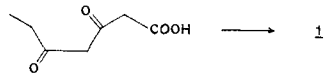
Table I. Precursor Incorporation Experiments with *S. Threomyceticus*

experiment no.	precursor ($^3H/^{14}C$)	% incorporation ($^3H/^{14}C$)	location of label
1	[U-^{14}C]-L-glutamic acid	0.03	
2	sodium [U-^{14}C]pyruvate	0.04	
3	sodium [1-^{14}C]acetate	1.0	
4	sodium (1-^{13}C)acetate	ca. 1.6	C-1, C-3
5	sodium (2-^{13}C)acetate	ca. 1.5	C-2, C-4
6	sodium (1,2-^{13}C)acetate	ca. 1.2	C-1, C-2 ($^1J_{CC}$ = 54 Hz) C-3, C-4 ($^1J_{CC}$ = 40 Hz)
7	sodium (1-^{13}C)propionate	ca. 7.3	C-5
8	DL-sodium [U-^{14}C]lactate	0.04	
9	sodium [1-^{14}C,2(*R*,*S*)-^{3}H]propionate (5.42)	6.0 (2.43)	

that of the agaric toxin muscarine (**2**) whose biosynthesis apparently proceeds from pyruvate and glutamate.[3] Nevertheless, experiments will now be outlined which prove that the biosynthetic pathways to **1** and **2** are unrelated.

Streptomyces threomyceticus (ATCC 15795) was cultivated according to the procedure of Katagiri et al.[1] and precursors were added after 72 h. Because of the structural similarity between furanomycin and muscarine, [U-^{14}C]-L-glutamate and sodium [U-^{14}C]pyruvate were initially evaluated as precursors. The results of these experiments (Table I, experiments 1 and 2) suggested that neither of these compounds was a direct precursor of furanomycin. On the other hand, administration of sodium [1-^{14}C]acetate to cultures of *S. threomyceticus* yielded antibiotic whose radioactivity corresponded to an incorporation figure of 1% (Table I, experiment 3). The specific incorporation of acetate was then demonstrated by administration of sodium (1-^{13}C)acetate to *S. threomyceticus*. This experiment produced furanomycin whose proton noise-decoupled NMR spectrum[4] revealed substantial enrichment at C-1 and C-3 of the antibiotic (Table I, experiment 4). This observation indicated that two acetate units are incorporated into furanomycin, a fact that was confirmed by an incorporation experiment with sodium (2-^{13}C)acetate. As expected, the furanomycin derived from this form of labeled acetate exhibited ^{13}C enrichment at C-2 and C-4 (Table I, experiment 5). A final confirmation of the incorporation of two intact acetate units into **1** was obtained by administration of sodium (1,2-^{13}C)acetate to the producing organism (experiment 6).

The experiments with ^{13}C-labeled acetate yielded furanomycin that exhibited no enrichment in C-5 to C-7. A logical precursor of this segment of the antibiotic was deemed to be propionate, and indeed, administration of sodium (1-^{13}C)propionate to *S. threomyceticus* yielded **1** exhibiting a high degree of enrichment at C-5 (experiment 7). We therefore conclude that furanomycin is derived from two acetate units and one propionate unit, with the latter serving as the starter unit (see eq 1).



1 (1)

