. H.; Phillion, D. P. *J. Org. Chem.* **1981**, *46*, 3209.
(3) Rastetter, W. H.; Phillion, D. P. *J. Org. Chem.* **1980**, *45*, 1535.
(4) Rastetter, W. H.; Phillion, D. P. *Tetrahedron Lett.* **1979**, 1469.
(5) A different preparation of crown ether **1** has been reported; see Kaplan L. J.; Weisman, G. R.; Cram, D. J. *J. Org. Chem.* **1979**, *44*, 2226.
(6) Newcomb, M.; Timko, J. M.; Walba, D. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6392.
(7) While the 2- (or 6) position of pyridine *N*-oxide is the preferred site for nucleophilic attack, 2,6-disubstituted species undergo attack exclusively at the 4-position; see ref 9.

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Table I. Association Constants (K_a) for Potassium Picrate Complexation[a]

compd	$10^{-3}K_a$, M^{-1}	$-\Delta G°$, kcal mol^{-1}
1	3590[b,c]	8.87[b,c]
2	109000[c]	11.0[c]
3	1.89	4.40
4	48.2	6.37

[a] $CDCl_3$ used as solvent at 23–26 °C. [b] Cram et al. determined $10^{-1}K_a = 3800\ M^{-1}$, $-\Delta G° = 8.98$ kcal mol^{-1}. [c] See ref 5.

3, especially toward anions, might be significantly different in the presence of complexing cations. In a competitive, multiple host system with limiting cation, the better host (i.e., 1) will sequester a preponderance of the available guests. The reactivities of 1 and 3 in such a competitive system should reveal the influence of the cation during reaction at the aromatic ring.

General Considerations

In their most straightforward form, the reductions of N-oxides 1 and 3 by K-Selectride are envisaged to proceed via direct hydride attack at the 4-position of the aromatic ring. Rearomatization would afford the pyridines 2 and 4, respectively.

Hydride transfer to the aromatic ring from a β position of the borane alkyl groups (*sec*-butyl groups) must also be considered. Similar β-hydride transfers are seen, for example, in the reactions of some Grignard reagents.[8]

Direct nucleophilic attack at the *N*-oxide oxygen atom of pyridine *N*-oxide and other heteroaromatic *N*-oxides is precedented.[9] Reduction by certain reagents (e.g., trivalent phosphorus compounds) is believed to occur in this fashion. Such reductions are strongly influenced by steric bulk about the *N*-oxide oxygen.[9]

Finally, a free-radical mechanism for the reduction of pyridine *N*-oxides, initiated by single electron transfer, must be considered. Free-radical reactions of pyridine *N*-oxides[10] and pyridine[11] are well-known. *N*-Oxides are found to undergo reduction in dissolving metal solutions,[9] presumably by sequential electron transfers.

Results

Syntheses. Crown ether 1[5] was prepared in 28% yield by the cyclization of 2,6-bis(bromomethyl)pyridine (5)[12] with tetraethylene glycol (NaH, THF, reflux). Oxidation of 2 with 3,5-dinitroperoxybenzoic acid[13] affords 1 (52%) as an oil. Oxidation of 4[6] with 3,5-dinitroperoxybenzoic acid[13] yields 3 (90%) as slightly brown crystals.

Kinetics of Reduction. The reductions of *N*-oxides 1 and 3 were performed in benzene/THF at 0 °C. The reactions of 1 and 3 with 1.0 equiv of K-Selectride proceed toward an asymptote near 50% reduction. Chromatography of each reaction mixture affords the remaining material as unreacted substrate. The reaction profiles

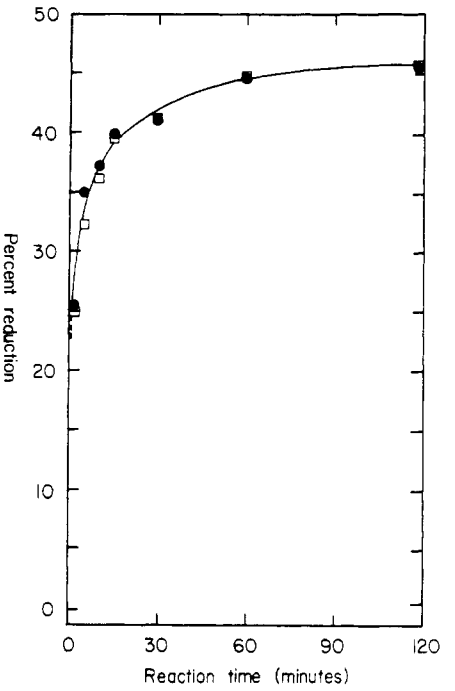

Figure 1. Reaction profile for the separate reductions of 1 (●) and 3 (□) by K-Selectride (*N*-oxide:K-Selectride = 1:1).

