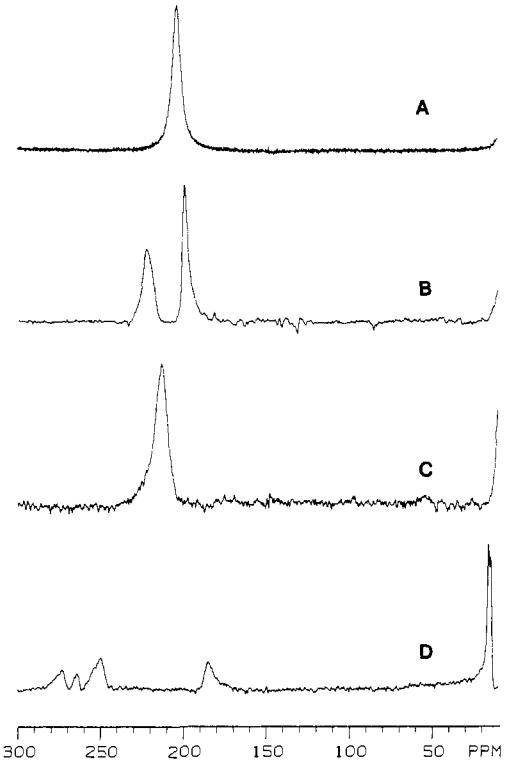

Figure 3. 300-MHz ^{1}H NMR spectra of tetrakis(alkylthiolate)-Fe(II) complexes in the region of 300-10 ppm. Complexes were prepared in D_2O as described.[14] Fe(II) complex with (A) 2-mercaptoethanol, (B) dithiothreitol, (C) glutathione, and (D) D,L-dihydrolipoate. Spectrum D is of a 2-fold diluted solution. All spectra were obtained at 25 °C.

Third, the spectra of Figure 3 show that similar isotropically shifted resonances can be obtained for a series of alkylthiolate-Fe(II) complexes.[14] We formulate these complexes as $[Fe(SR)_4]^{2-}$ (neglecting charges on the R groups) on the basis of the strong resemblance of their UV-vis[9] and ^{1}H NMR spectra to those of $[Fe(SCH_2CH_3)_4]^{2-}$.[15] The magnetic and spectral properties of this latter complex are indicative of tetrahedral coordination geometry.[16] For the complexes of Figure 3 we obtain resonances at 203 (β-mercaptoethanol); 221 and 199 (dithiothreitol); 213 (glutathione); and 271, 264, 250, and 185 ppm (D,L-dihydrolipoate), all at 25 °C. Each of the aforementioned resonances shifts upfield with increasing temperature and exhibits a linear dependence of the chemical shift on T^{-1} in the region of 5-55 °C. These resonances are all assigned to methylene hydrogens α to coordinated sulfur and, hence, correspond to the β-CH_2 groups of coordinated cysteinate in reduced Rd.[17] The multiple peaks observed in the cases of dithiotheitol and D,L-dihydrolipoate are presumably due to the S,S'-bidentate chelates formed with these dithiols. The chemical (though not necessarily magnetic) environment of α-CH of coordinated cysteinate in Rd would be expected to be most accurately approximated by the corresponding α-CH of S-coordinated glutathione (γ-glutamylcysteinylglycine). For this complex we observe a broad resonance centered at ~8 ppm (not shown), which we tentatively assign to the α-CH's of coordinated cysteinyl residues in glutathione. S,S'-Chelated dihydrolipoate has two methylenes β to coordinated sulfur, and the group of resonances between 13 and 16 ppm in Figure 3D we assign to these methylene hydrogens. These resonances shift upfield with increasing temperature. Thus, the resonances between 11 and 17 ppm in ^{1}H NMR spectra of reduced Rd have counterparts in at least one synthetic complex.

The results reported here represent a new spectroscopic probe of the iron site in at least one Rd and set the stage for examinations of iron sites in other Rds and in related proteins such as desulforedoxin[18] by ^{1}H NMR. Finally, this work clearly illustrates the usefulness of "synthetic analogues" in the clarification of properties of a metal site in a protein.[15]

Note Added in Proof. We have obtained ^{1}H NMR spectra of oxidized and reduced Rds from *Desulfovibrio vulgaris*. These spectra are similar to those in Figures 1 and 2.

Acknowledgment. This work was supported by the National Science Foundation (D.M.K., DMB-8216447, and J.L.G., DMB-8602789) and by a grant from Junta Nacional de Investigacão Cientifica e Tecnologica (Portugal). We thank the staff of the University of Georgia Fermentation Plant for growing the bacterial cells that were used in this study.

