The cyclic voltammogram for the reduction potential in DMSO of (*p*-nitrophenyl)diphenylmethane shown in Figure 1 is typical of those for the hydrocarbons containing one or more nitro groups.

The E_{re}(HA) value for 9-cyanoxanthene (9-CN-Xn) is in the same region as observed for most monosubstituted triphenylmethanes (-2.843), but 9-CN-Xn has a pK_{HA} about 20 kcal lower than most $GC_6H_4CHPh_2$ compounds. As a consequence, its $BDE_{HA\bullet-}$ value is also about 20 kcal lower. On the other hand, its $E_{ox}(A^{\bullet})$ and BDE_{HA} are of moderate size, and the $BDE_{HA\bullet+}$ value is 39 kcal, i.e., 50% *larger* than its $BDE_{HA\bullet-}$ value, rather than 50% smaller, which is the rule for the other $BDE_{HA\bullet+}$ values in Table III.

Experimental Section

Materials. The compounds used have all been prepared previously (see the footnotes in the tables for references).

Electrochemistry. The reduction potentials of the neutral weak acids and the oxidation potentials of the corresponding conjugate anions were measured in DMSO solution by cyclic voltammetry with 0.1 M tetraethylammonium tetrafluoroborate as supporting electrolyte. The working electrode for the measurements of the reduction potentials was a glassy carbon electrode, and that for the measurements of the oxidation potentials was a Pt electrode. The auxiliary electrode was Pt, and the reference electrode was Ag/AgI. The sweep rate was 100 mV/s, and the redox potentials reported were referenced to ferrocene-ferrocenium (Fc/Fc^+) couple ($E_{1/2}$ = 0.875 V).[8]