Table II. Rate Constants for K-Selectride Reductions

compd	10^3k_1, L mol^{-1} s^{-1}
1[a]	38.6 ± 3.2[c]
1[b]	40.4 ± 5.2[c]
3[a]	41.9 ± 9.3[c]

[a] Independent reduction of 1 or 3. [b] Reduction of 1 in the presence of 3; see text. [c] Error limits are standard errors of fit.

(Figure 1) of these reductions show systematic deviations from normal second-order behavior.

Frost and Schwemer[14–16] have investigated the kinetics of competitive, consecutive second-order reactions. In such systems, one of the products of the initial step (C, eq 1) reacts with a molecule of starting material (A, eq 2) to form

$$A + B \xrightarrow{k_1} C + D \quad (1)$$

$$A + C \xrightarrow{k_2} E \quad (2)$$

a species (E, eq 2) that is inert under the reaction conditions. These reactions often prove kinetically complex. Kinetic treatment is simplified, however, for certain specified stoichiometries and when the variable κ ($\kappa = k_2/k_1$; see equations 1 and 2) assumes certain values. When $\kappa = 0$, 0.5, or ∞, the treatment degenerates to one of simple second order.

The reductions of 1 and 3 were repeated at a stoichiometry of 0.5 equiv of K-Selectride/mol of *N*-oxide (see ref 14–16). With use of nonlinear regression and the Frost kinetic model,[14–16] the kinetic rate data for reduction of 1 and 3 were analyzed. The data prove a good fit for a competitive process with $\kappa = \infty$ ($k_2 \gg k_1$). The rate-determining, second-order rate constants (k_1) for the reductions are found in Table II. Crown ether 1 and ana-

(8) Whitmore, F. C.; George, R. S. *J. Am. Chem. Soc.* **1942**, *64*, 1239.
(9) Katrinsky, A. R. M.; Lagowski, J. M. "Chemistry of the Heterocyclic *N*-Oxides"; Academic Press: New York, 1971, and references therein.
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(11) (a) Newkome, G. R.; Hager, D. C. *J. Org. Chem.* **1982**, *47*, 599. (b) Kharash, M. S.; Schwartz, D.; Zimmerman, M.; Nudenberg, W. *Ibid.* **1953**, *18*, 1051.
(12) Newcomb, M.; Gokel, G. W.; Cram, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 6810.
(13) Rastetter, W. H.; Richard, R. J.; Lewis, M. D. *J. Org. Chem.* **1978**, *43*, 3163.
(14) Frost, A. A.; Schwemer, W. C. *J. Am. Chem. Soc.* **1952**, *74*, 1268.
(15) Schwemer, W. C.; Frost, A. A. *J. Am. Chem. Soc.* **1951**, *73*, 4541.
(16) Frost, A. A.; Pearson, R. G. "Kinetics and Mechanism", 2nd ed.; Wiley: New York, 1961.

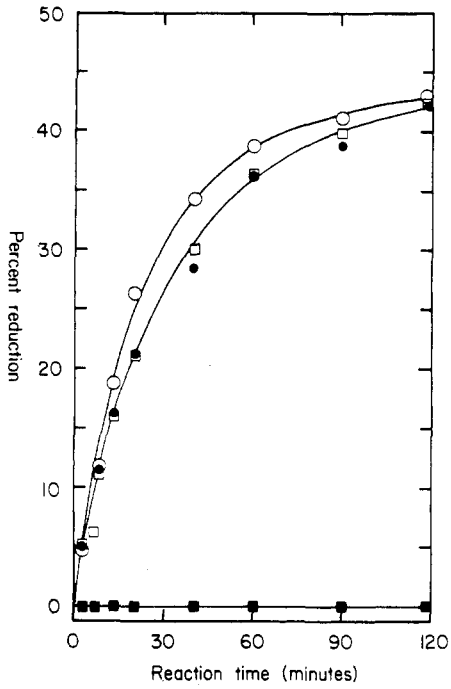
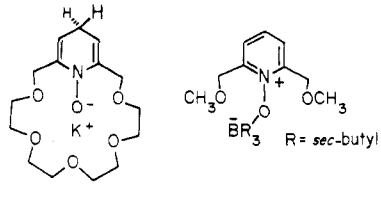


Figure 2. Reaction profiles for the separate and competitive reductions of 1 and 3 by K-Selectride (0.5 mol): 1 (●, 1 mol), 3 (□, 1 mol), competition of 1 and 3 (○, 1 mol and ■, 1 mol, respectively).

logue 3, within experimental error, are found to react with K-Selectride at the same rate.