Registry No. Fe, 7439-89-6; L-cysteine, 52-90-4.

Supplementary Material Available: Plots of chemical shifts vs. T^{-1} for isotropically shifted resonances of reduced *D. gigas* Rd and UV-vis absorption spectra of alkylthiolate-Fe(II) complexes (2 pages). Ordering information is given on any current masthead page.

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(15) A stimulus to the present work was the report by Hagen et al.[16] of ^{1}H NMR resonances of $[Fe(SCH_2CH_3)_4]^{2-}$ at 196 (CH_2) and 10 (CH_3) ppm downfield of Me_4Si.

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The Hydrated Methoxide Ion, $CH_3O^-\cdot 6H_2O$

Avi Bino

Department of Inorganic and Analytical Chemistry
The Hebrew University of Jerusalem
91904 Jerusalem, Israel

Received August 19, 1986

The interactions of very strong bases such as hydroxide and methoxide anions with water have been the subject of numerous experimental and theoretical studies. Experiments and calculations in the gas phase and in solutions have demonstrated the important role of solvation in determining molecular properties such as relative acidities, basicities, and nucleophilicities.[1-5]

While the hydrated hydroxide ion, $OH^-\cdot nH_2O$, has been characterized in several crystalline compounds,[6] the structure of the hydrated methoxide ion, $CH_3O^-\cdot nH_2O$, has not been reported in single-crystal X-ray studies.

We report here the results of an X-ray structural analysis of such a species, $CH_3O^-\cdot 6H_2O$, found in the crystal of $Na_5[Cr-$

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Table I. Bond Distances (Å) and Bond Angles (deg) for the $CH_3O^-\cdot 6H_2O$ Unit in **1** and **2**

	structure	
	1	**2**
H_3C-O	1.38 (1)	1.33 (2)
$H_3CO\cdots(H)OH(Ow4)$	2.721 (9)	2.80 (1)
$H_3CO\cdots OH_2(Ow3)$	2.95 (1)	2.95 (1)
$C_{me}-O_{me}-O(w4)$	126 (1)	128.8 (9)
$C_{me}-O_{me}-O(w3)$	91.0 (7)	91 (1)

$(PhC(O)=N(O))_3]\cdot I\cdot CH_3O\cdot 3CH_3OH\cdot 10^1/_2H_2O$ (**1**) and in the isostructural $Na_5[Co(PhC(O)=N(O))_3]\cdot Br\cdot CH_3O\cdot 3CH_3OH\cdot 10^1/_2H_2O$ (**2**).[7]

Compound **1** was originally prepared by Raymond et al. and was formulated as "$Na_3[Cr(PhC(O)=N(O))_3]\cdot NaI\cdot NaOH\cdot 9H_2O\cdot 3CH_3OH\cdot C_2H_5OH$".[8] Our attention was drawn to this compound in the course of a reexamination of single-crystal structures in which the existence of a distinct hydrated hydroxide ion had been claimed.

The presence of an OH^- ion in **1**, rather than an H_2O molecule of crystallization, was proposed in order to account for the mismatch of charges (3- for the chromium complex, 1- for the iodide, and 5+ for the sodium ions in each formula unit).[8] This compound was originally prepared by dissolving $[Cr(PhC(O)=NH(O))_3]$ in an aqueous solution of NaOH in the presence of iodide ions, ethanol, and methanol.[8] We have shown that the presence of the ethanol is not essential and that crystals of **1** are obtained with or without ethanol. The concentrations of the OH^- ion and of the methanol in the solution in which the crystals are grown are 4.4 and 7.4 M, respectively, and the calculated CH_3O^- ion concentration is about 1.8 M.

A crystal of **1**, prepared in our laboratory, was subjected to a low-temperature X-ray analysis and the results call for a revision of the original formula.[9] First, the assignment of the oxygen atom O(W3) as a hydroxide ion is erroneous since it resides in a 12-fold general position and hence exists in a 3:1 ratio of OH^-/Cr rather than 1:1. Since all the hydrogen atoms in **1** were located from the difference Fourier map in our study it is obvious from the hydrogen bonds scheme that O(W3) is a water molecule rather than an OH^- ion. Second, the "ethanol" molecule of crystallization, that was found residing on the threefold axis[8] is, in fact, a methoxide ion, CH_3O^-, hydrogen bonded to three water molecules and surrounded by three additional ones as shown in Figure 1.

