Communications to the Editor

Hydrogen Oxide Bridging Ligands in a Classical Coordination Compound

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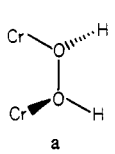
A new bridging ligand, hydrogen oxide ($H_3O_2^-$), was recently discovered in crystals of trinuclear, triangular clusters of molybdenum and tungsten.[1,2] The M-H_3O_2-M bridge is formed by a strong hydrogen bond between a water ligand coordinated to a metal atom of one cluster and a hydroxo ligand coordinated to a metal atom of another cluster.

It was suggested that the existence of this μ-H_3O_2 ligand may not be confined to metal cluster ions. Hydrogen oxide bridges may play a primary role in hydrolytic polymerization of ordinary transition-metal ions[2] and, eventually, in electron-transfer processes in aqueous solution, by means of an H atom transfer mechanism.[1] However, all species, reported to date, containing the H_3O_2 ligand were triangular clusters. There was no positive evidence for the existence of such bridges between ordinary, "classical", mononuclear metal complexes.

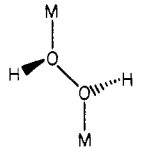
We now report the existence of hydrogen oxide bridges between two *mononuclear* octahedral complex ions. Neutralization of an aqueous solution of *cis*-[diaquabis(bipyridyl)chromium(III)] ion with NaOH to pH 5 causes deprotonation of one water ligand (pK_1 = 3.5) to yield what was generally accepted to be the corresponding hydroxoaqua ion $[Cr(bpy)_2(H_2O)(OH)]^{2+}$. Addition of KI, followed by a slow evaporation of the solution, produced crystals of the iodide salt. The structure of these crystals was determined by X-ray analysis.[3] The true formula of this compound was found to be $[(bpy)_2Cr(H_3O_2)_2Cr(bpy)_2]I_4 \cdot 2H_2O$. It consists of *dimeric* ions in which two chromium atoms are bridged by *two* $H_3O_2^-$ ligands as shown in Figure 1. Some important distances and angles are listed in Table I.

The two chromium atoms of the 4+ cation reside on a crystallographic 2-fold axis. Therefore, the two hydrogen oxide units are symmetry related. The O···O separation in the $H_3O_2^-$ unit is 2.444 Å. This distance is within the average range of 2.44–2.52 Å found in other compounds containing the μ-H_3O_2 ligand.[1,2] The two identical Cr–O(H_3O_2) distances, Cr(1)–O(1) and Cr(2)–O(2) (1.924 Å), indicate that the H_3O_2 unit is symmetric as previously found in other structures.[2] These distances are shorter than the average distance reported for the Cr–O(H_2O) bond (1.98 Å)[4] and slightly longer than those reported for Cr–O(OH) (1.90 Å)[5] as expected.

An interesting feature of the hydrogen oxide unit found in this compound is its "gauche" structure (a) rather than the anti



a



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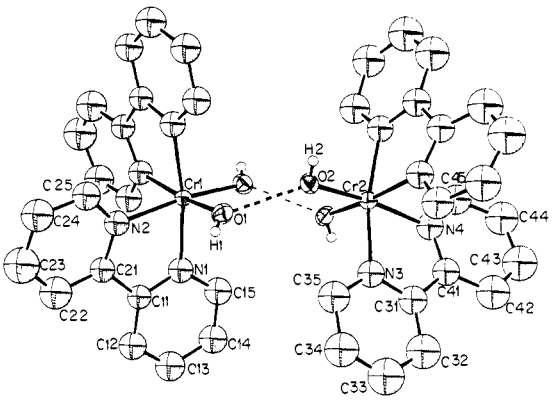

Figure 1. Structure of $[(bpy)_2Cr(H_3O_2)_2Cr(bpy)_2]^{4+}$. The O···H···O bonds in the H_3O_2 units are represented by the dashed lines. H(1) and H(2) were located from the difference Fourier.

Table I. Some Bond Distances (Å) and Angles (deg) in $[(bpy)_2Cr(H_3O_2)]_2I_4 \cdot 2H_2O$

Cr(1)–O(1)	1.921 (5)	Cr(1)–O(1)–O(2)	127.4 (3)
Cr(2)–O(2)	1.926 (6)	Cr(2)–O(2)–O(1)	126.5 (3)
O(1)–O(2)	2.444 (8)		

structure (b), found in the trinuclear systems. The Cr–O–O–Cr segment possesses a skew structure with a torsional angle of 64°.