In the competitive reduction of 1 (1 equiv) and 3 (1 equiv) by K-Selectride (0.5 equiv), only crown ether 1 is reduced (Figure 2). The reduction of 1 under these conditions follows *simple* second-order kinetics rather than the Frost kinetic model. Further, the second-order rate constant (k_1) for the reduction of 1 in the presence of 3, within experimental error, is the same as k_1 found in the separate reductions of 1 and 3 (see Table II).

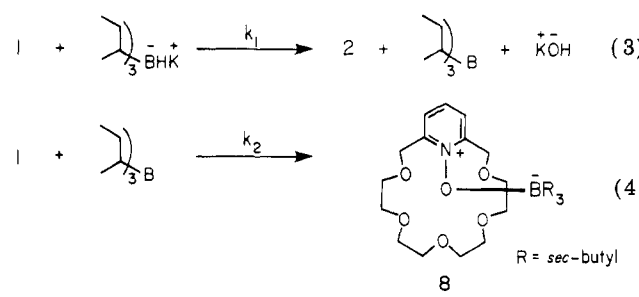
Mechanistic Studies. Tri-*sec*-butylborane is a likely product of the reaction of K-Selectride with *N*-oxides 1 and 3 (cf. eq 1). The possibility for complex formation between tri-*sec*-butylborane and the pyridine *N*-oxides (cf. eq 2) was investigated. The mixture of 1.0 equiv of tri-*sec*-butylborane and crown ether 1 (see complex 8) is unreactive toward K-Selectride under normal reducing conditions (vide supra). Addition of 1.0 equiv of cyclohexanone to the reaction mixture affords 0.99 equiv of cyclohexanol (GLC yield), demonstrating the persistence of an active reducing species in the presence of the complex (see 8). Similar results are observed for the complex (see 7) generated from tri-*sec*-butylborane and *N*-oxide 3.



6 7

Hydride addition to the 4-position of the aromatic ring of 1 would result in the formation of a 1,4-dihydropyridyl *N*-oxide intermediate (6). The spectroscopic observation of 6 was attempted numerous times. Several reductions of 1 were conducted in deuterated solvent mixtures and monitored by ^{1}H NMR. In every case, starting material (1) was seen to reduce cleanly to product (2) without any detectable intermediate.

Scheme I



8

Potassium tri-*sec*-butylborodeuteride, a potential deuteride donor, was prepared by the addition of potassium deuteride to a THF solution of tri-*sec*-butylborane.[17] Reaction of crown ether 1 with this reducing agent and characterization of the product (2) by ^{1}H NMR and mass spectrometry showed that *no deuterium had been incorporated into the aromatic ring.*

The reduction of crown ether 1 by K-Selectride was also performed in the cavity of an ESR spectrometer. The mixture, cooled to −196 °C, showed a weak, broad singlet (g = 2.004).

Discussion

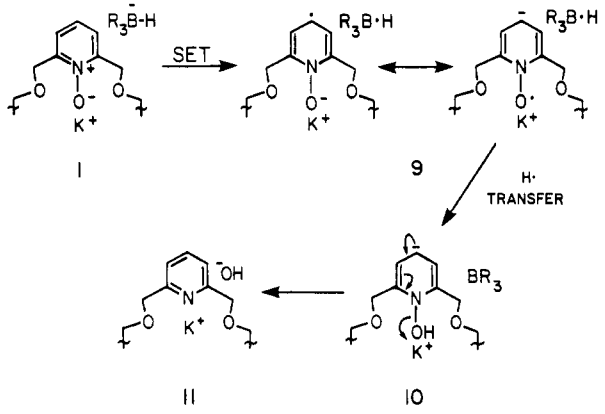
Scheme I for reduction of crown ether 1 is consistent with the demands of the Frost kinetic model. In the course of *N*-oxide reduction (eq 3, Scheme I), 1 equiv of tri-*sec*-butylborane is liberated. Complexation of the trialkylborane with unreacted substrate (eq 4, Scheme I) yielding an unreactive species (8) accounts for the observed 50% product yield. Assuming potassium cation–host complexation to be prerequisite for subsequent reduction, 8 might indeed be expected to prove inert owing to its neutral net charge and high steric crowding about the polyether ring. Complexation of the reduced pyridine species with tri-*sec*-butylborane is less likely.[18] The complex is disfavored both by competition of K^+ for the pyridine lone pair and by the bulk of the adjacent substituents on the aromatic ring.[19]

