stirred for 1 h, benzaldehyde (212 mg, 2.00 mmol) in THF (10 mL) was added dropwise. After being refluxed for 90 h, the reaction mixture was hydrolyzed. After the usual workup, preparative TLC afforded 1-phenylbut-3-en-1-ol in 85% yield.

Reaction of Benzaldehyde with Prenyltrichlorosilane–Dilithium α,α-Bis(trifluoromethyl)benzenemethanolato(2−)-C^2,O System. To a dilithium compound prepared from hexafluorocumyl alcohol (1.490 g, 8.00 mmol) in THF–hexane (ref 21, method **B**) were added allyltrichlorosilane (702 mg, 4.00 mmol) and THF (10 mL) at room temperature. After the resultant mixture was stirred for 1 h, benzaldehyde (212 mg, 2.00 mmol) in THF (10 mL) was added to the mixture. No allylation products of benzaldehyde were found in the reaction mixture by GLC analysis even after refluxing for 90 h.

Isolation of Bis(triphenylphosphoranylidene)ammonium Bis(1,2-benzenediolato)allylsilicate (3a). To dilithium catecholate (8.0 mmol) in THF–hexane was added allyltrichlorosilane (4.00 mmol) in THF (20 mL), and the mixture was stirred for 12 h at room temperature. After removal of the solvent under vacuum followed by the addition of PPN(Cl) (2.296 g, 4.00 mmol) in CH_2Cl_2 (40 mL), the mixture was stirred for 12 h at room temperature. Filtration of the produced LiCl under argon followed by removal of the solvent under vacuum afforded a solid of the title compound quantitatively. The salt was very unstable in air and moisture, preventing further purification, but it afforded satisfactory spectral data: ^{1}H NMR ($CDCl_3$) δ 7.7–7.2 (m, 30), 6.9–6.2 (m, 8), 6.2–5.5 (m, 1), 4.60 (d, J = 7 Hz, 1), 4.45 (d, J = 9 Hz, 1), 1.72 (d, J = 7.2 Hz, 2); ^{13}C NMR ($CDCl_3$) δ 149.0 (s), 136.5 (d), 133.1, 131.5, 131.2, 131.0, 129.1, 128.8, 128.5, 123.7, 117.2 (d), 110.6 (t), 110.3 (d), 24.1 (t); ^{29}Si NMR ($CDCl_3$) δ −78.8; negative-ion FAB MS m/e −285 (anion).

Bis(triphenylphosphoranylidene)ammonium Bis(1,2-benzenediolato)prenylsilicate (3b): ^{1}H NMR ($CDCl_3$) δ 7.7–7.2 (m, 30), 6.9–6.2 (m, 8), 5.37 (d, J = 8 Hz, 1), 1.61 (d, J = 8 Hz, 2), 1.40 (s, 3), 1.31 (s, 3); ^{13}C NMR ($CDCl_3$) δ 150.1 (s), 133.8, 132.2, 131.9, 131.7, 129.8, 129.4, 129.2, 124.4, 118.4 (d), 117.4 (s), 115.6 (d), 110.6 (d), 26.4 (t), 25.7 (q), 17.5 (q); ^{29}Si NMR ($CDCl_3$) δ −77.3; negative-ion FAB MS m/e −313 (anion).

Bis(triphenylphosphoranylidene)ammonium Bis[α,α-bis(trifluoromethyl)benzenemethanolato(2−)-C^2,O]allylsilicate (6a). To a dilithium compound of hexafluorocumyl alcohol in THF–hexane prepared with the literature method[21] by using hexafluorocumyl alcohol (1.952 g, 8.00 mmol) were added allyltrichlorosilane (4.00 mmol) and THF (20 mL) at room temperature, and then the mixture was stirred for 12 h. After filtration of LiCl salts, the organic layer was washed with water and dried over anhydrous Na_2SO_4 and the solvent was evaporated. The crude product was purified by reprecipitation from acetone–diethyl ether: 85% yield; white crystals; mp 145–148 °C; ^{1}H NMR ($CDCl_3$) δ 8.3–8.1 (m, 2), 7.7–7.0 (m, 36), 6.13 (ddd, J = 16.5, 9.0, 8.3 Hz, 1), 4.52 (dd, J = 16.5, 3.0 Hz, 1), 4.35 (dd, J = 9.0, 3.0 Hz, 1), 1.93 (d, J = 8.3 Hz, 2); ^{13}C NMR ($CDCl_3$) δ 144.6 (s), 141.2 (s), 141.0 (d), 137.9 (d), 133.8, 132.1, 132.0, 131.9, 129.6, 129.5, 129.4, 128.0 (d), 127.8 (d), 125.8, 123.3 (d), 108.9 (t), 81.9 (sep), 31.5 (t); ^{29}Si NMR ($CDCl_3$) δ −66.6; negative-ion FAB MS m/e −553 (anion).

