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.

[12] For example, over the Fe·BLM $A_2$ concentration range of 50–700 μM, the greatest difference in $C_3/C_{11}$ ratio observed was 9:91 vs. 17:83.

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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 ($3.94 \times 10^7$ 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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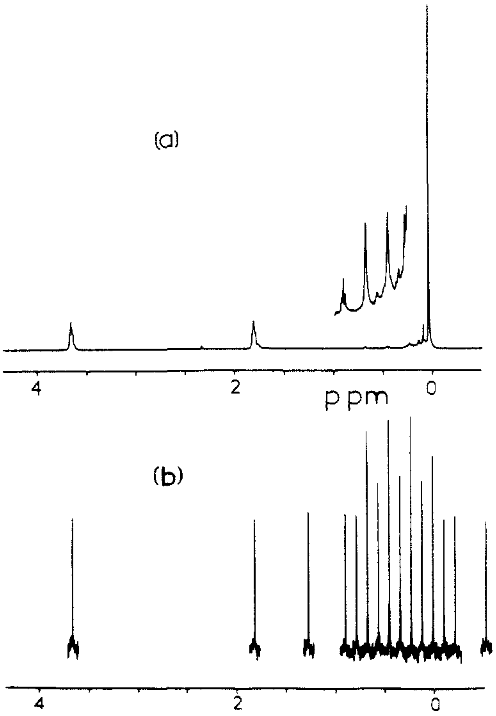
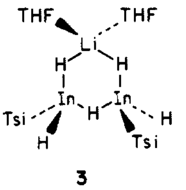


**Figure 1.** (a) $^1$H NMR spectrum of **2** obtained with a Bruker WM 360 spectrometer; (b) $^6$Li{$^1$H} spectra with irradiation centered at various positions in the proton spectrum. The $^6$Li spectra contained 8 K data covering 1805 Hz, giving a digital resolution of 0.44 Hz per point. Line widths were all ca. 1.2 Hz.

correlation time found from the molecular volume we obtained a Li···H distance of 2.2 Å. This is between the sum of the covalent and the sum of the van der Waals radii (1.71 and 3.0 Å, respectively).[10] There are few data in the literature on compounds with ($\mu$-H)$_3$ bridges between boron and another element but our results for **2** (Li···B 2.19, Li···H 2.2 Å) are similar to those for $Zr(BH_3)_4$ (Zr···B 2.31, Zr—H 2.21 Å) where the bridging hydrogens have been located by electron diffraction.[11]

Hydro[tris(trimethylsilyl)methyl]metalates of aluminum, gallium, and indium have also been isolated.[12] The $^6$Li spectra showed sharp singlets, but the signals for the metal hydride protons in the $^1$H spectra were too broad to be clearly detected. In each case, however, when the $^1$H region was irradiated successively at 180-Hz intervals there was a strong NOE on the $^6$Li signal, apparently generated by broad signals at $\delta_H$ (width at half-height (Hz) in parentheses) Al 3.25 (950), Ga 3.25 (2340), and In 4.75 (900). Thus these compounds, like **1** and **2**, appear to exist in toluene or THF with hydrogen bridges between M and Li. It is not possible from NOE measurements to determine how many hydrogen atoms are involved in each bridge, but from integration of THF and $Me_3Si$ signals in the $^1$H spectra, Li analyses, and molecular weight determinations, the structures do not appear to be completely analogous to that found for **1**. The presence of ($\mu$-H) bridges in the indium compound **3** has been confirmed by



**3**

an X-ray study;[12] the structures of the aluminum and gallium compounds are being investigated.

This work shows that selective $^6$Li{$^1$H} NOE experiments have potential (a) for the detection of weak broad resonances in $^1$H spectra and (b) for location of Li atoms relative to hydrogen atoms in organometallic compounds or hydrides. Both the reactivity and the regioselectivity of alkali metal hydrometalate reducing agents are known to depend on the alkali metal as well as the hydrometalate,[13] and it is likely that part of the explanation lies in the presence of species having the alkali metal close to the hydrometal center, probably in hydrogen-bridged species.

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## Asymmetric Induction via Addition–Elimination Process: Nitroolefination of $\alpha$-Substituted Lactones[1]

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Enantioselective construction of quaternary carbon centers is a stimulating subject in syntheses of complex natural products. Because of this, a number of methods to produce quaternary carbons in a highly enantioselective manner have been reported recently.[2] Here, we wish to report a new method for a chiral synthesis of quaternary carbon centers through the addition–elimination process using a chiral leaving group.

Advantage of asymmetric induction of chiral leaving groups includes the direct formation of chiral products, where the removal of the chiral auxiliary in the later stage is unnecessary. This type of chiral induction has lately attracted considerable attention from both mechanistic[3] and synthetic[4] points of view. Particularly, syntheses of chiral binaphthyls by nucleophilic aromatic substitution reported by Wilson and Cram[4c,d] are interesting, because the process involves ipso addition of arylmetal reagents in the initial stage before the elimination of the chiral group occurs. To the best of our knowledge, this was the first example of the chiral induction through an addition–elimination sequence in one pot. We describe another example of the same type of the chiral induction which is the first case in aliphatic systems.

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