The competitive, consecutive second-order kinetics proves a good model for the reduction of 1 and 3 by K-Selectride when $\kappa = \infty$ ($k_2 \gg k_1$). With this assumption ($\kappa = \infty$), the rate constant k_1 can be determined independently of the value of k_2. *N*-Oxides 1 and 3 are found to be reduced by K-Selectride, within experimental error, at the same rate (k_1, Table II). It is not possible to determine the rate of the competing complexation of *N*-oxide and trialkylborane (k_2, eq 2) from our results. The values of k_2 for the crown 1 and its analogue, 3, may in fact be quite different, but both rates must be of sufficient magnitude to meet the conditions of $\kappa = \infty$.

In the competitive reduction of 1 and 3 by K-Selectride, crown ether 1 is reduced in simple second-order fashion. This result suggests that 1 and 3 do not form borane complexes of equal stability. The second-order kinetics are most consistent with a scheme in which 3 complexes selectively with the trialkylborane product (see 7), leaving 1 free for reaction with K-Selectride. The polyether ring

(17) Brown, C. A. *J. Am. Chem. Soc.* **1973**, *95*, 4100.
(18) For examples of pyridine complexes with main group and transition metals, see (a) Ashby, E. C.; Goel, A. B. *J. Organometal. Chem.* **1981**, *204*, 139. (b) De Koning, A. J.; Boersma, J.; van der Kerk, G. J. M. *Ibid.* **1980**, *186*, 159. (c) Lansbury, P. T.; Peterson, J. O. *J. Am. Chem. Soc.* **1963**, *85*, 2236. Lansbury, P. T.; Peterson, J. O. *Ibid.* **1961**, *83*, 3537.
(19) For a discussion of steric interactions in pyridine–borane complexes, see (a) Brown, H. C.; Holmes, R. R. *J. Am. Chem. Soc.* **1956**, *78*, 2173. (b) Brown, H. C.; Horowitz, R. H. *Ibid.* **1955**, *77*, 1733.

Scheme II



of crown ether 1 forms a cavity for alkali-metal cations[5] but sterically encumbers complexation of the N-oxide oxygen with the bulky trialkylborane. Conversely, the lack of a polyether ring in 3 allows more stable trialkylborane complexation but precludes strong K^+ complexation (Table I).

The ligand properties of 1 and 3 determine their reactivity toward K-Selectride. The inability of 3 to compete with crown ether 1 for limiting K^+ accounts for its inertness in the competitive reduction. Thus, cation complexation is required for facile reduction of 3 by K-Selectride. By analogy, K^+ catalysis should facilitate the reduction of crown ether 1. In the independent reduction of 3, the ability of the model to weakly complex K^+ (Table I) is sufficient to ensure reduction.

Our results indicate that the reduction of 1 and 3 by K-Selectride (eq 3, Scheme I) probably does not involve direct hydride transfer. Dihyropyridine intermediates (e.g., 6) were not detected, and the products of reduction of 1 with the potential deuteride donor, potassium tri-*sec*-butylborodeuteride, were found to contain no deuterium.

Hydride (deuteride) transfer to the 2-position of N-oxides 1 and 3 followed by 1,2-elimination would result in reduction without incorporation of a hydrogen atom from K-Selectride (from either R_3BH^- or β-hydride position). The reactions of the unsubstituted substrates, pyridine-d_5 N-oxide and pyridine-d_5, with K-Selectride have been studied and will be reported in detail elsewhere.[20] Pyridine-d_5 N-oxide reduces to pyridine-d_5 without incorporation of ^1H into the ring. The product, pyridine-d_5, in a subsequent reaction, incorporates label (^1H) exclusively at the 4-position.[20] The transfer of hydride to the alkyl-substituted 2-positions of 1 and 3 and the β-hydride transfer to any ring position of the N-oxides, thus, is unlikely.[21]

Direct hydride transfer to the N-oxide oxygen of the 2,6-disubstituted 1 and 3 seems unlikely.[9] The complexed potassium polarizes electron density toward the N-oxide oxygen. Thus, direct hydride transfer to the oxygen atom should not be facilitated in the presence of K^+.

