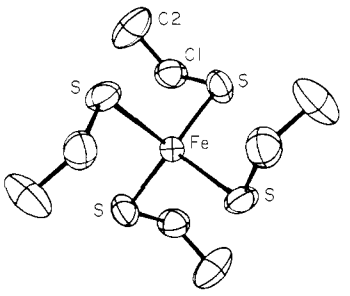

Figure 2. Anion of $[NPr_4][Fe^{III}(SEt)_4]$. The 2-fold disorder of the ethyl carbons is not shown.

of conformations, both of which have high idealized symmetry; they are the S_4 conformation observed for **1** or the D_{2d} conformation observed in **2**.[7,12] The same type of intramolecular interactions that causes the tetragonal elongation of the $[FeS_4]$ core in **2**[7] is responsible for the compression in **1**.

The $[Fe(SR)_4]^-$ unit in the recently reported $(NEt_4)[Fe^{III}$-(2,3,5,6-tetramethylbenzenethiolate)$_4]$ (**3**) also has S_4 symmetry;[4,13] however, the *o*-methyl groups prevent the phenyl rings in this complex from possessing the same conformation as in **1** and **2**. Rather, the planes of the phenyl rings in **3** are perpendicular to the Fe–S bonds. The sulfur p π lone pair orbitals are conjugated with the phenyl rings in **1** but are orthogonal to the rings in **3**. The effect of this change on the electronic properties of the iron(III) center will need to be carefully addressed by using theory and spectroscopy.

The ligand exchange reaction of alkylthiols with the iron(III) tetraphenolate complex also gives stable $[Fe^{III}(SR)_4]^-$ compounds. Stable but air-sensitive DMF solutions of $[Fe^{III}(SR)_4]^-$ (R = CH_2CH_3, CH_2Ph, CH_2CH_2Ph, and $C(CH_3)_3$), which are obtained by this reaction, display the characteristic rubredoxin-like electronic spectrum with two ligand-to-metal charge-transfer bands in the visible region.[14] $[Fe^{III}(SEt)_4][NPr_4]$ (**4**), which is isolated as black crystals in 70% yield from DMF/Et_2O, has been structurally characterized.[15,16] The $[Fe^{III}(SEt)_4]^-$ anion (Figure 2) has crystallographic S_4 symmetry. Interestingly, the FeS_4 core of $[Fe^{III}(SEt)_4]^-$ has nearly perfect T_d symmetry with the two S–Fe–S angles bisected by the S_4 axis equal to 109.43 (9)° and the four remaining angles equal to 109.49 (5)°. The Fe–S bonds are 2.272 (1) Å.

Attempts to understand the electronic structure of symmetric $[Fe(SR)_4]^{1-(2-)}$ complexes such as (**1**–**4**) are of direct biological importance since the geometry of the $[Fe(SCH_2)_4]$ unit of rubredoxin closely approximates D_{2d} symmetry.[1,4] Besides serving as models for oxidized rubredoxin, iron(III) tetrathiolates should be valuable reactants in the synthesis of iron–sulfide and iron–molybdenum–sulfide clusters.

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Registry No. 1, 86689-74-9; **4**, 86689-79-4; $[Fe^{III}(SCH_2Ph)_4]^-$, 86689-75-0; $[Fe^{III}(SCH_2CH_2Ph)_4]^-$, 86689-76-1; $[Fe^{III}(SC(CH_3)_3)_4]^-$, 86689-77-2; $(NEt_4)[Fe(2,6\text{-dimethylphenolate})_4]$, 86689-72-7.

Supplementary Material Available: Tables of fractional atomic coordinates and thermal parameters (3 pages). Ordering information is given on any current masthead page.

(12) A different ORTEP view of the anion of $[NEt_4]_2[Fe^{II}(SPh)_4]$ (Figure 8 in ref 7) would reveal its overall approximate S_4 symmetry.

(13) S_4 symmetry is common for many R_4M compounds: Karipides, A.; Iroff, L. D.; Mislow, K. *Inorg. Chem.* **1979**, *18*, 907.

(14) The electronic spectra of DMF solutions of the $[Fe^{III}(SR)_4]^-$ complexes are as follows: for R = CH_2Ph, λ = 498 nm (ϵ = 6000), 357 nm (11 000); R = CH_2CH_2Ph, 500 nm (6400), 362 nm (11 500); R = $C(CH_3)_3$, 505 nm (4800), 358 nm (9000). These spectra as well as those of **1** and **4** maintain greater than 90% of their intensities after standing at room temperature for 24 h under a nitrogen atmosphere.

