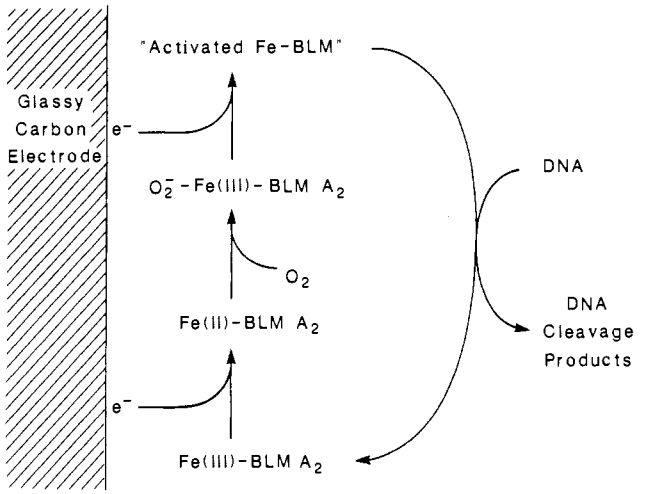
Scheme I. Proposed Catalytic Cycle for Fe·BLM Activation



mum current accessible in the present electrochemical cell, the products obtained via electrochemical and chemical activation were the same.[8,17]

Also studied was the effect of DNA on the electrochemical activation of Fe·BLM and on the putative self-inactivation of activated Fe·BLM. Admixture of excess CGCTAGCG or calf thymus DNA to Fe^{III}·BLM diminished the conversion to Fe(II)·BLM.[19] This paralleled a recent report[20] of the interaction of tris(1,10-phenanthroline)cobalt(III) with DNA and suggested that Fe^{III}·BLM was substantially bound to DNA under our experimental conditions. Quantitation of the current at high DNA concentrations indicated that Fe^{III}·BLM is reduced poorly, if at all, when bound to DNA.[21] Further, reductive activation of Fe^{II}·BLM under aerobic conditions at controlled potential was also inhibited at high DNA concentrations (not shown).

The presumed self-inactivation of Fe·BLM was studied by carrying out electrochemical activation in the presence and absence of DNA.[22] Aerobic electrolysis of Fe^{III}·BLM[23] resulted in a decrease in current to <20% (9.5 μA) of the initial value after passage of 10.2 electron equiv. Recovery of the electrolyzed Fe·BLM permitted verification that it had been substantially inactivated; by using fresh Fe(II), this sample degraded d($CGCT_3A_3GCG$) only 6% as well as a control sample of Fe·BLM. When the electrolysis was carried out in the presence of 0.63 mM d($CGCT_3A_3GCG$), the current was still 23.5 μA after passage of 14.4 electron equiv, indicating protection by DNA against Fe·BLM self-inactivation.

The foregoing data are consistent with a BLM activation mechanism involving initial reduction of Fe^{III}·BLM, followed by binding of O_2 and further reduction of the derived ternary complex (Scheme I). The data suggest strongly that both initial electrochemical reduction of Fe^{III}·BLM to Fe^{II}·BLM and reductive activation of Fe^{II}·BLM precede DNA binding. These observations place important constraints on the possible mechanistic schemes for Fe·BLM-mediated DNA degradation and should facilitate better definition of the individual steps involved.

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(17) Moreover, the specificity for modification at C_3 and $C_7(C_{11})$ as well as the strand selectivity (C_3 vs $C_7(C_{11})$), two characteristic features of individual activated BLMs,[8] were identical for electrochemically and chemically activated Fe·BLMs, suggesting that these species were the same. The maximum extent of DNA modification was also similar, presumably reflecting competitive self-inactivation of activated Fe·BLMs.[18] In fact, current flow diminished during the course of electrolysis.

(18) Although quantitation of the faradaic efficiency of Fe·BLM-mediated DNA degradation was hindered by the small volumes and limited amounts of substrates employed, the efficiency was clearly high in the context of the presumed stoichiometry of Fe·BLM activation.[7,8]

(19) In the presence of 1 and 2 mM calf thymus DNA, the current obtained with 500 μM Fe·BLM diminished from 1.19 to 0.94 and 0.63 μA, respectively.

