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# Direct Evidence for the Absence of Chelation with β-Silyloxy Aldehydes and Lewis Acids

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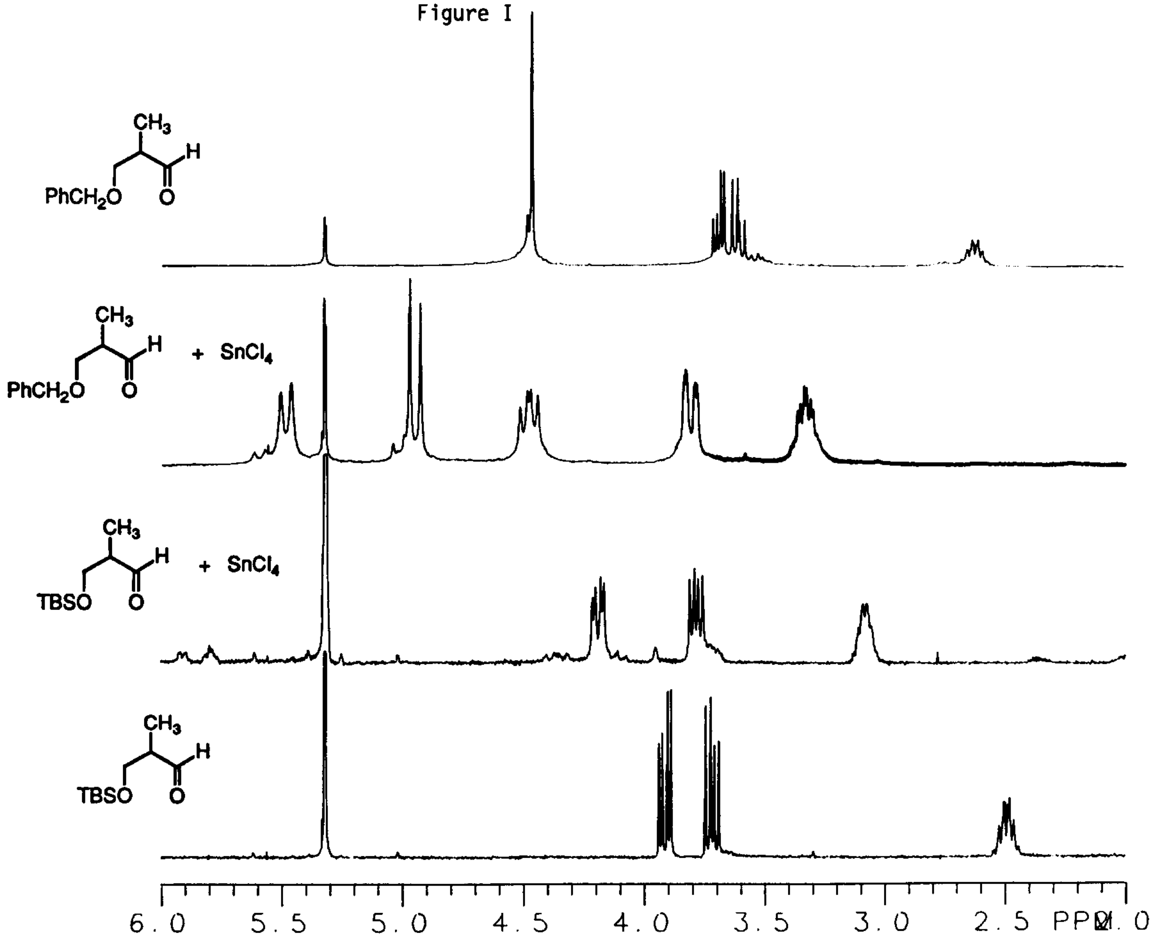
Summary: $^1$H and $^{13}$C NMR spectroscopy reveals no evidence for chelation with a TBDMS protected β-hydroxy aldehyde with $SnCl_4$ while the corresponding benzyl derivative forms a well behaved 1:1 chelate. Instead, a 2:1 aldehyde $SnCl_4$ complex is formed preferentially.