(15) The electronic spectrum of **4** in DMF is as follows: λ = 496 nm (ϵ = 5900), 356 nm (10 000), 284 nm (4400). Anal. Calcd for $FeS_4C_{20}H_{48}N$: C, 49.36; H, 9.94; N, 2.88; S, 26.35. Found: C, 49.58; H, 9.63; N, 2.83; S, 26.69.

(16) $[Fe^{III}(SEt)_4][NPr_4]$ crystallizes in the tetragonal space group $I\bar{4}$ with $a = b$ = 10.598 (2) Å, c = 12.588 (2) Å, V = 1413.8 (8) Å^3, Z = 2. The Fe is located at special position 2d and the nitrogen at position 2a. A crystallographic model with a 2-fold disorder of the methylene carbons of the cation and a 2-fold disorder of the ethyl groups of the anion was successfully refined. Final least-squares refinement gave R = 0.053 and R_w = 0.070 for 595 unique data with $I > 3\sigma(I)$. The analogous gallium compound $[Ga^{III}(SEt)_4][NPr_4]$ is isomorphous and isostructural with **4**.

Application of Proton NMR Spectral Editing Techniques for Selective Observation of N–H Protons in an Actinomycin D Complex with a Tetranucleotide Duplex

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The complexity of many biological molecules can make proton NMR spectral assignment a challenging task. This task would be facilitated by any technique allowing selective observation of a certain type of resonance. Such a technique is potentially furnished by editing methods that permit exclusive observation of protons directly bonded to a spin-$^1/_2$ nucleus.[1] If this nucleus can be introduced into a molecule selectively, the scope of the method is considerably increased. The assignment of N–H protons is of particular importance considering their role in the stabilization of protein and nucleic acid secondary structure. Two factors can complicate such assignments; analog to digital conversion limitations accompanying the necessity of working in H_2O, and possible overlap with other signals, especially in the aromatic region. The ready availability of many antibiotics biosynthetically enriched in ^{15}N provides the possibility of using editing techniques for spectral simplification in complexes of these antibiotics with suitable receptors.

Uniformly enriched actinomycin D[2] may be prepared from *Streptomyces parvulus* grown on a medium containing $Na^{15}NO_3$ as the sole nitrogen source. The complex formed between the drug and the duplex of the self-complementary tetranucleoside triphosphate d(A-G-C-T) is in slow exchange on the ^1H NMR time scale below 30 °C.[3] NMR spectra were acquired on a Bruker WH-400 modified to pulse protons and ^{15}N simultaneously and observe protons. Editing out of proton resonances other than those directly bonded to ^{15}N was achieved using the multinuclear pulse sequence

$$\pi/2[^1H,x] - 1/(2J) - \pi[^1H,x] - 1/(2J) - \text{acquire}\ \pi[^{15}N,1,0] \quad (1)$$

where J is the one-bond proton–^{15}N coupling constant (ca. 90 Hz), and ...1,0... signifies that the π-pulse on nitrogen is applied only on alternate scans. If these alternate scans are subtracted, signals result exclusively from ^{15}N–H protons (Figure 1); $\pi/2[^1H]$ = 35 μs and $\pi[^{15}N]$ = 50 μs. Experimental considerations vital to the success of the sequence are discussed elsewhere,[4] and its application

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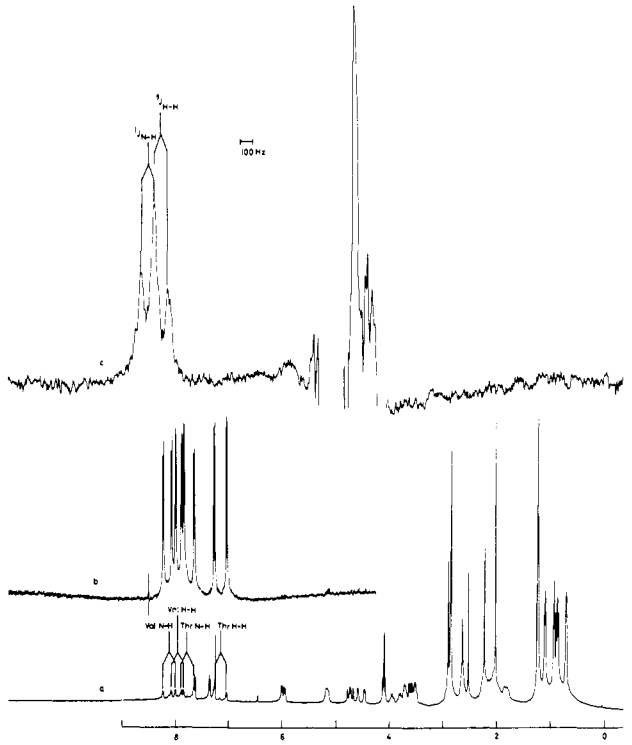

