Table I. Selected Average Bond Distances and Angles for Chemically Equivalent Atoms[a]

bond dist/Å		bond angles/deg	
$Zr-O_a$	1.958 (32, 6)	O_a-Zr-O_a	103.4 (12, 6)
Si_a-O_a	1.610 (36, 6)	$Zr-O_a-Si_a$	145.8 (14, 6)
Si_a-O_b	1.620 (29, 12)	$O_a-Si_a-O_b$	110.2 (13, 12)
Si_b-O_b	1.620 (24, 12)	$O_b-Si_a-O_b$	108.4 (13, 6)
Si_b-O_c	1.600 (46, 6)	$Si_a-O_b-Si_b$	151 (4, 12)
Si_c-O_c	1.619 (30, 6)	$O_b-Si_b-O_b$	110.6 (27, 6)
		$O_b-Si_b-O_c$	108.2 (17, 12)
		$Si_b-O_c-Si_c$	151 (5, 6)
		$O_c-Si_c-O_c$	108.0 (11, 6)

[a] The first numbers in parentheses are the root-mean-square deviations of chemically equivalent bonds or angles. The second numbers are the number of independent measurements used in the calculations.

the zirconium atom. The ^{13}C NMR spectrum also exhibits a 3:3:1 ratio of resonances for the cyclohexyl carbons attached to silicon (Figure 1B).[7]

We have also conducted a single-crystal X-ray diffraction study[11] on **3** in order to gain insight into the specific bonding capabilities of **1**. An ORTEP plot of **3** (Figure 2) shows that **1** can easily accommodate a large transition-metal atom without any unusual distortions to the siloxane framework. The Si–O bond distances, as well as the Si–O–Si and O–Si–O bond angles, are within the ranges observed[12] for structurally analogous POSS octamers **2**. The Zr–O bond distances and angles are also within the ranges expected for three-legged piano stool complexes of this type[13] (Table I).

In summary, we have described the synthesis and characterization of the first example from a new class of silicon–oxygen-based macromolecules which incorporate transition-metal atoms into a "cubelike" silsesquioxane framework (POMSS). We have demonstrated that such molecules can be easily synthesized and structurally characterized by using conventional spectroscopic techniques. The ease with which zirconium (one of the larger transition metals)[14] can be incorporated into the siloxane framework suggests that it will be possible to synthesize POMSS that contain a wide variety of different metals. Since the short-range (two–six atoms) molecular structure of **3** in the vicinity of the metal atom is very similar to those observed or proposed for some silica-supported transition-metal catalysts,[1] we believe that POMSS complexes such as **3** can be used to model reaction chemistry that occurs on a silica surface. We are currently synthesizing other related POMSS complexes which will allow us to test this hypothesis.

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Note Added in Proof. The X-ray crystal structure of **1**, obtained by recrystallization from pyridine/hexane, has been successfully solved. Details will be published in a subsequent article.

Supplementary Material Available: X-ray crystal data for **3** including experimental procedures, tables of crystal data, and perspective ORTEP plots (36 pages). Ordering information is given on any current masthead page.

(11) See the supplementary material for details regarding the X-ray crystal structure.

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DNA Strand Scission by Bleomycin: Catalytic Cleavage and Strand Selectivity

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The bleomycins (BLM's) are structurally related antitumor antibiotics that are now used routinely for the treatment of certain malignancies; the biochemical locus of action of bleomycin is thought to be DNA.[2] Oxidative DNA strand scission by bleomycin has been demonstrated in the presence of several metal ions, and the mechanism of DNA cleavage by these metallobleomycins has been studied extensively.[3] Of particular interest is the selectivity of bleomycin for certain sequences, notably G·pyrimidine sites,[4] and the ability of bleomycin to mediate double-strand breaks.[5]

Recently, we reported on $d(CGCT_3A_3GCG)$, a self-complementary dodecanucleotide that acts as an efficient substrate for cleavage by Fe^{II}·BLM + O_2; not surprisingly, most cleavage occurred at the (double-stranded) GC recognition site. By the use of this oligomer, we were able to identify and quantify all significant degradation products produced.[6] Analysis of the data suggested that each BLM-mediated DNA "event" required two electrons, consistent with earlier proposals for O_2 activation by BLM.[7] Presently, we extend our earlier observations concerning Fe·BLM–dodecanucleotide interaction and demonstrate that (i) bleomycin can act *catalytically* in DNA degradation, (ii) both ends of the BLM molecule participate in determining DNA binding specificity, (iii) BLM and decarbamoyl-BLM have different coordination geometries when bound to Fe, and (iv) BLM can probably assume two different orientations at double-strand cleavage sites.