The concept of "chelation" as a means to control the stereochemistry of numerous organic reactions, by temporary conversion of a conformationally mobile acyclic system to a more rigid cyclic one, enjoys a long and rich history in organic chemistry. Such processes would appear to have been first examined systematically by Cram,[1] although there are undoubtedly numerous previous examples, and more recently brought to the fore by Still in the framework of a total synthesis of monensin.[2] A much smaller body of literature exists which suggests that oxygen substitution is more important in determining the outcome of reactions involving "chelation control" than is generally recognized. In particular, the stereochemical outcome of certain processes of special interest to us suggests that "chelation control" is not stereochemically significant in the Lewis acid mediated additions of various allylstannanes to either α- or β-trialkylsilyloxy aldehydes. However, it is important to note that such hypotheses, based solely upon the stereochemical outcome of a reaction, provide only indirect evidence regarding the involvement of chelated intermediates, as such results may always be rationalized in a number of ways. For example, it is an a priori possibility that the sense of nucleophilic addition to such a putative chelate could be determined primarily by the geometry and disposition of substituents at the β oxygen rather than by the substituent at $C_2$. Although theoretical reasons for the absence of chelation with silyloxy groups have been previously advanced,[3] and very recently made more respectable (see preceding paper in this issue), no direct experimental data is yet available to support the notion that chelation with silyloxy oxygen is not involved in nucleophilic additions to α- or β-silyloxy aldehydes. We record herein the first definitive experimental evidence on this issue. Our approach[4] utilizes variable temperature high field $^1$H and $^{13}$C NMR spectroscopy of various derivatives of, e.g., β-hydroxy aldehydes, in conjunction with NMR studies of appropriate ethers and aldehydes, to assess the involvement of "chelation" under conditions which mimic those of reactions involving putative chelated structures.

Shown in Figure I are the 2-6 ppm regions of the 300 MHz $^1$H NMR spectra of the β-benzyloxy aldehyde **2a** and the β-silyloxy aldehyde **2b** and their "chelates" with $SnCl_4$ at -60° in $CD_2Cl_2$. Comparison of these spectra reveals that although the expected effects for bidentate chelation are observed with the benzyloxy compound **2a**, no evidence for bidentate chelation is found with the silyloxy compound **2b**. Downfield shifts observed with the silyloxy compound (note Table I) at $C_3$ are much smaller than those observed with the benzyloxy derivative, and are in excellent agreement with what one would expect based upon carbonyl complexation alone. Moreover, the vicinal coupling constants between the protons at $C_3$ and the methine proton at $C_2$ change very little for substrate **2b** upon complexation with $SnCl_4$; with **2a**, one coupling constant increases while the other decreases, consistent with a pseudoequatorial disposition of the methyl group in a six-membered ring chelate. Inspection of the data tabulated in Table I also reveals two

Figure I

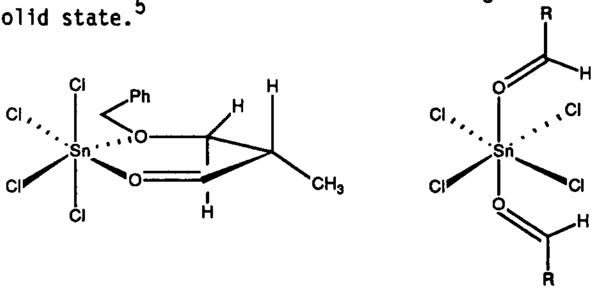


other significant differences between the two compounds, namely the chemical shifts observed for the formyl proton and the formyl carbon. In the bidentate complex derived from the benzyloxy compound **2a**, the downfield shift of the formyl proton is negligible, while in **2b** this proton is shifted downfield by 0.27 ppm. The carbon shifts for the aldehyde carbonyl, however, are comparable in both cases. These results strongly suggest that with $SnCl_4$ the $^1H$ chemical shifts at $C_1$ are determined primarily by magnetic anisotropy resulting from three dimensional structure while the $^{13}C$ shifts for the formyl carbon are primarily inductive, or charge induced, in origin.