(20) Carter, M. T.; Bard, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 7528.

(21) That this was not due to physical exclusion of the DNA-bound Fe·BLM from the electrode surface was suggested by a parallel observation in other BLM activating systems. See: (a) Burger, R. M.; Peisach, J.; Blumberg, W. E.; Horwitz, S. B. *J. Biol. Chem.* **1979**, *254*, 10906. (b) Albertini, J.-P.; Garnier-Suillerot, A.; Tosi, L. *Biochem. Biophys. Res. Commun.* **1982**, *104*, 557. (c) Ciriolo, M. R.; Magliozzo, R. S.; Peisach, J. *J. Biol. Chem.* **1987**, *262*, 6290. A slight shift in the redox potential of Fe·BLM to a more negative value was observed by differential pulse polargraphy upon admixture of moderate concentrations of DNA. The significance of this observation is unclear, however, since the current obtained from 0.16 mM Fe·BLM and high concentrations (14 mM) of sonicated calf thymus DNA was <1.5% of that obtained in its absence.

(22) For another approach, see: Nakamura, M.; Peisach, J. *J. Antibiot.* **1988**, *41*, 638.

(23) Electrolysis was carried out using 0.20 mM Fe^{III}·BLM A_2 in 1 mL of 50 mM Na cacodylate, pH 7.2, in a cell containing a 3.14 cm^2 glassy carbon plate electrode. The background current was negligible (<2% of the initial current).

Rate-Determining Complexation in Catalytic Hydrolysis of Unactivated Esters in Neutral Water

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Nature had a considerable head start[1] in developing catalysts that hydrolyze simple esters such as acetylcholine. In the past 40 years many research teams worldwide have been trying hard to catch up to nature. Much has been learned by mimicking various catalytic features of esterases with elegant enzyme models.[2-7] However, one critical difference between the esterases and their models is their reactivity.[7,8] Nature has a monopoly on true catalysts that hydrolyze unactivated esters under mild conditions. In model studies, the esters are either highly activated (e.g., *p*-nitrophenyl acetate[2] or methyl trifluoroacetate[7]) or they are permanently anchored to various catalytic groups preventing any catalytic turnover.[3-6] Currently there is considerable interest in developing artificial esterases and peptidases that hydrolyze unactivated esters and amides.[9] Here we report on the first nonenzymic, catalytic hydrolysis of methyl acetate and acetylcholine in neutral water at 25 °C.

$[(trpn)Co(OH)(OH_2)]^{2+}$ (**1**)-catalyzed hydrolysis of methyl acetate was monitored by the pH stat method (trpn: tris(aminopropyl)amine). In a typical kinetic experiment, methyl acetate (1 M) and $[(trpn)Co(OH_2)_2]^{3+}$ (1 mM) in 5 mL of water were stirred at 25 °C. The pH of the reaction solution was maintained at 7.6 with a Radiometer PHM63 pH meter equipped with a Radiometer RTS822 automatic titrator.[10] Figure 1 shows the acetic acid production vs time plot. Three turnovers of the catalyst

(1) By about 4 000 000 000 years.

(2) (a) Breslow, R.; Trainor, G.; Ueno, A. *J. Am. Chem. Soc.* **1983**, *105*, 2739. (b) Cram, D. J.; Lam, P. Y.; Ho, S. P. *J. Am. Chem. Soc.* **1986**, *108*, 839. (c) Lehn, J. M.; Sirlin, C. *J. Chem. Soc., Chem. Commun.* **1978**, 949.

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(8) Menger, F. M.; Ladika, M. *J. Am. Chem. Soc.* **1987**, *109*, 3145.

(9) (a) Kahn, D.; Still, W. C. *J. Am. Chem. Soc.* **1988**, *110*, 7529. (b) Janda, K. D.; Schloeder, D.; Benkovic, S. J.; Lerner, R. A. *Science* **1988**, *241*, 1188. (c) D'Souza, V. T.; Bender, M. L. *Acc. Chem. Res.* **1987**, *20*, 146. (d) Skorey, K. I.; Somayaji, V.; Brown, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 5205.