Although numerous studies have dealt with DNA cleavage by bleomycin, in virtually all cases the number of DNA lesions produced has failed to exceed the number of bleomycin molecules employed.[8] This observation and the mechanistic analogy between bleomycin and cytochrome P-450[9] have tended to support the

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Chart I

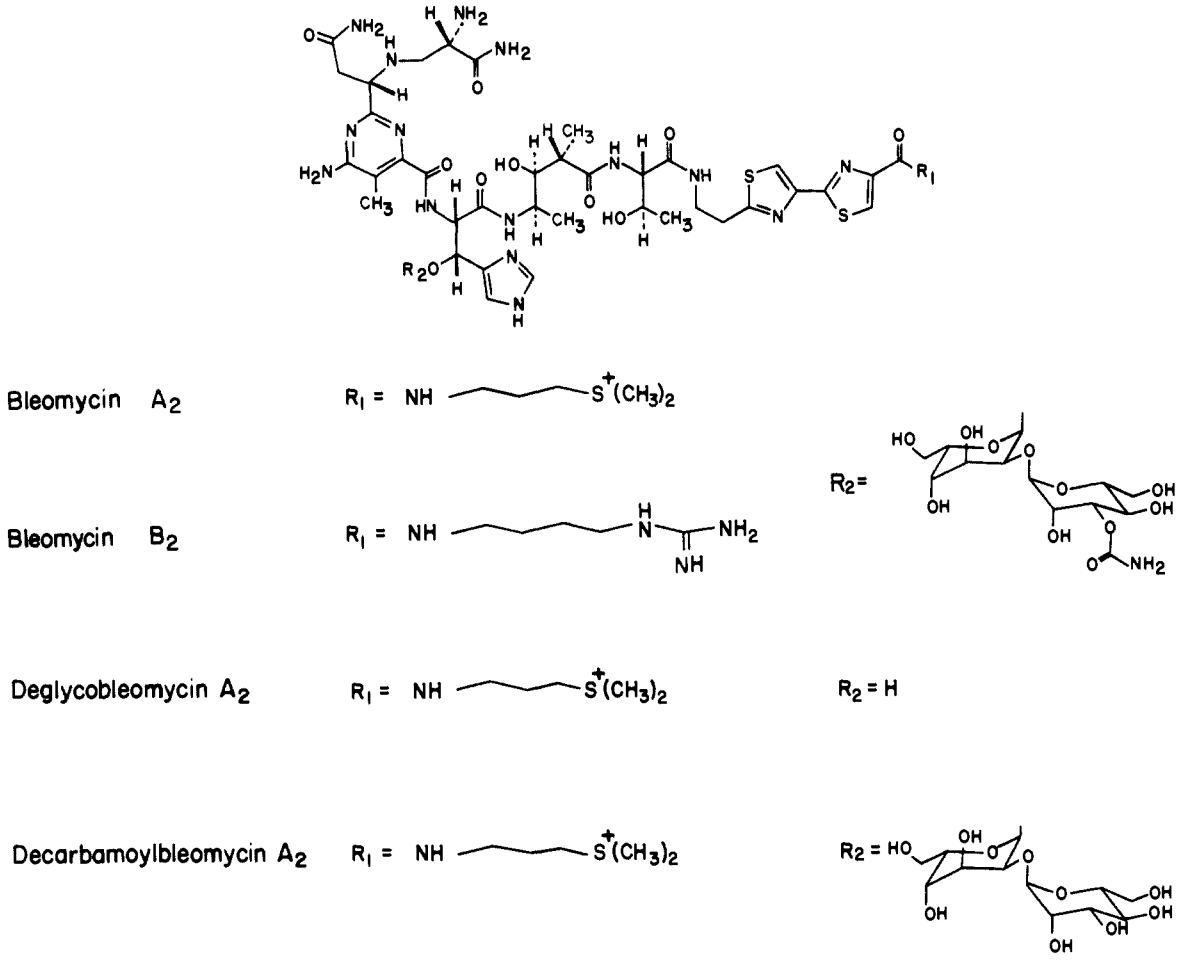

Table I. Quantitative Analysis of BLM-Mediated Product Formation from d($CGCT_3A_3GCG$) in the Presence of Ascorbic Acid[a]

Fe^{II}·BLM A_2, μM	dodecamer, mM	total product,[b] μM	total product/ Fe^{II}·BLM A_2
5	1	15	3.0
10	1	37	3.7
30	1	116	3.9
50	1	127	2.5
20[c]	2	213	10.7
20[c]	4	199	10.0