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Registry No. 1, 86-73-7; **2**, 34484-03-2; **4**, 143959-25-5; **5**, 144017-24-3; **6**, 607-57-8; **7**, 90405-77-9; **8**, 7596-59-0; $8^{\bullet-}$, 144017-27-6; $8^{\bullet+}$, 116997-79-6; **10**, 144017-34-5; 2-$PhSO_2FlH_2$, 59014-85-6; 2-$PhSO_2FlH_2^{\bullet-}$, 143959-24-4; 2-$CNFlH_2$, 2523-48-0; 2-Me_2NFlH_2, 13261-62-6; 9-$PhSO_2FlH$, 22010-78-2; 9-$PhSO_2FlH^{\bullet-}$, 144017-25-4; 9-CO_2MeFlH, 3002-30-0; 9-$CO_2MeFlH^{\bullet-}$, 135256-58-5; 2,7-Br_2-9-CO_2MeFlH, 73838-62-7; 2,7-Br_2-9-$CO_2MeFlH^{\bullet-}$, 135356-41-1; 9-EtOFlH, 2868-70-4; 9-$EtOFlH^{\bullet-}$, 143959-26-6; 9-EtSFlH, 60147-53-7; 9-$EtSFlH^{\bullet-}$, 143959-27-7; $FlH_2^{\bullet+}$, 34985-70-1; 9-PhFlH, 789-24-2; 9-$PhFlH^{\bullet-}$, 38691-37-1; 9-$PhFlH^{\bullet+}$, 113566-64-6; 9-mesityl-FlH, 18153-40-7; 9-mesityl-$FlH^{\bullet-}$, 144017-26-5; 9-mesityl-$FlH^{\bullet+}$, 113533-48-5; 9-Me_2NFlH, 53156-46-0; 9-$Me_2NFlH^{\bullet-}$, 83936-72-5; 9-$Me_2NFlH^{\bullet+}$, 117065-69-7; 9-piperidino-FlH, 3333-06-0; 9-piperidino-$FlH^{\bullet-}$, 144017-28-7; 9-piperidino-$FlH^{\bullet+}$, 116997-80-9; 9-$PhCH_2$(Me)NFlH, 102478-64-8; 9-$PhCH_2$(Me)$NFlH^{\bullet-}$, 144017-29-8; 9-$PhCH_2$(Me)$NFlH^{\bullet+}$, 141320-02-7; 9-(*i*-Pr)$_2$NFlH, 109495-00-3; 9-(*i*-Pr)$_2$$NFlH^{\bullet-}$, 144017-30-1; 9-(*i*-Pr)$_2$$NFlH^{\bullet+}$, 116997-76-3; 9-(2,6-dimethylpiperidino)FlH, 116997-66-1; 9-(2,6-dimethylpiperidino)$FlH^{\bullet-}$, 144017-31-2; 9-(2,6-dimethylpiperidino)$FlH^{\bullet+}$, 116997-81-0; 9-(2,2,6,6-tetramethylpiperidino)FlH, 116997-84-3; 9-(2,2,6,6-tetramethylpiperidino)$FlH^{\bullet-}$, 144017-32-3; 9-(2,2,6,6-tetramethylpiperidino)$FlH^{\bullet+}$, 141320-04-9; 4-$NO_2C_6H_4CH_3$, 99-99-0; 4-$NO_2C_6H_4CH_3^{\bullet-}$, 34509-96-1; Ph_2CH_2, 101-81-5; $Ph_2CH_2^{\bullet-}$, 34512-70-4; $Ph_2CH_2^{\bullet+}$, 82189-87-5; (4-$NO_2C_6H_4)_2CH_2$, 1817-74-9; (4-$NO_2C_6H_4)_2CH_2^{\bullet-}$, 34533-75-0; Ph_3CH, 519-73-3; $Ph_3CH^{\bullet-}$, 75366-18-6; $Ph_3CH^{\bullet+}$, 88424-77-5; 4-$PhCH_4CHPh_2$, 745-36-8; 4-$PhC_6H_4CHPh_2^{\bullet-}$, 143959-28-8; 4-$PhSC_6H_4CHPh_2$, 85554-39-8; 4-$PhSC_6H_4CHPh_2^{\bullet-}$, 143959-29-9; 3-$CF_3C_6H_4CHPh_2$, 13865-59-3; 3-$CF_3C_6H_4CHPh_2^{\bullet-}$, 143959-30-2; 3-$NO_2C_6H_4CHPh_2$, 6630-83-7; 3-$NO_2C_6H_4CHPh_2^{\bullet-}$, 143959-31-3; 4-$PhSO_2C_6H_4CHPh_2$, 85554-27-4; 4-$PhSO_2C_6H_4CHPh_2^{\bullet-}$, 143959-32-4; 4-$PhCOC_6H_4CHPh_2$, 7375-38-4; 4-$PhCOC_6H_4CHPh_2^{\bullet-}$, 144017-33-4; 4-$PhCOC_6H_4CHPh_2^{\bullet+}$, 141320-07-2; 4-$NO_2C_6H_4CHPh_2$, 2945-12-2; 4-$NO_2C_6H_4CHPh_2^{\bullet+}$, 141320-08-3; (4-$NO_2C_6H_4)_3CH$, 603-49-6; (4-$NO_2C_6H_4)_3CH^{\bullet-}$, 143959-33-5; (4-$NO_2C_6H_4)_3CH^{\bullet+}$, 144017-36-7; 4-$NO_2C_6H_4$(4-$MeOC_6H_4)_2CH$, 128527-22-0; 4-$NO_2C_6H_4$(4-$MeOC_6H_4)_2CH^{\bullet-}$, 143959-34-6; 4-$NO_2C_6H_4$[2,4-$(MeO)_2C_6H_3]_2CH$, 143959-23-3; 4-$NO_2C_6H_4$[2,4-$(MeO)_2C_6H_3]_2CH^{\bullet-}$, 143959-35-7; 4-$NO_2C_6H_4$(4-$MeC_6H_4)_2CH$, 69361-51-9; 4-$NO_2C_6H_4$(4-$MeC_6H_4)_2CH^{\bullet-}$, 143959-36-8; 4-$NO_2C_6H_4$-(2,4-$Me_2C_6H_3)_2CH$, 98293-92-6; 4-$NO_2C_6H_4$(2,4-$Me_2C_6H_3)_2CH^{\bullet-}$, 143959-37-9; Xn, 92-83-1; $Xn^{\bullet-}$, 41174-13-4; $Xn^{\bullet+}$, 41174-12-3; 9-PhXn, 3246-80-8; 9-$PhXn^{\bullet-}$, 58378-46-4; 9-$PhXn^{\bullet+}$, 141394-69-6; 9-CNXn, 85554-24-1; 9-$CNXn^{\bullet-}$, 144017-35-6; 9-$CNXn^{\bullet+}$, 130920-17-1.