Evidence for the existence of hydrogen oxide bridging ligands in species of the type reported here supports the assumption of the widespread occurrence of this bridging ligand between metal ions.[2] The main difficulty of proving this assumption lies in the close relationship which may exist between the formation reaction of μ-H_3O_2 bridges (eq 1) and the formation reaction of μ-hydroxo

$$[L_5M(H_2O)]^{n+} + [(HO)ML_5]^{(n-1)+} \rightarrow [L_5M(H_3O_2)ML_5]^{(2n-1)+} \quad (1)$$

$$[L_5M(H_3O_2)ML_5]^{(2n-1)+} \rightarrow [L_5M(OH)ML_5]^{(2n-1)+} + H_2O \quad (2)$$

bridges (olation, eq 2). μ-Hydroxo bridges exist in solution of most metal ions.[6] The greater thermodynamic stability of μ-hydroxo bridges and their rapid rate of formation by reaction 2 result in a very low steady-state concentration of the μ-H_3O_2 bridged species and frustrate attempts to trap them in stable crystalline compounds. This situation is altered in substitution-inert species such as the trinuclear cluster ions reported previously[1,2] and some mononuclear ions, e.g., chromium(III) complexes. The rate of reaction 2 with such species is usually slow since it requires the breaking of a metal–oxygen bond, whereas reaction 1 remains extremely rapid (probably diffusion controlled). It is therefore to be expected that inert ions may yield high concentrations of hydrogen oxide bridged species under favorable thermodynamic conditions (high total metal concentration and a pH that equals the pK_1 of the aqua ion). These considerations directed our choice of systems that led to the positive results reported here.

Chromium(III) and cobalt(III) salts of the di-μ-hydroxo ions $[L_4M(OH)_2ML_4]^{4+}$ are traditionally obtained by heating salts of the corresponding mononuclear *cis*-$[L_4M(H_2O)(OH)]^{2+}$ ions to 110 °C. Our findings, indicating that some cis "monomers" may indeed be dimeric $[L_4M(H_3O_2)_2ML_4]^{4+}$ ions, throw new light

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(3) The red compound crystallizes in space group *Pbcn* with a = 15.511 (2) Å, b = 15.115 (2) Å, c = 20.955 (3) Å, and Z = 4. The structure was refined by least-squares methods using 3120 unique reflections with $I > 3\sigma(I)$ to a conventional R factor of 0.042.
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on the olation reaction. The two H_3O_2 bridges in this dimer hold the two metal atoms in a mutual orientation suitable for the olation reaction. This reaction may proceed by a water molecule elimination from each of the two H_3O_2 bridges, leaving two μ-hydroxo bridges between the two metal atoms. This mechanism may also operate in the olation of aquo ions such as $Cr(H_2O)_5OH^{2+}$ in which the "Chromic Dimer"[7] $[(H_2O)_4Cr(OH)_2Cr(H_2O)_4]^{4+}$ is formed. In some cases, the formation of these species may be followed by the rupture of one bridge to form a singly bridged species[8] as in eq 3.

$$[Cr(OH)_2Cr]^{4+} + H^+ \rightarrow [Cr(OH)Cr]^{5+} + H_2O \quad (3)$$

Work is in progress on the isolation of other crystalline compounds with μ-H_3O_2 bridges. The existence of bridged species of these complex ions in solution will be investigated.

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Registry No. $[Cr(bpy)_2(H_2O)_2]^{3+}$, 36513-26-5; $[(bpy)_2Cr(H_3O_2)_2Cr(bpy)_2]I_4 \cdot 2H_2O$, 87764-12-3.

Supplementary Material Available: Tables of atomic positional and thermal parameters (2 pages). Ordering information is given on any current masthead page.

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Sequence-Specific Double-Strand Cleavage of DNA by Bis(EDTA-distamycin·Fe^{II}) and EDTA-Bis(distamycin)·Fe^{II}