[a] Reaction mixtures (50 μL total volume) contained d(CGCTTTAAAGCG) (1–4 mM final nucleotide concentration), 50 mM sodium cacodylate (pH 7), 2 mM ascorbic acid, and the indicated amount of Fe(II)·BLM A_2. Reaction was initiated by addition of Fe(II) and incubated at 0 °C for 15 min, then analyzed by HPLC.[6] [b] Total product is equal to the sum of all free bases and base propenals.[6] [c] 5 mM ascorbic acid.

thesis that oxygenated BLM may also undergo self-inactivation,[10] which could preclude a catalytic role for this species in DNA degradation. Our recent finding[6] that activation of Fe^{II}·BLM in the presence of O_2 may well require an additional electron prompted us to study d($CGCT_3A_3GCG$) degradation by Fe^{II}·BLM in the presence of reducing agents. The results obtained with ascorbic acid are shown in Table I. As indicated, 5 μM Fe^{II}·BLM A_2 produced 15 μM products from d($CGCT_3A_3GCG$) at 1 mM final nucleotide concentration, i.e., essentially the same as that produced by 50 μM Fe^{II}·BLM A_2 in the absence of ascorbic acid.[6] At higher (10, 30 μM) concentrations of Fe^{II}·BLM A_2, total product formation was almost 4 times greater than the number of BLM molecules employed. When larger amounts of substrate were used, 10–11 DNA events were obtained for each Fe^{II}·BLM A_2 molecule. Thus, in the presence of an efficient substrate,[6] Fe·BLM A_2 can function catalytically in DNA degradation.[11]

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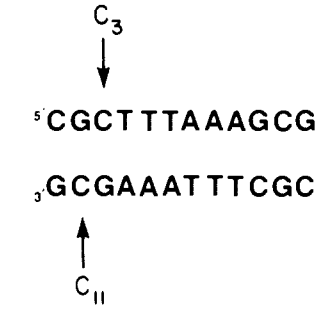

Figure 1. Preferred Fe^{II}·BLM cleavage sites on a self-complementary dodecanucleotide.

Table II. Position of d($CGCT_3A_3GCG$) Cleavage by BLM Congeners[a]

BLM	total events at C_3, C_{11},[b] μM	specificity,[c] %	cleavage position (%) C_3	C_{11}
Fe^{II}·BLM A_2	62	78	15	85
Fe^{II}·BLM B_2	42	75	17	83
Fe^{II}·deglyco-BLM A_2	52	98	79	21
Fe^{II}·decarbamoyl-BLM A_2	60	90	72	28

[a] Reaction mixtures (50 μL total volume) contained d($CGCT_3A_3GCG$) (1 mM final nucleotide concentration), 50 mM sodium cacodylate, pH 7, and 300 μM Fe^{II}·BLM derivative. Reaction was initiated by the addition of Fe(II), incubated at 0 °C for 15 min, and then analyzed by HPLC as described.[6] [b] Equal to the sum of cytosine + cytosine propenal.[6] [c] Proportion of oligonucleotide modification occurring at C_3 or C_{11}.

Previously, we have reported that degradation of d-($CGCT_3A_3GCG$) occurred primarily (76–96%) at the GC sequences (Figure 1) over a wide range of Fe^{II}·BLM concentrations.[6] Interestingly, analysis of the data indicated that most of the GC modifications involved C_{11} rather than C_3 (Table II). Attempts to alter this ratio by variation of Fe^{II}·BLM concentration or other experimental parameters led to the surprising observation that the C_3/C_{11} modification ratio could not be altered significantly.[12] In the belief that this ratio must reflect the orientation of Fe·BLM on the duplex prior to dodecanucleotide modification, we next studied BLM B_2, as this species differs structurally from BLM A_2 in that portion of the molecule believed to be responsible for DNA binding.[13] As indicated in the table, however, the proportion of cleavage at C_3 and C_{11} was not significantly different than that observed for BLM A_2. Moreover, efforts to change the C_3/C_{11} ratio were again unsuccessful, suggesting that this ratio reflected some intrinsic property of Fe^{II}·BLM B_2.