Dimethyl Phosphate Hydrolysis at Neutral pH

Jung Hee Kim and Jik Chin*

Contribution from the Department of Chemistry, McGill University, Montreal, Quebec, Canada H3A 2K6. *Received June 23, 1992*

Abstract: $[(cyclen)Co(OH_2)_2]^{3+}$ (**1**) hydrolyzes dimethyl phosphate with a second-order rate constant of 6.2×10^{-7} M^{-1} s^{-1} at 60 °C, pD 6.3 (cyclen: 1,4,7,10-tetraazacyclododecane). In contrast, $[(tetren)Co(OH_2)]^{3+}$ (**2**) does not hydrolyze the diester to any observable extent, even when the reaction solution is heated to 100 °C for 1 month (tetren: tetraethylenepentamine). The mechanism for **1**-promoted hydrolysis of dimethyl phosphate involves joint Lewis acid activation and metal hydroxide activation.

Nature has chosen the ester linkage for lipids, the amide linkage for proteins, and the phosphate diester linkage for nucleic acids. Among the three types of linkages, phosphate diesters are by far the most stable. Under basic conditions, dimethyl phosphate[1] is about 10^6 times more stable than *N*-methylacetamide,[2] which in turn is about 3×10^5 times more stable than methyl acetate[3] (Table I). Perhaps not surprisingly, the linkage that is by far the most difficult to hydrolyze is the one that nature chose to preserve the genetic material. Over the years, there has been considerable interest in developing catalysts that hydrolyze unactivated phosphate diesters like DNA. Although artificial restriction enzymes that cleave DNA oxidatively with amazing sequence specificity have been synthesized,[4,5] those that cleave DNA hydrolytically have yet to be developed. It has recently been shown that ribozymes activated by metal ions hydrolyze DNA sequence specifically.[6,7] However, the mechanistic role of metal

Table I. Second-Order Rate Constant (k_{OH}) for Hydroxide-Catalyzed Hydrolysis of Substrates at 25 °C

substrate	k_{OH} (M^{-1} s^{-1})
$NaOP(O)(OCH_3)_2$	6.8×10^{-12}
$CH_3C(O)NHCH_3$	5.0×10^{-6}
$CH_3C(O)OCH_3$	1.5×10^{-1}

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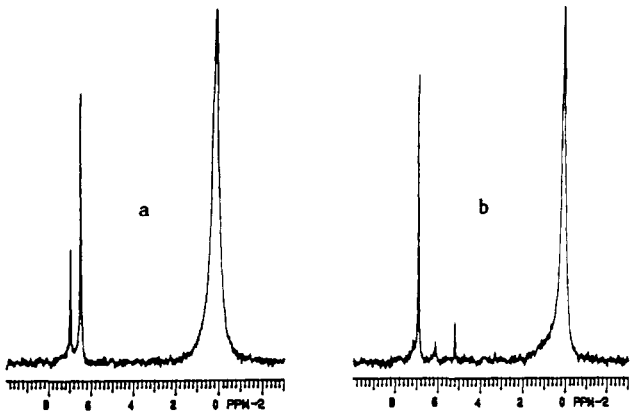
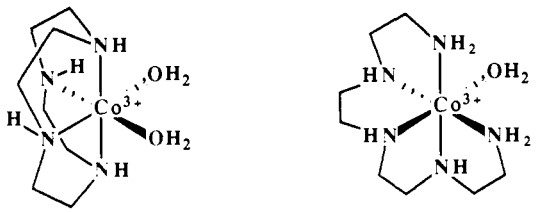


Figure 1. ^{31}P NMR for binding of dimethyl phosphate (0.1 M) to **1** (0.1 M, a) and **2** (0.1 M, b) at pD 2, 22 °C.