Figure 1. (a) ^1H NMR spectrum of 2 mg of uniformly enriched [^{15}N]actinomycin D in $CDCl_3$; 32 fids were accumulated. (b) ^1H NMR spectrum of actinomycin D in chloroform edited to select ^{15}N-H protons. (c) ^1H NMR spectrum of the actinomycin D complex with d(A-G-C-T) at 25 °C edited to select ^{15}N-H protons. A recycle time of 8 s was used, and 3600 fids were accumulated.

to a solution of ^{15}N-enriched actinomycin D is shown in Figure 1, a and b. ^{15}N decoupling has been used as an alternative approach to the same result in tRNAs.[5]

A solution of about 2 mg of d(A-G-C-T) with a quantity of ^{15}N-enriched actinomycin D equimolar with nucleotide duplex was made up in 10% D_2O/H_2O at pH 7.0 containing 100 mM NaCl and 50 mM phosphate buffer. Although the pulse sequence (1) should eliminate the strong H_2O signal after one cycle, a hard π-pulse followed by a wait period of 2.4 s was inserted before its implementation in order to avoid receiver overload. The ^1H spectrum of the complex at 25 °C is shown in Figure 1c, edited to show only protons directly bonded to ^{15}N. As no ^{15}N broadband decoupling was employed during acquisition, each N-H proton is manifested as a doublet. A maximum of six ^{15}N-H doublets are expected from actinomycin D; the two amino group N-Hs, however, certainly exchange too fast with H_2O to be observed. There are two pairs of peptide N-Hs that should be resolved under favorable exchange conditions, however, and ideally the two L-threonyl and two D-valyl N-Hs should be seen. Figure 1c shows only two doublets instead of the four expected, although the line widths are such that it is possible that the observed signal corresponds to overlap of the two pairs.

Crystal structure analyses of actinomycin D complexed with nucleosides[6] and oligonucleotides[7] suggest that the threonyl N-Hs are involved in hydrogen bond formation with the guanine bases of DNA, while the D-valyl N-Hs participate in hydrogen bonds linking the two pentapeptide rings of the drug. We conjecture that only one N-H pair is observed and that it corresponds to the intramolecularly hydrogen bonded N-Hs, i.e., the D-valyl N-Hs. Attempts to observe both pairs at reduced temperature are complicated if a hard pulse is used to initiate the inversion-recovery H_2O suppression procedure; the complex is outside the extreme narrowing regime, and a decrease in temperature increases T_1 in the complex while decreasing it for H_2O. Thus, whereas at 20 °C T_1s in the complex were much shorter than $T_{1(H_2O)}$, at temperatures low enough to slow the exchange, T_1s in the complex and of H_2O are comparable, and nulling of the complex signals occurs.

If the above conjecture is correct, some kinetic restrictions are placed upon the amide NH exchange processes. The D-valyl N-Hs are required to exchange with water at a rate considerably less than $^1J_{^{15}N-^1H}$ (i.e., 90 Hz), or this coupling would not be resolved (although this rate is not necessarily that of breaking of the intramolecular hydrogen bonds). On the other hand, the proposed intermolecular hydrogen bond to the nucleotide is broken at a rate faster than the chemical shift separation of H_2O and the threonyl N-Hs (in slow exchange), i.e., $>\sim 1000$ Hz at 400 MHz.

Experiments utilizing a soft pulse to selectively suppress the H_2O resonance at low temperature are in progress. We are also hoping to use selectively labeled drugs to assign the N-Hs unambiguously.

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Stereochemical Control in the Addition of Isothiocyanatoacetate Esters to Boron Trifluoride Activated 3-Thiazolines. A Novel Synthesis of *d*-Biotin

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Considerable effort has been directed recently toward the total synthesis of the biological cofactor *d*-biotin (**1**).[1] The three contiguous asymmetric centers of the molecule provide a key hurdle that a successful synthesis must surmount. We were intrigued with the possibility of establishing the requisite biotin stereochemistry by adding an ester enolate of specific geometry bearing a masked α-amino functionality to a suitably substituted imine containing the biotin valeric acid side chain (Scheme I). In so doing, we wished to determine whether the wealth of recent data surrounding the aldol condensation[2] could be extended to the chemistry of imines.[3]

Treatment of α-bromoheptanal[4] with sodium hydrogen sulfide followed by acetone and ammonia generated 3-thiazoline **2**[5,6]

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