Bis(triphenylphosphoranylidene)ammonium Bis[α,α-bis(trifluoromethyl)benzenemethanolato(2−)-C^2,O]prenylsilicate (6b): 81% yield, white crystals; mp 151–151.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.3–8.1 (m, 2), 7.7–7.0 (m, 36), 5.42 (t, J = 8 Hz, 1), 1.78 (d, J = 8 Hz, 2), 1.45 (s, 3), 1.38 (s, 3); ^{13}C NMR ($CDCl_3$) δ 145.1 (s), 141.1 (s), 137.7 (d), 133.8, 132.2, 131.9, 131.7, 129.8, 129.4, 129.2, 127.6 (d), 127.4 (d), 125.3 (d), 124.5, 123.0 (d), 119.2 (s), 26.0 (t), 24.5 (q), 17.4 (q); ^{29}Si NMR ($CDCl_3$) δ −65.4.

Reaction of 3a with Benzaldehyde. A mixture of **3a** (1.648 g, 2 mmol), benzaldehyde (110 mg, 1.00 mmol), and THF (10 mL) was refluxed for 90 h under argon. The usual workup afforded 2,2-dimethyl-1-phenylbut-3-en-1-ol in 90% yield, which was determined by GLC.

Reaction of 3b with Benzaldehyde. A mixture of **3b** (1.704 g, 2.00 mmol), benzaldehyde (110 mg, 1.00 mmol), and THF (10 mL) was refluxed under argon for 90 h. The usual workup afforded 2,2-dimethyl-1-phenylbut-3-en-1-ol in 80% yield. No other regioisomers were detected by GLC and ^{1}H NMR spectra.

Reaction of 6b with Benzaldehyde. A mixture of **6b** (2.184 g, 2.00 mmol), benzaldehyde (110 mg, 1.00 mmol), and THF (10 mL) was refluxed for 90 h. No allylation products were found in the reaction mixture. A similar experiment in the presence of excess CsF did not give the desired products.

Modeling Chemical Reactivity. 9. The Role of the Metal in Controlling the Stereochemistry of Nucleophilic Additions of Organometallic Reagents

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Abstract: The stereochemistry of nucleophilic addition of organometallic reagents to unsaturated organic substrates depends on at least three factors: (1) the accessibility of the metal, (2) the degree of reagent ion pairing in solution, and (3) the ability of the substrate to discriminate between the nucleophilic and electrophilic character of the reagent. Reagents such as $LiAl(CH_3)_4$ behave as if they were fully separated ion pairs; the lithium cation plays little if any role in the selectivity of tetramethylaluminate anion. A similar situation prevails for reagents such as methyltitanium triisopropoxide, the metal that is shielded from the substrate by its ancillary ligands. On the other hand, Grignard, dialkylmagnesium, and alkyllithium compounds incorporate accessible and highly electrophilic metal centers, which are able to interact with the substrate and influence the stereochemical outcome of the addition process. It is suggested that nucleophiles that are associated with an accessible electrophilic metal will show opposite stereochemical preferences from "free" nucleophiles or compounds where the metal center is shielded from the substrate. Available experimental data on stereoselectivities of Michael additions to chiral vinylic sulfoxides with different reagents provide support for such a classification of nucleophilic reagents. The effects of solvent upon asymmetric additions involving nucleophilic reagents are addressed. It is argued that solvation is of relatively minor importance in determining reaction asymmetries in this class of additions.