ions in ribozymes is not known. Numerous studies on the effect of simple metal complexes on the hydrolysis of phosphate esters have been reported. Although simple metal complexes efficiently hydrolyze activated phosphate diesters[8] and RNA,[9] they have been shown to be inactive[10] for hydrolyzing unactivated phosphate diesters like dimethyl phosphate and DNA. Indeed, hydrolysis of dimethyl phosphate (P–O bond cleavage) has never been detected at neutral pH. It is important to study the effect of catalysts on unactivated substrates, since the mechanism for hydrolyzing activated substrates may not necessarily be the same as that for hydrolyzing unactivated substrates. Herein we report on the reactivities of **1** and **2** for hydrolyzing dimethyl phosphate and its implications on the mechanistic role of metal ions in ribozymes.



1 2

Experimental Section

Instruments. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded in D_2O on a Varian XL-300 spectrometer.

Materials. 1,4,7,10-tetraazacyclododecane (cyclen) and tetraethylenepentamine (tetren) were purchased from Aldrich. $[Co(cyclen)(OH_2)_2](ClO_4)_3$ and $[Co(tetren)OH_2]Cl(ClO_4)_2$ were prepared according to literature procedures.[8,11,12]

$[Co(cyclen)CO_3]ClO_4$. A solution of cyclen (1 mmol) in water (5 mL) was added to a solution of $Co(ClO_4)_2 \cdot 6H_2O$ (1 mmol) in water (5 mL). To this mixture were added PbO_2 (1.5 mmol) and $NaHCO_3$ (1 mmol). The resulting suspension was stirred overnight at ambient temperature, and the pH of the solution was adjusted to about 6.5 with dilute perchloric acid. After filtration of the solution, the filtrate was evaporated to dryness in vacuo. The crude residue was triturated with absolute ethanol and recrystallized from water (80% yield): ^{13}C NMR (75.4 MHz, D_2O, (dioxane)) δ 167.43 (CO_3), 56.47, 54.02, 50.02, 47.91.

Anal. Calcd for $C_9H_{20}ClCoN_4O_7$: C, 27.67; H, 5.16; N, 14.34; Cl, 9.07; Co, 15.09. Found: C, 27.43; H, 4.76; N, 14.26; Cl, 8.93; Co, 15.19.

$[Co(cyclen)(OH_2)_2](ClO_4)_3$. To a solution of $[Co(cyclen)CO_3]ClO_4$ (1 mmol) in water (0.5 mL) was added dropwise 70% aqueous $HClO_4$ (2.5 mmol) and the mixture was stirred at ambient temperature until CO_2 evolution ceased. The mixture was then stirred under reduced pressure for 0.5 h and evaporated to dryness in an ice-water bath. The residue was triturated with anhydrous ethyl ether, filtered, and dried in vacuo over P_2O_5: ^{13}C NMR δ 57.97, 54.6, 50.6, 48.6.

$[Co(tetren)Cl](ClO_4)_2$. The cobalt complex was prepared according to published procedures.[12] It is well known that this cobalt complex undergoes rapid aquation to $[Co(tetren)OH_2]Cl(ClO_4)_2$ in water.[13]

Anal. Calcd for $C_8H_{23}Cl_3CoN_5O_8$: C, 19.91; H, 4.8; N, 14.51; Cl, 22.04; Co, 12.21. Found: C, 19.87; H, 5.27; N, 14.47; Cl, 21.91; Co, 12.11.

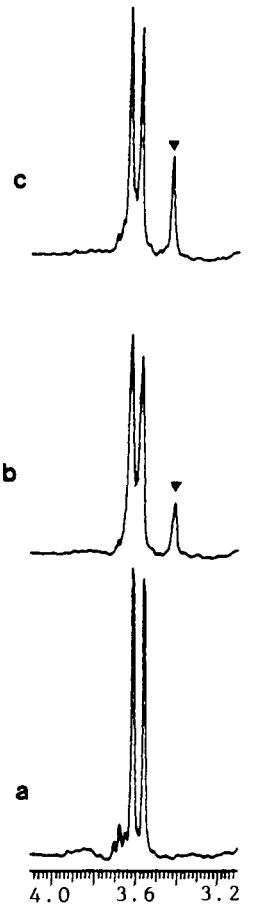


Figure 2. ^{1}H NMR of dimethyl phosphate (0.5 M) after adding **1** (0.2 M) at pD 5.5, 80 °C. (▼) methanol. Elapsed time: (a) 0 h, (b) 115 h, (c) 480 h.