In Scheme II, 1 and 3 are reduced without hydride transfer by a SET-intitated mechanism.[22] The yellow reaction mixtures (λ_{max} 328 nm) from 1 and 3 with K-Selectride are weakly ESR active. While the observed ESR signal in the reduction of 1 is consistent with a SET mechanism, the weakness of the signal precludes the characterization of our proposed diradical intermediate 9. The SET mechanism, however, is consistent with the results of the isotope-labeling experiments since deuterium is transferred to oxygen and subsequently eliminated.

MO calculations of spin densities in the pyridine N-oxide radical anion show maximum unpaired electron density on the N-oxide oxygen.[11] This is consistent with hydrogen atom transfer (**9** → **10**) to the oxygen atom prior to the elimination–rearomatization (**10** → **11**). It should be noted that no dimerization of the radical species was observed during the course of this study. The radical pair 9 must collapse to products (**9** → **10** → **11**) at a rate more rapid than dimer formation.

Uncomplexed N-oxide 3, and by analogy uncomplexed 1, are not reduced by K-Selectride while the potassium cation complexes are reduced to the corresponding pyridines (2 and 4, respectively). Similarly, pyridine N-oxide was found[23] not to be reduced electrochemically, while its conjugate acid, bearing a net positive charge, is reduced to pyridine.

The data gathered on the reductions of pyridine N-oxides by K-Selectride reemphasize the role a cation may play in facilitating nucleophilic[2-4] or electron-transfer reactions of anions. Substrate recognition and binding, and charge/dipole-driven catalysis seen here and in similar crown ether examples,[2-4] serve as simple models for the often complex interactions of substrates with macromolecular protein catalysts, the enzymes. The range of substrates that can be studied as crown ether–cation complexes is limited by the very nature and size of the crown ether cavity. Nevertheless, the same principles demonstrated here may be applied in the future to de novo design and synthesis of macromolecular protein catalysts using newer synthetic methodologies.[24]

Experimental Section

General Procedures. ^1H NMR spectra were obtained on a Varian T-60 (60 MHz), Perkin-Elmer R-24B (60 MHz), JEOL FX-90Q (90 MHz), Bruker WM-250 (250 MHz), or Bruker WM-270 (270 MHz) NMR spectrometer. Chemical shifts are reported downfield from tetramethylsilane (Me_4Si) on the δ scale. Internal Me_4Si reference was utilized at 60 MHz and residual $CHCl_3$ was utilized at 90, 250, and 270 MHz. Gas–liquid chromatographic (GLC) analyses were carried out on a Varian Series 3700 chromatograph using He as carrier gas. An 8 ft × $^1/_8$ in. 4.1% Carbowax column on Chromosorb G and a flame-ionization detector were used. Mass spectra were obtained on a Varian MAT-44 mass spectrometer. Liquid chromatographic (LC) analyses were carried out on a Waters ALC/GPC 204 system. Two Bondapak C_{18} analytical columns in series and UV detection (254 nm) were used. Gradient elution using CH_3OH/CH_3CN (1:1) and 5 mM NaOAc aqueous buffer (pH 4.7) was used. Peak areas were determined by mass. GLC and LC peaks were identified by coinjection with authentic samples. Melting points are uncorrected. Kinetic

(20) Wagner, W. R.; Rastetter, W. H., manuscript in preparation.

(21) The presence of an intact trialkylborane species is central to the kinetics observed in these reactions. β-Hydride transfer would yield 1-butene and di-*sec*-butylborane. Recombination should predominantly give *n*-butyl-di-*sec*-butylborane; see Brown, H. C. "Hydroboration"; W. A. Benjamin: New York, 1961. Oxidation (H_2O_2, NaOH) of the trialkylborane(s) resulting from the reduction reaction mixtures to their corresponding alcohols afforded only *sec*-butyl alcohol (GLC analysis), suggestive of the persistence of tri-*sec*-butylborane.