The incorporation of propionate into **1** involves the introduction of oxygen at C-2 of propionate. A priori, this could occur either before or after the assembly of a putative seven-carbon diketo acid. If C-2 of propionate were oxidized before the assembly process, then lactic acid would be a likely intermediate in furanomycin biosynthesis. This possibility was evaluated by an incorporation experiment with DL-sodium [U-^{14}C]lactate. The low incorporation figure that was observed (Table I, experiment 8) makes it unlikely that propionate is hydroxylated to lactate prior to the assembly process. Some additional insight into the mechanism of oxidation of C-2 of propionate was obtained by utilizing sodium 2(*R*,*S*)-[2-^{3}H]propionate as a precursor. The tritiated acid was prepared by generation of the anion of *n*-butyl propionate with LDA[5] followed by quenching with [^{3}H]trifluoroacetic acid. The resulting tritiated ester was then converted to its sodium salt and mixed with sodium [1-^{14}C]propionate. Administration of the doubly labeled propionate to *S. threomyceticus* yielded furanomycin that retained 45% of the tritium label (experiment 9). This result rules out the possible formation of a keto function at C-2 of propionate during the biosynthesis, and it indicates that the formation of the ether linkage in furanomycin involves the loss of one hydrogen atom from the prochiral center at C-2 of propionate. Future experiments will examine the stereochemistry of formation of the ether linkage and the origin of the oxygen atom as well as the mechanism of nitrogen introduction at C-2 of the furanomycin skeleton.

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Transmission of Magnetic Interactions in a Molecular Metal Oxide Cluster

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Molecular metal oxides and alkoxides have recently been considered to be useful models of condensed-phase metal oxides[1,2] that may provide valuable information about catalytic chemistry on bulk oxide surfaces and about the interaction of metal catalysts with such surfaces.[3,4]

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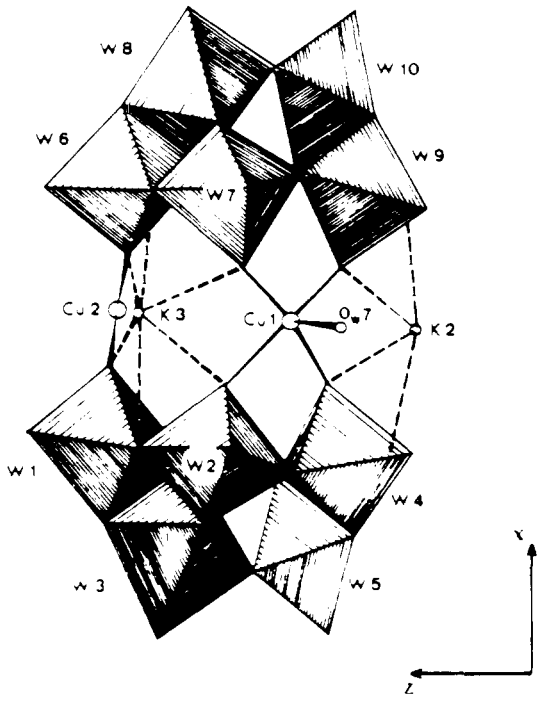

Figure 1. $(W_9AsO_{33})_2Cu_3(H_2O)_2^{12-}$ anion viewed along *b* (reproduced from ref 6).

Important to a full development of the chemistry of metal oxide clusters and surfaces is a better understanding of interactions between metal centers separated by several intervening M–O units.[5] We report here the characterization by EPR spectroscopy and magnetic susceptibility measurements of metal oxide mediated spin exchange in $W_{18}As_2O_{66}Cu_3(H_2O)_2^{12-}$, a novel polymetallic cluster whose X-ray crystal structure (Figure 1) reveals three Cu(II) ions sandwiched between two W_9AsO_{33} cages[6] and that exhibits the first $\Delta m = 2$ and 3 transitions observed in a trimeric Cu(II) cluster complex.[7]