Equilibrium. The equilibrium constants for the binding of dimethyl phosphate to the cobalt complexes **1** and **2** were measured by ^{31}P NMR (Figure 1). Sodium dimethyl phosphate (0.1 M) was allowed to react with the cobalt complexes (0.1 M) in D_2O. Equilibrium for complexation of dimethyl phosphate to the cobalt complexes was established within hours at pD 2 and 20 °c.

Kinetics. Hydrolysis of dimethyl phosphate was monitored by ^{1}H NMR (Figure 2). In a typical experiment, dimethyl phosphate (0.5 M) was allowed to react with **1** (0.2 M) in D_2O at pD 6.3 and 60 °C. Each kinetic run was reproducible to within 10% error.

Results and Discussion

The equilibrium constants for complexation of dimethyl phosphate to **1** and **2** as measured by ^{31}P NMR are 2.8 M^{-1} and 2.4 M^{-1}, respectively. Dimethyl phosphate coordinates to **1** (δ 6.48 and 6.97 relative to free dimethyl phosphate) and **2** (δ 6.90) as a monodentate ligand (Figure 1). The two water molecules in **1** are not equivalent as a result of asymmetric complexation of cyclen to cobalt.[14] Dimethyl phosphate can replace either water molecule in **1**, resulting in the two ^{31}P NMR signals. Dimethyl phosphate does not chelate to **1**. The ^{31}P NMR chemical shift

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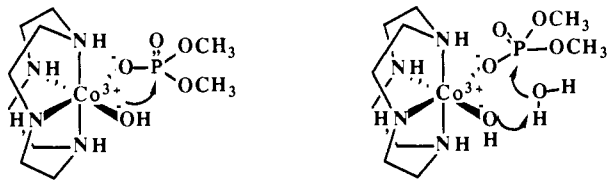
Scheme I



a b

would have been about twice as large as observed if there were any chelation.[15]

Hydrolysis of dimethyl phosphate was monitored by ^{1}H NMR (Figure 2). With the progress of the hydrolysis reaction, the NMR signal due to methanol (δ 3.42 relative to DSS) increased with a concomitant decrease in the signal due to dimethyl phosphate (δ 3.57, d). Concentration of monomethyl phosphate did not accumulate to an observable extent during the hydrolysis reaction. It is well known that *cis*-diaqua cobalt complexes efficiently hydrolyze phosphate monoesters.[10a,15] The second-order rate constant for **1**-promoted hydrolysis of dimethyl phosphate is 6.2×10^{-7} M^{-1} s^{-1} at pD 6.3 and 60 °C and 2.2×10^{-6} M^{-1} s^{-1} at pD 5.5 and 80 °C. Since the equilibrium constant for complexation of dimethyl phosphate to **1** is 2.8 M^{-1}, the first-order rate constant for hydrolysis of the cobalt-bound diester is approximately 2×10^{-7} s^{-1} at 60 °C. When **1** was replaced with **2**, there was no observable hydrolysis of dimethyl phosphate, even when the reaction solution was heated at 100 °C for 1 month.

We propose that the mechanism for **1**-promoted hydrolysis of dimethyl phosphate involves coordination of the diester to the metal complex, followed by intramolecular metal hydroxide attack (Scheme Ia). Such a mechanism had been proposed for the hydrolysis of esters, amides, nitriles, and phosphate mono- and diesters.[16] It is unlikely that the metal hydroxide is an intramolecular general base catalyst (Scheme Ib). Effective molarities[17] of intramolecular general base-catalyzed reactions are too low to account for the large difference in the reactivities of **1** and **2** for hydrolyzing dimethyl phosphate. Oxidative cleavage[18] of dimethyl phosphate can be ruled out on the basis that 2 equiv of methanol are produced upon cleavage of the diester.