(22) A wide variety of complex metal hydrides have been found to react with diverse substrates by electron-transfer mechanisms; see (a) Ashby, E. C.; Goel, A. B. *Tetrahedron Lett.* **1981**, 3729. (b) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *Ibid.* **1981**, 4355. (c) Ashby, E. C.; Goel, A. B.; DePriest, R. N.; Prasad, H. S. *J. Am. Chem. Soc.* **1981**, *103*, 973. (d) Ashby, E. C.; Goel, A. B. *J. Org. Chem.* **1981**, *46*, 3934. (e) Ashby, E. C.; Goel, A. B. *Tetrahedron Lett.* **1981**, 4783. (f) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *J. Am. Chem. Soc.* **1980**, *102*, 7779. (g) Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545.

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analyses using nonlinear regression were obtained on an IBM 370/168 computer with the NLIN procedure of the SAS data package (Gauss-Newton method).

2,6-Pyrido-18-crown-6 (8).[12] A suspension of NaH (3.14 g, 61% oil suspension, 80.0 mmol) in THF (300 mL) was heated to reflux. Separate solutions of 2,6-bis(bromomethyl)pyridine (**5**;[12] 5.25 g, 19.8 mmol) in pyridine (150 mL) and tetraethylene glycol (3.85 g, 19.8 mmol) in THF (150 mL) were simultaneously added dropwise over a 3-h period. The mixture was cooled and evaporated in vacuo and the resulting solid was dissolved in CH_2Cl_2 (10 mL). Residual NaH was decomposed by careful addition of H_2O (5 mL). The organic layer was removed and the aqueous layer extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried ($MgSO_4$) and evaporated to a viscous brown oil. Elution of the oil through neutral alumina (60 mesh) with EtOAc and trituration from cold Et_2O (-78 °C) yielded the crown ether (1.69 g, 28%) as fluffy white crystals: mp 40.0-41.5 °C (lit.[12] mp 40-41 °C); ^1H NMR (250 MHz, $CDCl_3$) δ 3.57-3.63 (8 H, m), 3.64-3.79 (8 H, m), 4.76 (4 H, s), 7.24 (2 H, d, J = 7.7 Hz), 7.66 (1 H, t, J = 7.7 Hz); IR (KBr pellet) 3040, 2830, 1589, 1570, 1453, 1343, 1242, 1100 cm^{-1}.

2,6-Pyrido-18-crown-6 *N*-Oxide (1).[5] 2,6-Pyrido-18-crown-6 (**2**; 200 mg, 0.673 mmol), Na_2CO_3 (1.00 g, 4.92 mmol), and 4,4'-thiobis(6-*tert*-butyl-*m*-cresol) (30 mg, 1% wt of peracid) were stirred into 1,2-dichloroethane (20 mL). 3,5-Dinitroperoxybenzoic acid[13] (521 mg, 2.46 mmol of active oxygen) was added and stirred at room temperature for 2.5 h. Filtration through sintered glass and evaporation in vacuo gave a yellow oil, which was chromatographed through basic alumina with THF to yield oxidized product **1** (110 mg, 52%) as a light-yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 3.41 (8 H, s), 3.59-3.62 (4 H, m), 4.96 (4 H, s), 7.29-7.48 (3 H, m); IR (NaCl) 2860, 1440, 1405, 1350, 1295, 1245, 1108, 1020, 940, 780 cm^{-1}.

2,6-Bis(methoxymethyl)pyridine *N*-Oxide (3). Compound **3** was prepared as slightly colored crystals (mp 51.5-52.0 °C) in 70% yield by oxidation of **4**[12] as described for the preparation of crown ether **1** (vide supra). Data for **3**: ^1H NMR (250 MHz, $CDCl_3$) δ 3.49 (6 H, s), 4.66 (4 H, s), 7.25-7.39 (3 H, m); IR (CCl_4) 2990, 2925, 2820, 1590, 1535, 1400, 1370, 1242, 1194, 995, 968 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.23; H, 7.43; N, 7.63.

Potassium Tri-*sec*-butylborodeuteride (8).[17] The oil was removed from potassium deuteride (1.0 g, 20-25% suspension by repeated washings with Et_2O) under a nitrogen atmosphere. To the dry KD was added tri-*sec*-butylborane (18 mL, 1 M in THF) with water bath cooling. The mixture was stirred 1 h and transferred via cannula to a septum-capped flame-dried tube. This solution showed no appreciable loss of reducing power when stored under nitrogen at room temperature for several months.