Further support for this hypothesis comes from investigation of the stoichiometry of complexation in these cases. Although the benzyloxy compound **2a** forms a discrete, well behaved 1:1 complex with $SnCl_4$ whose NMR spectrum is essentially independent of temperature between -80°C and -20°C, titration experiments with the silyloxy compound **2b** clearly show that the stoichiometry in this case is 2:1 (**2b**: $SnCl_4$). Thus, upon adding $SnCl_4$ in increments to a 0.1 M solution of **2b** in $CD_2Cl_2$, the spectrum changes until 0.5 equivalents of $SnCl_4$ are added, past this point (up to 2.0 eq.) no further change is noted. This is exactly what is observed with simple aliphatic aldehydes possessing no ligating substituents other than the aldehyde oxygen.

Based upon the data discussed above, we suggest that with **2a** a 1:1 chelate of the gross structure shown in Figure II is formed with $SnCl_4$, while with **2b**, a 2:1 complex is formed in which the geometrical disposition of the Lewis acid is considerably different than in the complex formed with **2a**. Thus, the stereochemistry of complexation is forced to be E in the case of the bidentate complex derived from **2a**, while the 2:1 complex formed from **2b** or other simple aldehydes is presumably Z, which nicely accounts for the greater downfield shift for the formyl proton upon complexation of **2b** with $SnCl_4$. This interpretation is also consistent with a recent report that the complex formed from benzaldehyde and $BF_3$ is of E stereochemistry, both in solution and in the solid state.[5]

Figure II



Parallel behavior is observed using $MgBr_2$ as Lewis acid (note Table I). Thus, a bidentate chelate is formed from **2a** with $MgBr_2$, but only aldehyde complexation is observed with **2b**.

It is of course possible that chelation with β-silyloxy aldehydes could be observed with more potent Lewis acids. However, it seems unlikely that such will be the case, as **2b** with

$TiCl_4$ at -80° underwent extensive decomposition over the time period required to prepare the sample, shim the magnet, and collect data; some decomposition is observed even with $SnCl_4$. It is of interest to note in this regard that we have found $MgBr_2$ to be considerably more effective than either $SnCl_4$ or $TiCl_4$ in complexing sterically demanding β-alkoxy aldehydes,[6] yet no chelation of **2b** was observed with $MgBr_2$.

Table I

| Compound | Lewis Acid | CHO | $C_3$-H | $C_2$-H | $C_2$-H' | $^{13}$CCHO |
|---|---|---|---|---|---|---|
| **2a** | none | 9.60 | 2.59 | 3.64, dd<br>J = 9.1, 6.5 | 3.57, dd<br>J = 9.1, 4.5 | 204.6 |
| **2a** | $MgBr_2 \cdot OEt_2$ | 9.68<br>(-0.08) | 2.95<br>(-0.36) | 3.91, dd<br>J = 11.2, 7.9<br>(-0.27) | 3.62, dd<br>J = 11.2, 3.9<br>(-0.05) | 216.9<br>(-12.3) |
| **2a** | $SnCl_4$ | 9.61<br>(-0.01) | 3.28<br>(-0.69) | 4.46, dd<br>J = 13, 3.5<br>(-0.82) | 3.68, dd<br>J = 13, 8.8<br>(-0.11) | 220.1<br>(-15.5) |
| **2b** | none | 9.66 | 2.50 | 3.88, dd<br>J = 10.2, 4.5 | 3.77, dd<br>J = 10.2, 6.2 | 204.5 |
| **2b** | $MgBr_2 \cdot OEt_2$ | 9.85<br>(-0.19) | 2.79<br>(-0.29) | 4.01, dd<br>J = 10.3, 4.5<br>(-0.13) | 3.84, dd<br>J = 10.3, 6.1<br>(-0.07) | 216.0<br>(-11.5) |
| **2b** | $SnCl_4$ | 9.93<br>(-0.27) | 3.08<br>(-0.58) | 4.19, dd<br>J = 10.3, 3.8<br>(-0.31) | 3.78, dd<br>J = 10.3, 5.6<br>(-0.01) | 221.3<br>(-16.8) |

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