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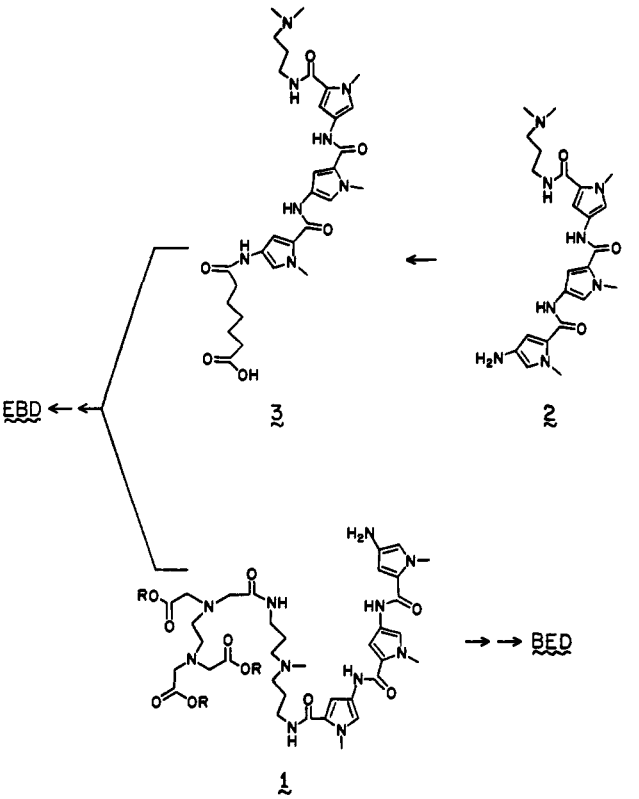
Restriction enzymes (type II) cleave double-helical DNA on opposite strands at or close to a defined recognition site four-six base pairs in size.[3] The ability of these enzymes to cleave DNA into unique fragments is useful for DNA sequencing, chromosome analyses, gene isolation, and recombinant DNA manipulations. Attachment of EDTA·Fe^{II} to a DNA binding molecule creates a DNA cleaving molecule.[4] Distamycin-EDTA·Fe^{II} (DE·Fe^{II}) and EDTA-distamycin·Fe^{II} (ED·Fe^{II}), which contain EDTA tethered to the amino or carboxy terminus of an *N*-methylpyrrole tripeptide DNA binding unit, single strand cleave DNA adjacent to five base pair A + T recognition sites.[5] The pentapeptide penta-*N*-methylpyrrolecarboxamide-EDTA·Fe^{II} (P5E·Fe^{II}) achieves double-strand cleavage of DNA adjacent to a six-seven base pair A + T recognition site in a catalytic reaction.[6] One general approach for designing double-strand DNA-cleaving molecules with defined target sequences and binding-site sizes would be to couple sequence-specific DNA binding molecules of similar (or diverse) base pair specificities and attach one (or more) DNA cleaving moieties such as EDTA·Fe^{II}.

We report the synthesis of two sequence-specific double-strand DNA cleaving molecules, bis(EDTA-distamycin·Fe^{II}) (BED·Fe^{II}) and EDTA-bis(distamycin)·Fe^{II} (EBD·Fe^{II}) (Chart I). These molecules contain two *N*-methylpyrrole tripeptide units[7] coupled at the amino termini via a flexible tether with EDTA attached to one or both carboxy termini. In the presence of O_2 and dithiothreitol (DTT), *nanomolar* concentrations of BED·Fe^{II} and EBD·Fe^{II} cleave DNA (25 °C, pH 7.9). BED·Fe^{II} and EBD·Fe^{II} cleave pBR 322 plasmid DNA (4362 base pairs) on opposite strands to afford *discrete* DNA fragments. High-resolution gel electrophoresis of an end-labeled restriction fragment containing a major binding site reveals cleavage contiguous to an *eight* base pair sequence 5′-TTTTTATA-3′.

Reaction of 2 equiv of amine **1** with the di-*N*-hydroxysuccinimide ester of heptanedioic acid followed by hydrolysis (0.25 M, LiOH), acidification, and chromatography (silica gel, NH_3/MeOH) afforded BED. Condensation of diamine **2** with an excess of the monoimidazolide of heptanedioic acid afforded the amino acid **3**. Reaction of the imidazolide of **3** with amine **1** followed by hydrolysis, acidification, and chromatography (silica gel, NH_3/MeOH) afforded EBD. BED and EBD were rendered



metal free by supporting each on Amberlite XAD-2 and washing with 5% aqueous Na_2EDTA and deionized water and eluting with methanol.[8]

The DNA cleavage efficiency of BED·Fe^{II} and EBD·Fe^{II} was followed by monitoring the conversion of supercoiled pBR 322 plasmid DNA (form I) to open circular (form II) and linear forms (form III).[9,10] One single-strand scission converts form I to form

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(10) The correction factor for the decreased stainability of form I pBR-322 DNA is 1.22.[4]

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