(10) Maximum efficiency of the cobalt complex was obtained at about pH 7.6.

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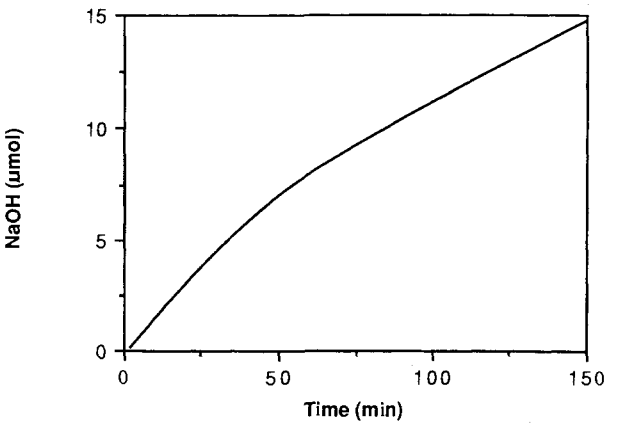
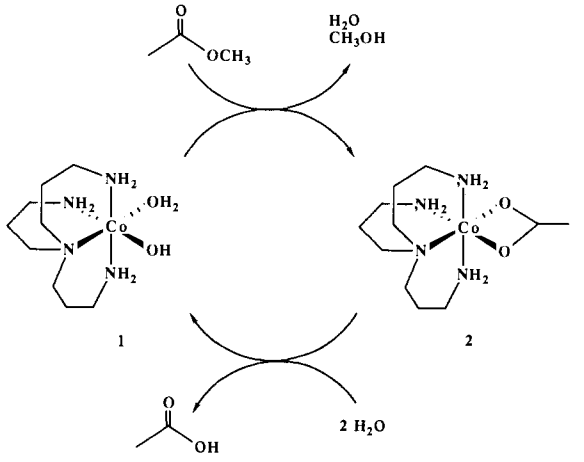


Figure 1. Consumption of NaOH with time in $[(trpn)Co(OH_2)_2]^{3+}$ (5 μmol)-catalyzed hydrolysis of methyl acetate (1 M) at pH 7.6, 25 °C.

Scheme I



take place within 150 min. Production of methanol was confirmed by ^1H NMR. In sharp contrast, when $[(tren)Co(OH_2)_2]^{3+}$ is used in the above procedure instead of $[(trpn)Co(OH_2)_2]^{3+}$, acetic acid production is too slow to be observed (tren: tris(aminoethyl)-amine).

The catalytic cycle for $[(trpn)Co(OH)(OH_2)]^{2+}$-catalyzed hydrolysis of methyl acetate is shown in Scheme I. **1** has been fully characterized previously.[11] **2** was synthesized by adding 1 equiv of NaOAc to $[(trpn)Co(OH_2)_2]^{3+}$ in water followed by precipitation with $NaClO_4$. The crude product was recrystallized from water.[12] A number of bidentate acetate metal complexes have been reported in the literature.[13]

Although **2** forms readily upon addition of NaOAc to $[(trpn)Co(OH_2)_2]^{3+}$, the corresponding bidentate acetate did not form upon addition of NaOAc to $[(tren)Co(OH_2)_2]^{3+}$. ^{13}C NMR of a D_2O solution of ^{13}C enriched NaOAc (98% at the carboxyl carbon) and $[(tren)Co(OH_2)_2]^{3+}$ (10 mM each) consists of four signals (δ 185.4, 186.4, 186.8, and 188.2) due to acetate bound to the cobalt complex (monodentate) and one signal due to free acetic acid (δ 185).[14] Since the two aquo positions on the cobalt complex are nonequivalent, mono- and diacetates of the cobalt complex should give a total of four ^{13}C NMR signals (Figure 2, bottom: a, b, c, and d). In sharp contrast, when $[(trpn)Co(OH_2)_2]^{3+}$ is used instead of $[(tren)Co(OH_2)_2]^{3+}$ a major new signal appears (f: δ 197.0) at the expense of the other five signals (Figure 2, top). The new signal is due to the formation of a bidentate acetate complex (**2**). It is interesting that $[(trpn)Co(OH_2)_2]^{3+}$ forms the four-membered ring bidentate complex, whereas $[(tren)Co(OH_2)_2]^{3+}$ does not. **2** provides the first direct evidence for the tetraamine ligand effect in stabilizing four-membered rings.[11c] Strongly basic bidentate ligands such as carbonate can form four-membered ring carbonato complexes with either $[(trpn)Co(OH_2)_2]^{3+}$ or $[(tren)Co(OH_2)_2]^{3+}$.[15]