In $(W_9AsO_{33})_2Cu_3(H_2O)_2^{12-}$, two types of copper ions, Cu(1) and Cu(1′), related by symmetry, and Cu(2) are arranged in an equilateral triangle with d[Cu(1)–Cu(1′)] = 4.669 Å and d-[Cu(1)–Cu(2)] = 4.707 Å; Cu(2) is in a square-planar environment and Cu(1) and (1′) have square-pyramidal coordination cores. The 9-GHz room-temperature EPR spectrum of the Na^+ salt of this cluster[8] is shown in Figure 2. It reveals three resonances at approximately 3000, 1500, and 1000 G due, respectively, to the $\Delta m = 1$, 2, and 3 transitions; the highest field feature in the $\Delta m = 1$ region corresponds to a well-defined parallel component. The intensities of these signals are 10^4:10^2:1, in good agreement with the expected ratio of $1:(D/H)^2:(D/H)^4$ where D is the zero-field splitting parameter in the axial symmetrical spin Hamiltonian (vide infra) and H is the resonance field. A detailed analysis of the $\Delta m = 2$ and 3 spectral region provides experimental values for the magnetic parameters: $g_\parallel = 2.075$ (6), $g_\perp = 2.243$ (9) and $D = 1.9$ (1) $\times 10^{-2}$ cm^{-1}.[9] These data have been used to effect a computer simulation of the entire X-band quartet spectrum which agrees to within experimental error with that in Figure 1. EPR spectra have also been obtained at 63 GHz and used to obtain an upper limit on the deviation from axial behavior. Since $E \leq 30$ G and $g_x - g_y \leq 0.01$, we infer that the copper trimer is situated in an environment having essentially axial symmetry. Because of the geometrical arrangement of the Cu(II) centers and the axial appearance of the spectra, the effective molecular values, g(m), i.e., those for each Cu(II) and its first coordination shell, should be given by $g_\parallel = g(m)_\perp$ and $g_\perp = {}^1/_2[g(m)_\parallel + g(m)_\perp]$. From the 9- and 63-GHz spectra, $g(m)_\perp = 2.075$ and $g(m)_\parallel = 2.411$, which leads to the important result, which will be used below, that the unpaired electrons reside primarily in $3d_{x^2-y^2}$ orbitals.[10]

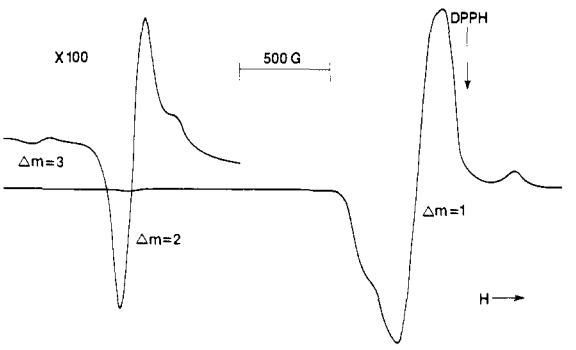

Figure 2. Room-temperature 9-GHz EPR spectrum of $Na_{12}(W_9AsO_{33})_2Cu_3(H_2O)_2 \cdot 11H_2O$.

Clear observation of the $\Delta m = 3$ transition at room temperature implies significant population of the $S = {}^3/_2$ quartet state of the copper trimer in $(W_9AsO_{33})_2Cu_3(H_2O)_2^{12-}$.[11] In addition, although the broad resonance features of the two $S = {}^1/_2$ states are nearly obscured by the quartet absorption and relaxation effects, other EPR features associated with their presence are observed in the X-band spectra between 77 and 300 K. Magnetic susceptibility data from 4 to 300 K were fitted to $\chi = (Ng^2\beta^2/(4kT)[(1 + 5\exp(3J/kT))/(1 + \exp(3J/kT))]$, an expression suitable for an exchange-coupled trimer with three equivalent magnetic centers[12] to yield −1.7 (3) cm^{-1} for the exchange interaction J. This value may be compared with −34.9 cm^{-1} found for α-$SiV_3W_9O_{40}H_3^{7-}$.[13] However, we note that Hatfield has pointed out difficulties associated with establishing a direct relationship between J and the importance of spin-exchange interactions.[14,15]

Because of the large Cu–Cu separations in $(W_9AsO_{33})_2Cu_3(H_2O)_2^{12-}$, direct metal–metal interactions seem quite unlikely and, therefore, stabilization of the collective $S = {}^3/_2$ state must involve a magnetic interaction that propagates through the W_9AsO_{33} caps on both sides of the copper trimer. Indeed, the Cu $3d_{x^2-y^2}$ orbitals, in which the spin density is concentrated, are directed along the Cu–O vectors, which leads logically to the observed collective magnetic behavior.

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