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ever, assignment of overall geometry requires further characterization. Dimeric structures are characteristic of Cu(II)–TEEN complexes reported here and elsewhere.[15]

The reaction chemistry of II is consistent with the formation of a dioxygen complex. Addition and removal of dioxygen cause the metal ion to shuttle between the +1 and +2 oxidation states. Adding dioxygen to methanol solutions of I produces II; this reaction is reversed by bubbling ethylene through the solution to produce I in nearly quantitative yield. Similarly, bubbling carbon monoxide through solutions of II yields the Cu(I)–carbonyl complex [Cu(TEEN)(CO)ClO$_4$].[8]

The decomposition reactions of II are characteristic of a peroxide complex. Stirring solutions of II under nitrogen at room temperature or low temperature yields the hydroxy-bridged copper(II) dimer III. The complex produced in this reaction has been identified by analytical, spectroscopic, and X-ray diffraction techniques.[16] This complex also precipitates from methanol solutions of II when a dioxygen atmosphere is not maintained over the solution and when dioxygen is added to I in the presence of excess ethylene. III may result from formation and disproportionation of hydrogen peroxide, a reaction characteristic of copper–dioxygen chemistry.[1,3]

The reaction chemistry of II under an atmosphere of dioxygen at room temperature is different from that under nitrogen. We have isolated and characterized by analytical, spectroscopic, and X-ray diffraction techniques a second bis(μ-hydroxy)dicopper(II) complex in which one of the eight ethyl groups of the two TEEN ligands has been hydroxylated, [Cu$_2$(TEEN)(TEEN+OH)(OH)$_2$]X$_2$ (IV) (X = ClO$_4$, BF$_4$).[17] The copper coordination spheres in this dimeric product are very similar to those in III with the addition of a weakly coordinated hydroxyl group of the TEEN+OH ligand to one copper ion in the dimer. The complex with X = ClO$_4$ shows OH stretches at 3595 and 3565 cm^{-1} corresponding to the ethylhydroxyl and bridging hydroxyl groups. Hydroxylation of alkyl groups is not usually observed in the reactions of Cu(I) complexes with molecular oxygen, although hydroxylation of aromatic substrates is well-established.[1,3,18] The complex IV is obtained at least in part because the copper ions hold both the reduced oxygen moiety and the alkyl group in the proper orientation for reaction. Also, the oxygen atmosphere is critical. Experiments are in progress to determine the source of the incorporated oxygen atom. Oxidation of the ethyl groups of this ligand has been suggested in reactions of other Cu(I)–TEEN complexes with dioxygen.[15]

Three important properties of copper–dioxygen coordination chemistry emerge from this initial study. First, stable copper(II) peroxide complexes can be prepared with the proper choice of ligands and reaction conditions. Choice of the other ligands in the copper coordination sphere is critical. Use of less sterically hindered ligands does not yield stable dioxygen complexes; rather, only Cu(II) products and fully reduced oxygen species (water, hydroxide, oxide) are obtained.[1,3] Second, bound oxygen can be displaced. All copper proteins for which a μ-peroxodicopper(II) active-site structure has been proposed show reversible dioxygen binding.[2] Finally, the isolation of IV demonstrates that Cu(II)–peroxide species are potent oxidizing agents, provided the reduced oxygen species and substrate are held in the proper orientation. However, the chemistry of these dioxygen complexes is dominated by the disproportionation reaction.

Acknowledgment. The excellent technical assistance of R. M. Swiatek is gratefully acknowledged.

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(16) (a) Anal. Calcd for C$_{20}$H$_{50}$Cl$_2$Cu$_2$N$_4$O$_{10}$: C, 34.09; H, 7.15; N, 7.95. Found: C, 34.13; H, 7.34; N, 7.87. (b) Crystallization from dichloromethane/petroleum ether yielded the β-form of the complex.[11a]

(17) (a) Thompson, J. S.; Tulip, T. H., manuscript in preparation. (b) The blue BF$_4$ salt crystallizes in the monoclinic space group $P2_1/c$ with a unit cell of dimensions a = 7.613 (2) Å, b = 15.416 (3) Å, c = 14.129 (2) Å, and β = 103.05 (1)°. Least-squares refinement of 198 variables led to R = 0.039 and R_w = 0.038 for 2267 reflections having $F_o^2 > 3\sigma(F_o^2)$.