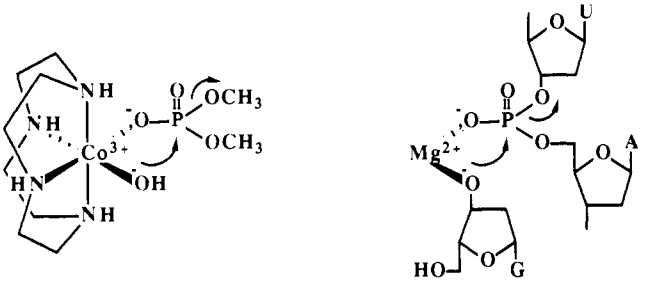
It has been shown that *cis*-diaqua cobalt complexes ($[Co(N_4)(OH_2)_2]^{3+}$, where N_4 represents a tetramine ligand) are highly efficient at hydrolyzing activated phosphate diesters.[8] *cis*-Diaqua cobalt complexes like **1** can provide joint Lewis acid activation and intramolecular metal hydroxide activation in hydrolyzing phosphate diesters, whereas monoaqua cobalt complexes like **2** can provide either Lewis acid activation or metal hydroxide activation but not both at the same time. The reactivities of *cis*-diaqua cobalt complexes are highly sensitive to their structures.[8] Specifically, the reactivity increases dramatically with a decrease in the angle that the two coordinated water molecules make at the metal center. **1** is one of the most reactive *cis*-diaqua cobalt complex for hydrolyzing activated phosphate diesters. One of the main reasons why **1** is so efficient at hydrolyzing dimethyl phosphate is its stability. Other *cis*-diaqua cobalt complexes, such as $[Co(trpn)(OH_2)_2]^{3+}$, that efficiently hydrolyze activated phosphate diesters undergo deligation of the tetramine ligand during the extended time period required to hydrolyze unactivated phosphate diesters (trpn:tris(3-aminopropyl)amine).

The second-order rate constant for **1**-promoted hydrolysis of dimethyl phosphate is 6.2×10^{-7} M^{-1} s^{-1} at 60 °C. This represents an enormous rate acceleration for dimethyl phosphate hydrolysis. The second-order rate constant for hydroxide-catalyzed hydrolysis of dimethyl phosphate at 25 °C is 6.8×10^{-12} M^{-1} s^{-1}.[1] Dimethyl phosphate is 2–3 orders of magnitude more stable than cyclic 3′:5′-nucleotides and 7 orders of magnitude more stable than cyclic 2′:5′-nucleotides.[19] The water rate for dimethyl phosphate hydrolysis (P–O bond cleavage) can be estimated as follows. Kirby and Younas[20] showed that there is a linear free energy relationship between the water rate for phosphate diester hydrolysis (P–O bond cleavage) at 100 °C and the conjugate acid pK_a of the leaving group (eq 1). The water rate for dimethyl phosphate hydrolysis

$$\log k = 1.57 - 0.97pK_a \quad (1)$$

at 100 °C is expected to be 3.4×10^{-14} s^{-1} (pK_a of methanol = 15.5). This represents a half-life of over 600 000 years for the P–O bond cleavage reaction at 100 °C. Kirby and Younas[20] measured the activation entropy for the water rate for bis(2,4-dinitrophenyl) phosphate hydrolysis ($\Delta S^{\ddagger} = -25.5$ eu). If it is assumed that the activation entropy for the water rate is independent of the diester being hydrolyzed,[1] then the activation enthalpy for dimethyl phosphate hydrolysis should be 35.5 kcal. The water rate for dimethyl phosphate hydrolysis calculated from the activation parameters is 1.9×10^{-19} s^{-1} at 25 °C and 9.3×10^{-17} s^{-1} at 60 °C.[21] The rate of hydrolysis of dimethyl phosphate bound to **1** is some 10^{10} times greater than the water rate for free dimethyl phosphate hydrolysis. In general, simple Lewis acid activation gives 2–3 orders of magnitude rate acceleration for hydrolyzing phosphate diesters.[22] Hence, intramolecular metal hydroxide activation in **1**-promoted hydrolysis of dimethyl phosphate is expected to give 7–8 orders of magnitude rate acceleration.