The equilibrium constant for formation of **2** from $[(trpn)Co(OH_2)_2]^{3+}$ and NaOAc was measured by potentiometric titration

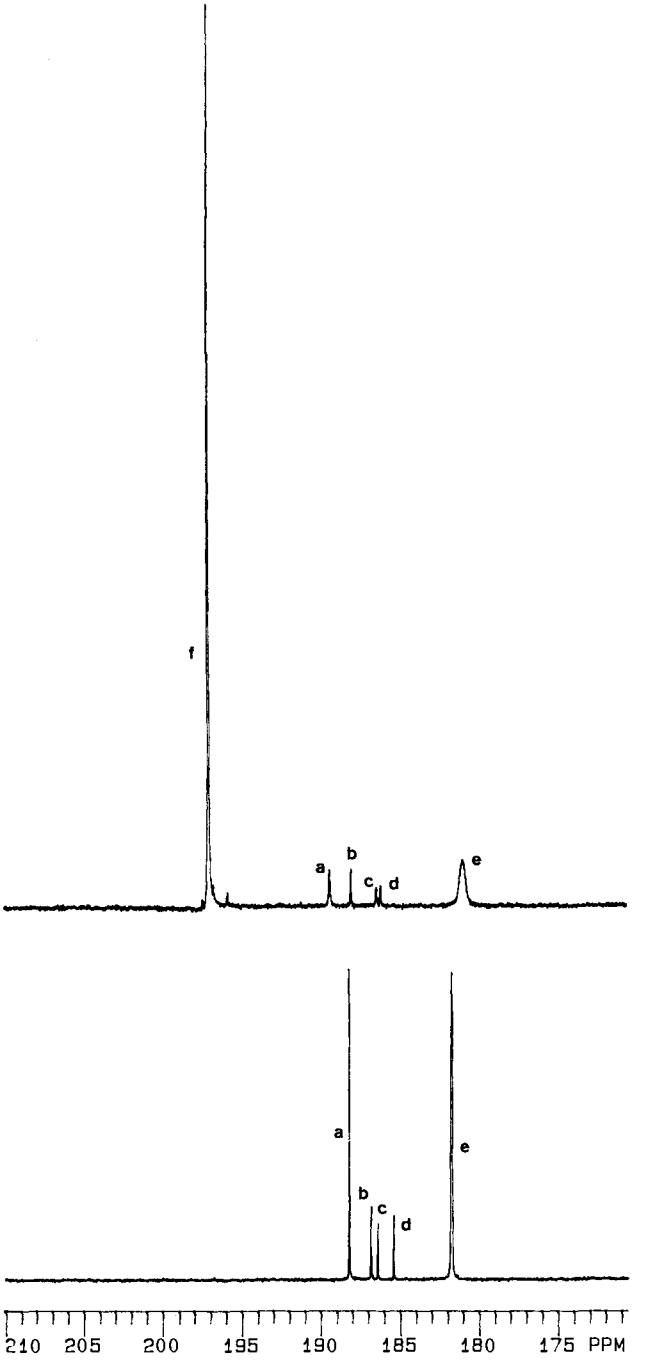


Figure 2. ^{13}C NMR carboxyl carbon. Bottom: a = $[(tren)Co(OAc)(H_2O)]^{2+}$; c = $[(tren)Co(H_2O)(OAc)]^{2+}$; b and d = $[(tren)Co(OAc)_2]^{+}$; e = AcOH. Top: a = $[(trpn)Co(OAc)(H_2O)]^{2+}$; b = $[(trpn)Co(H_2O)(OAc)]^{2+}$; c and d = $[(trpn)Co(OAc)_2]^{+}$; e = AcOH; f = $[(trpn)Co(OAc)]^{2+}$.