The distances of the three (symmetry related) hydrogen bonds, $H_3CO\cdots O(W3)$ in **1** and **2** and of the three $H_3CO\cdots O(W4)$ contacts are given in Table I. Both O(W3) and O(W4) are part of the hydration sphere of the CH_3O^- anion and of some of the sodium cations. The positive charge of the 20 Na^+ cations in the cell is balanced by the negative charge of the four CH_3O^-, four $[Cr(PHC(O)=N(O))_3]^{3-}$, and four iodide anions.

Several theoretical studies on the hydrated methoxide ion in the gas phase were performed but most of them dealt with the monohydrate, $CH_3O^-\cdot H_2O$.[3,5a] In some of these calculations, the proposed H_3C-O^- distances are in the range of 1.33-1.37 Å and they resemble the values found in the crystals of **1** and **2** (Table I). In previous structural studies of simple salts of the methoxide ion such as $M(CH_3O)_2$ (M = Ca, Sr, Ba), the H_3C-O distances were in the range of 1.39-1.40 Å.[10]

(7) Compound **2** was prepared by reacting $CoCl_2\cdot 6H_2O$ (0.5 g) and potassium benzohydroxamate (1.1 g) in methanol (25 mL). The pink slurry of $[Co(PhC(O)=NH(O))_3]$ was added to a hot solution of NaOH (15 g) and NaBr (5 g) in H_2O(60 mL). Green crystals were obtained after several hours. The crystals are trigonal, space group $P\bar{3}c1$, a = 13.541 (2) Å and c = 25.981 (3) Å. Anal. Calcd for $BrCoNa_5O_{20.5}N_3C_{25}H_{48}$: C, 30.88; H, 4.98; N, 4.32. Found: C, 30.14; H, 4.83; N, 4.22.

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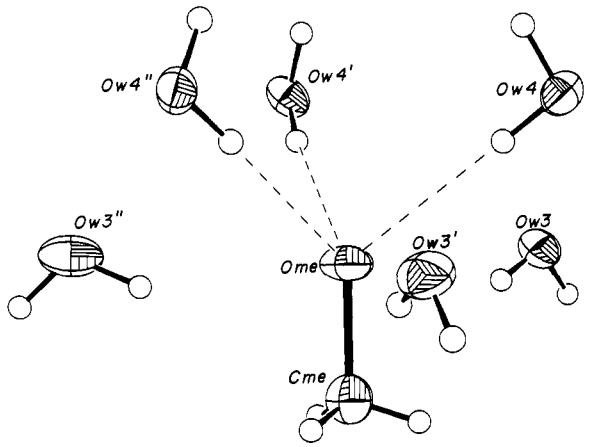

Figure 1. Structure of $CH_3O^-\cdot 6H_2O$. The atoms O_{me} and C_{me} reside on a crystallographic threefold axis. The dotted lines represent the hydrogen bonding between the CH_3O^- ion and the water molecules, O(W4)-O(W4)". All hydrogen atoms have been located from the difference Fouriers.

The calculated O-O distances of the $H_3CO\cdots(H)OH$ hydrogen bond are in the range of 2.57-2.64 Å,[3,5a] and they differ significantly from the corresponding distances found in the crystals of **1** and **2** (Table I). These variations are probably the result of the difference between the hydration number in the crystal and those in the theoretical calculations as well as of the interactions with the counterions in the solid.

Jorgensen et al. estimated the average solvation number of CH_3O^- in methanol and of OH^- in H_2O to be about 5.[11] This work shows that in the solid state, the CH_3O^- ion is surrounded by six water molecules, in a trigonal symmetry, and it is not unlikely that a similar hydration system exists in the aqueous solution of CH_3O^-.

Supplementary Material Available: Tables of atomic positional parameters for **1** and **2** and a structure of the $CH_3O^-\cdot 6H_2O$ system and the nearest sodium cations (4 pages). Ordering information is given on any current masthead page.

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A Total Synthesis of Acivicin

S. Mzengeza, C. M. Yang,† and R. A. Whitney*

Department of Chemistry, Queen's University
Kingston, Ontario, Canada K7L 3N6

Received August 25, 1986

Acivicin (AT-125) (**1**) is an antimetabolite antibiotic, produced by *Streptomyces sviceus*, for which the isolation and structure elucidation were reported by Martin et al.[1] in 1973. The antitumor properties associated with this compound are a consequence of irreversible inhibition of a number of glutamine-requiring enzymes involved in the de novo biosynthesis of purine and pyrimidine nucleotides.[2] Initial phase II clinical trials have indicated that acivicin may be useful in the treatment of non-small cell lung cancer;[3] additional clinical trials are ongoing and underscore the

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