Scheme II



In an elegant study, Cech and Herschlag[6] showed that DNA bound to an RNA enzyme derived from the self-splicing intervening sequence of *Tetrahymena thermophila* is hydrolyzed sequence-specifically with a half-life of about 69 min at 50 °C. By comparison, dimethyl phosphate bound to **1** is hydrolyzed with a half-life of about 40 days at 60 °C. According to eq 1, the water rate for DNA hydrolysis should be somewhat greater than that for dimethyl phosphate hydrolysis, since the hydroxyl group in methanol is less acidic than the 3′-hydroxyl or the 5′-hydroxyl groups of nucleosides. Simple metal complexes that efficiently hydrolyze RNA molecules have been previously reported.[9] However, in those cases the 2′-hydroxyl group of the ribose is directly involved in the hydrolysis reaction as an intramolecular nucleophilic catalyst. Such intramolecular catalysis can give up to 10^8-fold rate acceleration.[17] An intriguing feature of the self-splicing RNA from *T. thermophila* is that the 2′-hydroxyl group is not directly involved in the hydrolysis reaction.[23] Perhaps the mechanistic role of Mg^{2+} in ribozymes for catalyzing trans-

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(21) The water rate for dimethyl phosphate had been previously overestimated by several orders of magnitude (2×10^{-14} s^{-1} at 25 °C[1] and 5×10^{-14} s^{-1} at 50 °C[6]). The first estimate[1] was based on the rate of dimethyl phosphate hydrolysis at 100 °C between pH 1 and 5, where the water rate is insignificant. The second estimate[6] was based on the hydroxide rate for dimethyl phosphate hydrolysis and the assumption that β_{nuc} for 2,4-dinitrophenyl methyl phosphate is the same as that for dimethyl phosphate hydrolysis. However, according to the reactivity–selectivity principle, β_{nuc} for dimethyl phosphate hydrolysis is expected to be greater than β_{nuc} for 2,4-dinitrophenyl methyl phosphate. Indeed, the ratio of the hydroxide rate to the water rate for diphenyl phosphate hydrolysis is much greater than that for bis(2,4-dinitrophenyl) phosphate hydrolysis.[20] Since ΔpK_a of hydronium and water is large (17.4), a small change in β_{nuc} could affect the estimate of the water rate by several orders of magnitude.
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esterification of DNA molecules is related to the mechanistic role of **1** for hydrolyzing dimethyl phosphate (Scheme II).

In conclusion, **1** efficiently hydrolyzes dimethyl phosphate at neutral pH. The equilibrium constant for complexation of dimethyl phosphate to **1** is 2.8 M^{-1}. The cobalt-bound phosphate diester is hydrolyzed with a half-life of 40 days at neutral pH and 60 °C. By comparison, the half-life for the water rate for dimethyl phosphate hydrolysis at 100 °C is estimated to be 600 000 years. **1**-Promoted hydrolysis of dimethyl phosphate represents the first hydrolysis of an unactivated phosphate diester at neutral pH.

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Acid-Catalyzed Amino-Migration of *O*-Phenylhydroxylamines

Naoki Haga,[†] Yasuyuki Endo,*[,†] Ken-ichiro Kataoka,[†] Kentaro Yamaguchi,[‡] and Koichi Shudo[†]

Contribution from the Faculty of Pharmaceutical Sciences, University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113, Japan, and Faculty of Pharmaceutical Sciences, Showa University, 1-5-8, Hatanodai, Shinagawa-ku, Tokyo 142, Japan. *Received February 28, 1992. Revised Manuscript Received August 18, 1992*