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Phosphorus–Oxygen Bond Order in Adenosine 5′-*O*-Phosphorothioate Dianion

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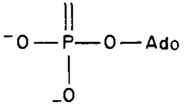
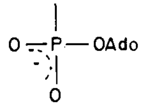
Structural formulas for nucleoside phosphorothioate anions are generally written with P═S double bonds, P—O single bonds, and negative charges localized on oxygens.[1a–e] These assignments originated with the analysis of the crystal and molecular structure of the triethylammonium salt of *endo*-uridine-2′,3′-phosphorothioate.[2] In this paper we report new data bearing on charge distribution and P–O bond order of adenosine 5′-phosphorothioate (AMPS) dianion in water.

The structure of AMPS may be represented as **1a**, with P–O



$^{-}\mathrm{O}-\underset{\underset{^{-}\mathrm{O}}{|}}{\overset{\overset{\mathrm{S}}{\|}}{\mathrm{P}}}-\mathrm{O}-\mathrm{Ado}$

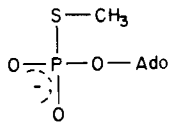
1a



$\mathrm{O}\overset{-}{\cdots}\underset{\underset{\mathrm{O}}{\vdots|}}{\overset{\overset{\mathrm{S}^{-}}{|}}{\mathrm{P}}}-\mathrm{OAdo}$

1b

bond orders of 1 and charges localized on oxygen, or **1b**, with P–O bond orders of 1.5, one charge localized on S and the second delocalized between two oxygens. Both structural formulas imply little or no involvement of S in charge delocalization. The data in Table I support **1b** as the more accurate representation of charge distribution and bonding for AMPS dianion in water. An effect of ^{18}O substituted for ^{16}O in phosphates is to shift the ^{31}P NMR signal upfield by an amount directly proportional to the P–O bond order.[3a–c] This upfield shift is the ^{18}O-isotope shift, $\Delta\delta_P$. The values of $\Delta\delta_P$ given in Table I for [α-^{18}O]AMPS, [α-^{18}O$_2$]AMPS, *S*-methyl-[α-^{18}O]AMPS, and *S*-methyl-[α-^{18}O$_2$]AMPS are the same for all species.[4] Since the P–O bond orders in *S*-methyl-AMPS (**2**) are 1.5 and the ^{18}O-isotope shifts for *S*-methyl-[α-^{18}O]AMPS are the same as those for [α-^{18}O]AMPS, the P–O bond orders in AMPS must also be 1.5. The $\Delta\delta_P$ values in Table



$\mathrm{O}\overset{-}{\cdots}\underset{\underset{\mathrm{O}}{\vdots|}}{\overset{\overset{\mathrm{S}-\mathrm{CH_3}}{|}}{\mathrm{P}}}-\mathrm{O}-\mathrm{Ado}$

2

[†] University of Wisconsin.

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(4) Spectra were recorded at 81 MHz by using a Nicolet 200-MHz or JOEL FX 200 Fourier transform NMR spectrometer, field frequency locked on the deuterium resonance of the solvent. Samples were dissolved in 90% D$_2$O at pH 8. For AMPS spectra 8K data points and 1000-Hz spectral width were used to acquire the free induction decay. A 14.5-μs pulse, 2.05-s acquistion time, and broad-band proton decoupler power of 23.0 W were used to collect 600 transients. For *S*-methyl-AMPS 8K data points and 320-Hz spectra width were used to collect the free induction decay. A 6-μs pulse, 6.4-s acquisition time, and 2.0-W decoupler power were used to collect 400 transients. Temperature was 30 °C. *S*-Methyl-[α-^{18}O]AMPS was synthesized from [α-^{18}O]AMPS as described by Connolly and Eckstein.[5]

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Table I. Effects of ^{18}O on ^{31}P NMR Chemical Shifts of AMPS and *S*-Methyl-AMPS

^{18}O species	δ_P[a]	$\Delta\delta_P$[b]
AMPS	43.200	
[α-^{18}O]AMPS	43.167	0.033
[α-$^{18}O_2$]AMPS	43.134	0.033
S-methyl-AMPS	22.642	
S-methyl-[α-^{18}O]AMPS	22.607	0.035
S-methyl-[α-$^{18}O_2$]AMPS	22.572	0.035

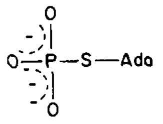
[a] ^{31}P NMR chemical shift relative to an external standard of 85% H_3PO_4, in ppm. Spectra recorded at pH 8.5. [b] $\Delta\delta_P$ is defined as the absolute difference beteen δ_P for the ^{18}O-containing species relative to ^{16}O species and divided by the number of chemically equivalent ^{18}O's in the species, in ppm.