Investigated next was deglyco-BLM A_2, a derivative shown to exhibit DNA sequence specificity similar to that of BLM itself[14] in spite known differences in metal coordination geometry.[15] As shown in Table II, Fe^{II}·deglyco-BLM A_2 was highly specific (98%) for cleavage at C_3 and C_{11}; although the chemical products of cleavage at C_3 and C_{11} were the same as those obtained with Fe^{II}·BLM A_2,[6] the C_3/C_{11} cleavage ratio was just the reverse! Since deglyco-BLM A_2 and BLM A_2 differ only at their N-termini, i.e., the portion of the molecule responsible for metal ion binding and oxygen activation,[13] the differences in DNA cleavage specificity must be due to this structural difference. Thus, while the C-terminus of bleomycin is necessary to achieve DNA binding, it is not a sufficient determinant of specificity.[16]

Also studied was decarbamoyl-BLM A_2,[14c] a derivative that differs from BLM A_2 only by the absence of a carbamoyl group on mannose. Cleavage of d($CGCT_3A_3GCG$) by Fe^{II}·decarbamoyl-BLM A_2 also occurred primarily at C_3 and C_{11} and resulted in the formation of the same chemical products produced by Fe^{II}·BLM A_2. For this derivative, the specificity of cleavage at C_3 and C_{11} was similar to that of Fe^{II}·BLM A_2, but the C_3/C_{11} cleavage ratio was much closer to that of Fe^{II}·deglyco-BLM A_2. These data suggest that the geometry of Fe^{II}·decarbamoyl-BLM A_2 at its N-terminus differs significantly from that of Fe^{II}·BLM A_2. This implies a role for the carbamoyl moiety in the determination of metal coordination geometry, consistent with earlier evidence that the carbamoyl group may be a ligand for Fe.[17]

Given the general similarities in GC specificity for BLM, deglyco-BLM, and decarbamoyl-BLM and the fact that all three mediate the same chemical transformations concomitant with DNA cleavage, the simplest intepretation of the dramatic differences noted for the C_3/C_{11} cleavage ratio is that BLM can bind to DNA at a given (GC) site in each of two complementary orientations. The stoichiometry of Fe·BLM activation/DNA cleavage suggests that the observed double-strand DNA cleavage[5] must result from two activated Fe·BLM's;[6] presumably cleavage of each strand would require a separate orientation.

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(11) This observation also serves to eliminate the possibility that the stoichiometry observed previously for d($CGCT_3A_3GCG$) by BLM was due to self-inactivation of BLM.

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Utilization of the $^6Li\{^1H\}$ Nuclear Overhauser Effect. The Structures of Hydro[tris(trimethylsilyl)methyl]metalates of Boron, Aluminum, Gallium, and Indium in Solution

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The ^6Li nucleus ($I = 1$) has been largely neglected by spectroscopists. The low natural abundance (7.4%) and low magnetogyric ratio (3.94×10^7 rad T^{-1} s^{-1}) give a sensitivity which is about 400 times lower than that of the commonly observed ^7Li ($I = {}^3/_2$) though still 3.6 times that of ^{13}C. However, the quadrupole moment of ^6Li is smaller than that of any other isotope, so ^6Li behaves in isotropic solutions like a spin-$^1/_2$ nucleus,[1] and in environments where signals from ^7Li are broad and difficult to observe, ^6Li may give narrow lines.[2,3] Whereas quadrupole relaxation is dominant for ^7Li, dipolar interactions with the nearest protons dominate relaxation of ^6Li.

We judged that it should thus be possible by gated decoupling experiments with careful selective narrow-band irradiation of the ^1H spectrum to use the nuclear Overhauser effect (NOE)[4] to identify those protons in an organolithium compound or lithium hydride that are close to a ^6Li nucleus, and we have shown the validity of this approach[5] by examining the structure in solution of some alkyltrihydrometalates (compounds of a type important as reducing agents in organic synthesis[6]).

The structure of the boron compound $(Me_2PhSi)_3CB(\mu\text{-}H)_3Li(thf)_3$ (**1**) in the solid has been established by X-ray diffraction.[7] That the BH_3 fragment is present in solutions of **1** and of $(Me_3Si)_3CB(\mu\text{-}H)_3Li(thf)_3$ (**2**) is shown by the 1:3:3:1 quartets in the ^{11}B spectra and the 1:1:1:1 quartets in the ^1H spectra. Though ^7Li–^1H coupling has recently been observed[8] under rather restricted conditions, we have not detected it in our work. In gated decoupling experiments, broad-band irradiation of the proton spectra gave an NOE on the ^6Li signals of ca. 2.2 as measured by integration (the theoretical maximum is 3.4[1]). With weak (≈0.13 mW) selective irradiation (i) near the resonances of the two THF multiplets. (ii) at 40 Hz (i.e. $^1/_2J(BH)$ intervals over the hydride region, and (iii) in the empty parts of the spectrum, ^6Li spectra such as those in Figure 1 were obtained. Enhancements were found only when the irradiation was centered on the four peaks corresponding to the BH_3 protons, indicating that these are close to the ^6Li nuclei[4] and thus that **1** and **2** probably retain their hydrogen-bridged structures in solution.

In an attempt to determine the Li···H distance in solution, we measured the rate of buildup of the NOE. Using the established relation between this rate and the internuclear distance[9] and the

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