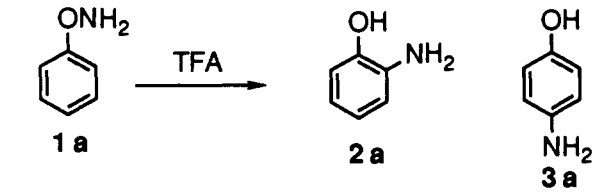
Abstract: The mechanism of amino-migration of *O*-phenylhydroxylamine (**1a**) was studied. It was found that **1** rearranges to give 2-aminophenol (50%) and 4-aminophenol (7%) in trifluoroacetic acid (TFA). The predominance of the ortho rearrangement of **1** clearly distinguishes this process from the Bamberger rearrangement. From cross-coupling experiments employing stable isotopes, it was clarified that the ortho rearrangement proceeds intramolecularly and the para rearrangement involves both intra- and intermolecular processes. Good first-order kinetics were obtained for the rearrangement. The Hammett plot (σ^+) with a large negative slope ($\rho = -7.8$) indicates that initial heterolytic N–O bond cleavage of **1** occurs and generates a positive charge on the oxygen atom with considerable delocalization into the aromatic ring. An ion–molecule pair involving a phenoxenium ion and an ammonia molecule as an intermediate rationalizes all of the results. In this pair, intramolecular combination to the ortho position proceeds preferentially over that to the para position. Formation of catechol and hydroquinone can be explained in terms of nucleophilic attack of TFA on the phenoxenium ion in a solvent-separated pair.

Introduction

Rearrangement of *N*-phenylhydroxylamine[1] to 4-aminophenol in aqueous sulfuric acid is well-known as the Bamberger rearrangement, which was discovered at the end of the nineteenth century. It has been believed that in this rearrangement the hydroxyl group is introduced into the aromatic ring via nucleophilic attack of a hydrosulfate ion upon the anilenium ion that is generated by the heterolytic N–O bond cleavage of O-protonated *N*-phenylhydroxylamine. Bamberger carried out the rearrangement of *N*-phenylhydroxylamine in nucleophilic solvents such as alcohols, hydrogen halides, phenols, and anilines and observed that they are incorporated into the aromatic ring.[2] Ingold et al.[3] examined the rearrangement of *N*-phenylhydroxylamine in ^{18}O-rich acidic water and found that the products are ^{18}O-enriched. Gassman et al. carried out the methanolysis of a series of *N*-*tert*-butyl-*N*-chloroanilines in the presence of silver trifluoroacetate.[4] The products obtained from these solvolyses differ greatly, depending on the nature of the substituent on the aromatic ring. The stronger the electron-donating power of the substituent, the higher the yield of anisidines and cyclohexadienones. In general, it has been proposed that the formation of all of these products involves the initial formation of a positively charged aromatic species.

In contrast to *N*-phenylhydroxylamine, *O*-phenylhydroxylamine is a relatively new compound, synthesized by Bungardner and Lilly in 1962,[5] so its properties have been less well studied. Among analogs of *O*-phenylhydroxylamines, *N*-acyl-*O*-phenylhydroxylamines have been studied by Endo et al. They reported acid-catalyzed rearrangements of *N*-benzoyl-*O*-phenylhydroxylamine to catechol derivatives,[6] *N*-alkyl-*N'*-phenoxyureas to *N*-alkyl-*N*-(2-hydroxyphenyl)ureas,[7] and *O*-aryl-*N*-acetoacetylhydroxylamines to benzofurans.[8] All of these reactions are considered

Scheme I



to involve concerted [3,3] sigmatropic rearrangements. In addition, the authors described acid-catalyzed nucleophilic substitutions of *N*-acyl-*O*-phenylhydroxylamines in the presence of aromatic nucleophiles such as benzenes.[9] A typical example is the reaction of *N*-tosyl-*O*-phenylhydroxylamine with benzene to give 2-hydroxybiphenyl and 4-hydroxybiphenyl in a mixture of trifluoromethanesulfonic acid (TFSA) and trifluoroacetic acid (TFA). Endo has proposed the intermediacy of phenoxenium ion, in which the positive charge is not on the electronegative oxygen but is delocalized on the aromatic ring, generated by the rate-

[†] University of Tokyo.
[‡] Showa University.

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