Preparation and Attempted Reduction of Complex 6. A flame-dried 5-mL flask was fitted with a magnetic stir bar and sealed under nitrogen with a rubber septum. A solution of **1** (10 μL, 0.366 M, 3.66 μmol) in benzene was charged into the flask. After the contents were cooled to 0 °C in an ice-water bath, tri-*sec*-butylborane (3.7 μL, 1.0 M, 3.70 μmol) was added. After an additional 2 h of stirring, an aliquot was removed and quenched into 0.1 mL of CH_3OH. LC analysis showed no reduced crown products to be present in the reaction mixture. Cyclohexanone (10.3 mg, 10.5 μmol, 3 equiv) was added to the reaction mixture. After 30 min, GLC analysis revealed 33% reduction of cyclohexanone to cyclohexanol. An identical procedure was used with identical results for the attempted reduction of complex **7**.

Reduction of 2,6-Pyrido-18-crown-6 *N*-Oxide (1) by Potassium Tri-*sec*-butylborodeuteride. Crown ether **1** (24.5 mg, 72.0 μmol) was dissolved in benzene-d_6 (0.5 mL, sieve-dried) and cooled to 0 °C in an ice-water bath. Reducing agent (72 μL of a 1 M THF solution) was added and the mixture was concentrated in vacuo. Chromatography (basic alumina, THF) yielded 9.1 mg (42%) of reduced product: ^1H NMR, same as that reported for crown ether **2**; mass spectrum, m/e 297 (M^+ for **2**).

Kinetic Experiments. A flame-dried flask equipped with a magnetic stir bar was capped with a rubber septum and flushed with dry nitrogen. Into the flask was syringed a solution of **1** (9 μL, 0.370 M, 34 μmol) in dry benzene, additional dry benzene (124 μL), and dry THF (114 μL). After the contents were cooled to 0 °C in an ice-water bath, K-Selectride (17.5 μL, 1.0 M in THF, 17.5 μmol) was added. The final mixture was 0.1 M in **1** and 0.05 M in K-Selectride. The solution quickly became yellow. Aliquots (2 μL) were periodically removed and quenched into CH_3OH (100 μL). LC analyses of the quenched aliquots were carried out as outlined (vide supra). An identical procedure was used for the kinetic analyses of **3**. The competitive reductions were conducted in this manner also, except that 95 μL of a 0.370 M solution of analogue **3** (in dry benzene) was substituted for 95 μL of benzene in the reaction mixture.

Spectroscopic Determination of Association Constants (K_a). All association constants were determined with potassium picrate solution, using the method reported by Cram.[25]

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Registry No. 1, 69928-23-0; 1 potassium picrate complex (1:1), 69942-89-8; **2**, 53914-89-9; **2** potassium picrate complex (1:1), 69942-98-9; **3**, 84051-59-2; **4**, 64726-18-7; **6**, 84051-60-5; **7**, 84051-61-6; K^+, 24203-36-9; 2,6-bis(bromomethyl)pyridine, 7703-74-4; tetraethylene glycol, 112-60-7; tri-*sec*-butylborane, 1113-78-6.

Sulfenylation of Ortho Esters. A Novel Preparation of 2-[(Trihalomethyl)thio]alkanoic Acids[1]

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Trifluoromethanesulfenyl chloride reacts readily with ortho esters of acetic acid as well as ortho esters of higher aliphatic carboxylic acids to yield 1,1,1-trialkoxy-2-[(trifluoromethyl)thio]alkanes **4a-c**. In the presence of an excess of trifluoromethanesulfenyl chloride, disubstitution of triethyl orthoacetate was observed, giving 1,1,1-triethoxy-2,2-bis[(trifluoromethyl)thio]ethane (**6**), which underwent facile thermal elimination to yield 1,1-diethoxy-2,2-bis[(trifluoromethyl)thio]ethene (**8**). The trialkoxyethanes **4a-c** are easily transformed into the corresponding [(trihalomethyl)thio]alkanoic acids and lower alkyl esters. Trichloromethanesulfenyl chloride, a less reactive sulfenyl halide, reacts at elevated temperature in a similar manner with trimethyl and triethyl orthoacetate to furnish 1,1,1-trialkoxy-2-[(trichloromethyl)thio]ethanes **10a** and **10b**. A radical chain mechanism is proposed for the formation of **10a** and **10b**.

As a consequence of the physical and chemical properties of trifluoromethanethiol[2] (bp -37 °C), rather tedious methods are utilized for the introduction of the (trifluoromethyl)thio moiety into aliphatic compounds.

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