Few classes of compounds have contributed to selective carbon–carbon bond forming reactions as significantly as have metalated organic reagents.[1] The variety of organic substrates known to undergo facile transformations upon treatment with organometallic compounds has prompted development of reagents for novel synthetic applications and has spurred efforts toward

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elucidation of organometallic addition mechanisms.[2] Despite such efforts over many years, surprisingly little detailed information exists on the fundamental dictates of organometallic additions.

Difficulties in characterizing the actual reactive organometallic species in solution have complicated experimental mechanistic studies.[2] Solvation and aggregation of organometallic reagents likely alters their structure and reactivity,[3] although it remains to be established what if any role these factors play in directing reaction stereoselectivity.

Reported here are the results of a theoretical study, the aim of which has been to establish connections between reagent and substrate structure and selectivity and thereby provide a basis for the description of the stereoselectivity of organometallic reagents. The key to the analysis lies in correlating known differences in stereoselectivities of several commonly employed organometallic nucleophiles, namely Grignard and dialkylmagnesium reagents, lithium aluminates and alkyltitanium alkoxides, with differences in reagent structure. This has been accomplished utilizing previously described chemical reactivity modeling techniques,[4,5] which suggest that product stereochemistry is dictated early along the reaction coordinate on the basis of electrostatic considerations. Complex nucleophiles, with both nucleophilic and electrophilic sites, will add to complex substrates with complementary sites in order to maximize favorable electrostatic interactions.

The asymmetry brought on by sulfoxide functionality, coupled with the nucleophilic sulfur lone pair and sulfoxide oxygen (available to bind the metal), suggests the utility of vinyl sulfoxides to study the asymmetric dictates in addition reactions involving organometallic reagents. Stereochemical data for Michael additions to chiral vinylic sulfoxides show a marked dependence on nucleophilic reagent and can be rationalized in terms of conditional (depending on reagent) stereodirection of nucleophilic agents via interaction of accessible electrophilic site(s) on the organometallic reagent (the metal) with basis site(s) on the substrate.

Computational Methods

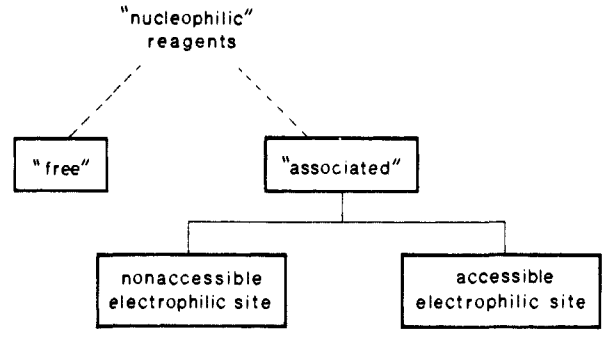
All calculations have been carried out at the single-determinant (Hartree–Fock) level with the 3-21G split-valence basis set[6a,b] (3-21G* for molecules containing second-row elements[6c]). Geometries obtained at these levels compare favorably with higher level theoretical[7] as well as experimental[8] equilibrium structures, and have been utilized throughout. All ab initio calculations were performed with the GAUSSIAN 85 program system,[9] as implemented on Harris H800 and Control Data 180/830 digital computers. Electrostatic and hydride potentials have been obtained from the resultant wave functions, according to methods described in detail elsewhere,[10] and have been superimposed onto substrate electron-density surfaces corresponding to $\psi^2 = 0.002$ electrons/bohr^3.[11] Accessible "atomic" surface areas are defined according to

$$\text{area (Å}^2) = 4\pi r^2(\text{accessible surface points})/(\text{total surface points})$$

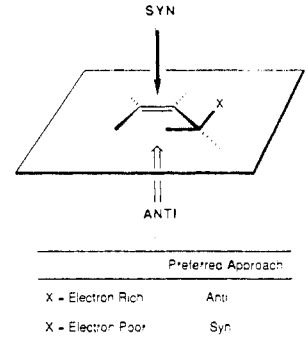
where the atomic radii r and the number of accessible surface points are obtained from procedures described elsewhere.[12] These "atomic" surface areas provide an alternative assessment of steric accessibility and have been utilized throughout to complement visual inspection of computer-generated space-filling models. It should be noted that our use of "accessibility" is similar to previous efforts[13] that have been concerned with evaluating solvent accessible surfaces and their effects on reactivity and selectivity in biomolecular systems.