(11) (a) Tafesse, F.; Massoud, S. S.; Milburn, R. M. *Inorg. Chem.* **1985**, *24*, 2952. (b) Chin, J.; Banaszczyk, M.; Jubian, V.; Zou, X. *J. Am. Chem. Soc.* **1989**, *111*, 186. (c) Chin, J.; Banaszczyk, M.; Jubian, V. *J. Chem. Soc., Chem. Commun.* **1988**, 735.

(12) ^{13}C NMR (300 MHz, D_2O, (dioxane)) 197.0 (carboxyl carbon); UV/vis λ_{max} = 361 nm (ε = 151), 531 nm (ε = 69). Anal. Calcd for $C_{11}H_{27}N_4O_2Co\cdot 2ClO_4\cdot H_2O$: C, 25.25; H, 5.59; N, 10.71; Co, 11.26; Cl, 13.55. Found: C, 25.43; H, 5.49; N, 10.74; Co, 11.51; Cl, 13.56.

(13) Burk, M. J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1987**, *109*, 8025.

(14) The peaks were easily assigned by varying the amount of acetate (Supplementary Material, Figures 3 and 4). For ^{13}C NMR of Co(III) bound carboxylates, see: Taura, T. *Inorg. Chem.* **1988**, *27*, 2845.

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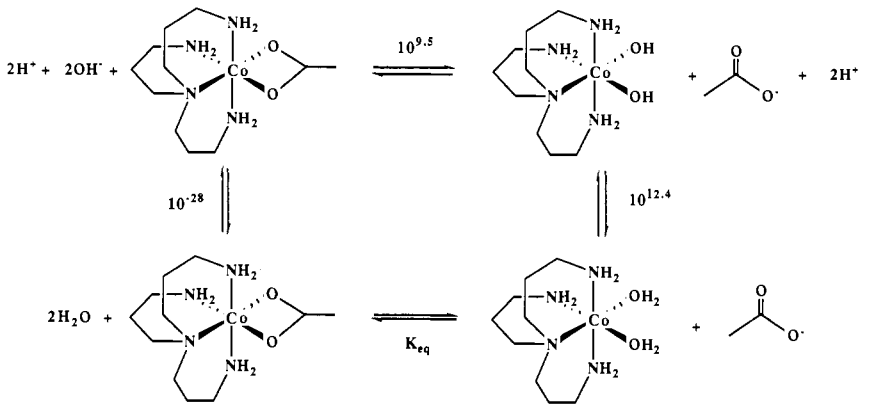
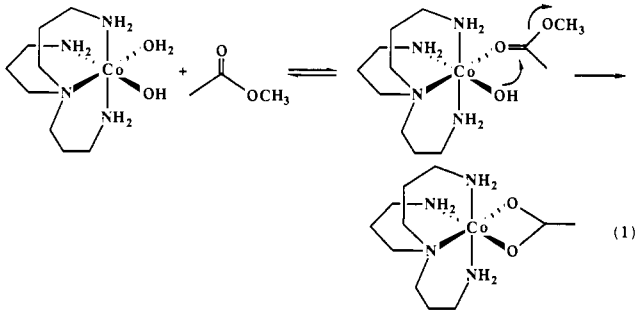
Scheme II