I are consistent with bond orders of 1.5 since the $\Delta\delta_p$ value for single-bonded ^{18}O in phosphorothioates is 0.022.[6a,b]

If **1a** accurately represented the P–O bonding in AMPS, methylation to **2** would increase the P–O bond order from 1 to 1.5; and this would be reflected in a proportional increase in the ^{18}O-isotope shift. As shown in Table I, this transformation is accompanied by only a slight increase in the ^{18}O-isotope shift.

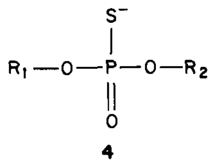
The small difference between $\Delta\delta_p$ for [^{18}O]AMPS and *S*-methyl-[^{18}O]AMPS may be within experimental error. If significant, it could reflect slightly higher P–O bond order in *S*-methyl-AMPS compared with AMPS. In this case, taking 1.5 as the P–O bond order in *S*-methyl-AMPS (**2**), the P–O bond order in AMPS could be as small as 1.4, which would not alter our conclusion that **1b** is a reasonably accurate representation of bonding in AMPS, whereas **1a** is not.

Ash et al.[7] have suggested that differences in ^{31}P NMR chemical shifts such as those for AMPS and *S*-methyl-AMPS in Table I reflect differences in P–S bond orders, that for *S*-methyl-AMPS being 1.0. These differences should not be attributed solely to bond order, however, since the ^{31}P NMR chemical shift for *S*-5′-adenosyl phosphorothioate, **3**, is 12.4 ppm[8] compared with 22.6 ppm for **2**, despite the fact that sulfur is bridging with a P–S single bond in both compounds. Differences in ^{31}P chemical shifts among phosphorothioates are poorly understood, but appear not to be determined by bond order alone and may be dominated by other factors.



3

The structure **1b** for AMPS suggests structure **4** for nucleoside phosphorothioates in general. This formulation is consistent with the differences in ^{18}O-isotope shift effects on the ^{31}P NMR resonances of nucleoside phosphorothioates such as ADPαS and ATPβS with bridging and nonbridging ^{18}O.[6a,b,9] It is also consistent with the vibrational spectra of thiophosphate trianion and dianion in aqueous solutions[10a,b] as well as with the relative acid strengths of phosphoric and thiophosphoric acids.[11]



$$R_1{-}O{-}\overset{\displaystyle S^-}{\underset{\displaystyle O}{P}}{-}O{-}R_2$$

4

R_1 = 5′-nucleoside; R_2 = H, 3′-nucleoside, PO_3^{2-}, $P_2O_7^{3-}$

Structural formulation **4** should guide rationalizations of nucleoside phosphorothioate interactions with enzymes. For example, S_P 3′,5′-cyclic AMPS activates 3′,5′-cyclic AMP dependent protein kinase, whereas the R_P epimer binds but does not activate.[12a,b] Since the configuration at phosphorus governs the regulatory properties of these compounds, it is very likely that an intimate interaction of the phosphorothioate center with the regulatory protein is involved in activation. Charge localization and bond orders at this center might be crucial factors in determining regulatory function. Secondary structure in sulfur analogues of oligonucleotides and polynucleotides may also be influenced by configuration and charge distribution at phosphorothioate diester centers.

It is emphasized that structure **4** refers to species not complexed with metal ions. The charge distribution in Mg^{2+} or Cd^{2+} complexes can vary, shifting from O in the presence of the former to S in the presence of the latter,[12-14] depeneding on the hardness or softness of the metal.

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Hydride-Rich Zirconium-Osmium and Zirconium-Rhenium Dimers

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Heterobimetallic compounds offer the advantage of cooperativity between two adjacent, yet electronically different, metal centers and hold promise in the reduction of dipolar substrates such as CO or CO_2.[1,2] While many such dimeric species are known,[1-9] few have exhibited catalytic behavior in reactions of

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