of **2**. Two equiv of NaOH are consumed in forming $[(trpn)Co(OH)_2]^+$ and NaOAc from **2** (Scheme II). The midpoint of the titration curve is at pH = 7.6 when the initial concentration of **2** is 1 mM. Therefore, the equilibrium constant for displacement of acetate from **2** with 2 equiv hydroxide is $10^{9.5}$ M^{-1} (Scheme II). Since $K_w = 10^{-14}$ and the pK_{a1} and pK_{a2} values of $[(trpn)Co(OH_2)_2]^{3+}$ are 4.8 and 7.6, respectively,[11b] the equilibrium constant for formation of **2** from $[(trpn)Co(OH_2)_2]^{3+}$ and NaOAc can be obtained from the cycle in Scheme II ($K_{eq} = 10^{6.1}$ M^{-1}). Due to the tight association of NaOAc to $[(trpn)Co(OH_2)_2]^{3+}$, there is considerable product inhibition during $[(trpn)Co(OH_2)(OH)]^{2+}$-catalyzed hydrolysis of methyl acetate below pH 7.6.

The rate constant for dissociation of acetate from **2** at pH 7.6 was measured by the pH stat method ($k = 2.3 \times 10^{-2}$ s^{-1}). Since the turnover time (30 min) of the catalyst is much greater than the half-life (30 s) for dissociation of acetate from **2**, the rate-determining step in the catalytic cycle (Scheme I) should not be the dissociation step. Therefore the rate-determining step should be either the complexation step or the ester bond cleavage step (eq 1).[16] Interestingly, the second-order rate constants for formation of **2** from $[(trpn)Co(OH_2)(OH)]^{2+}$ and methyl acetate (5.5×10^{-3} M^{-1} s^{-1}), *p*-nitrophenyl acetate (7.4×10^{-3} M^{-1} s^{-1}), or acetylcholine (4.0×10^{-3} M^{-1} s^{-1}) are comparable (at pH 7.0, 25 °C), indicating that complexation of the ester to the cobalt complex is the rate-determining step.[17]



(1)

The water rate for methyl acetate hydrolysis is very slow (3.16×10^{-10} s^{-1} at 25 °C, half-life = 70 years).[18] We have demonstrated for the first time, efficient catalytic hydrolysis of methyl acetate and acetylcholine in neutral water at 25 °C. The rate-determining step in the catalytic cycle is complexation of the ester to the catalyst. A key four-membered ring intermediate $[(trpn)Co(OAc)]^{2+}$ in the catalytic cycle has been isolated for the first time. The stability of the four-membered ring intermediate is highly sensitive to the tetraamine ligand structure.

Acknowledgment. We thank Suzanne Lilker for preliminary work. This work was supported by the Natural Sciences and Engineering Research Council of Canada.

Supplementary Material Available: Figures of ^{13}C NMR spectra of carboxyl carbon (2 pages).[14] Ordering information is given on any current masthead page.

(16) Direct intermolecular metal-hydroxide mechanism can be ruled out since monoaquo metal complexes are not active.[7]

(17) The second-order rate constants were obtained from the rate of formation of **2**. In a typical kinetic experiment, methyl acetate (0.1 M) was allowed to react in a buffered solution (pH 7, 0.02 M collidine; ionic strength 0.1 M with $NaClO_4$) of $[(trpn)Co(OH_2)(OH)]^{2+}$ (10 mM) at 25 °C. Formation of **2** was monitored by following the increase in the visible absorption at λ_{max} for **2** (531 nm).

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Reversible Redox Processes in Main-Group/Transition-Metal Clusters: The $[Sb_2Co_4(CO)_{10}(\mu\text{-}CO)]^{-/2-}$ Couple

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Elaborate theories have developed over the past 20 years to aid in understanding structure and bonding in small metal clusters.[1-7] Dahl and co-workers have performed numerous studies focusing on the geometric effects caused by changes of electronic configurations in various metal clusters.[8] They have found that many

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(7) (a) King, R. B.; Rouvray, D. H. *J. Am. Chem. Soc.* **1977**, *99*, 7834. (b) King, R. B. *Inorg. Chem. Acta* **1986**, *116*, 99. (c) King, R. B. *Inorg. Chem. Acta* **1986**, *116*, 119. (d) King, R. B. *Inorg. Chem. Acta* **1986**, *116*, 125.

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