Results and Discussion

Nucleophilies may be grouped into two distinct categories, depending on whether or not a metal is associated with the reagent. "Free" nucleophiles, devoid of an incorporated metal, are exemplified by nonionic electron-rich species such as piperidine, or alternatively, by the anion component of fully separated ion pairs in the presence of cation-complexing cryptands or crown ethers.[14] Conversely, organometallic nucleophiles, e.g., cuprate, alkyllithium, alkyltitanium, dialkylmagnesium, and Grignard reagents are representative of the group of reagents that incorporate an eleectrophilic, i.e., Lewis acidic, metal center. This latter class of reagents may be further subdivided into those in which the metal is accessible to the substrate and those where it is not. Such a categorization provides the basis on which the stereochemistry of nucleophilic additions may be discussed.



In the absence of severe steric crowding, "free" nucleophiles (type A nucleophiles) should add to asymmetric olefins according to electrostatic dictates;[4] addition should occur preferentially onto the olefin face that is the more removed from electron-rich functionality, i.e.,



(2) For example, for discussion of the mechanisms of Grignard additions, see: Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545.

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(11) See: Francl, M. M.; Hout, R. F., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1984**, *106*, 563.

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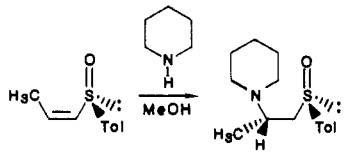
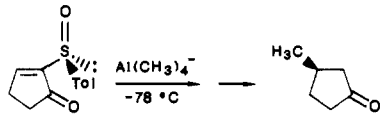
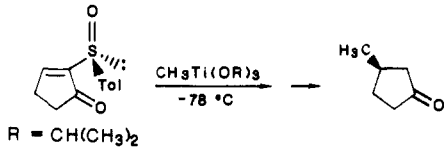
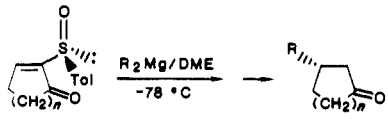
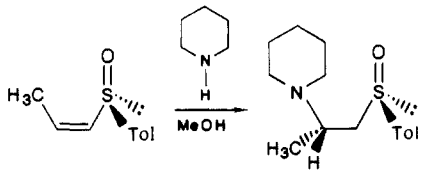
Table I. Experimental Stereochemistry of Michael Additions to Vinyl Sulfoxides

reaction	side of nucleophilic attack	selectivity	ref
	tolyl	3:1	16
	tolyl	19:1	17b
	tolyl	14–49:1	17b, 19
	lone pair	3–49:1	22
	lone pair	4–49:1	23

Experimental data collected for conjugate additions to chiral vinylic sulfoxides[15] (Table I) provides a self-consistent base of information with which to probe the limits of such a hypothesis.

Addition of piperidine (a type A nucleophile) to (−)-(*R*)-(*Z*)-propenyl *p*-tolyl sulfoxide is reported to occur anti to the electron-rich lone pair on sulfur, even at the expense of encountering the bulky tolyl group.[15,16]



$MeTi(i\text{-}PrO)_3$ also participates in conjugate additions to chiral vinylic sulfoxides in a highly diastereoselective fashion[17b,19] and with the same asymmetric biases already discussed for piperidine and for lithium tetramethylaluminate. While the alkyltitanium reagent incorporates an electropositive and highly oxophilic metal, the metal is not accessible to the substrate, at least at an early stage along the reaction coordination where stereoselectivity is determined (cf. ref 5f). Inspection of space-filling models (see also Table II) reveals the titanium (in the model compound $MeTi(OMe)_3$) to be effectively shielded by the three σ-bound

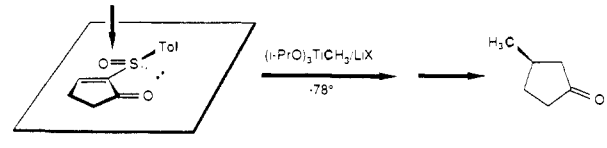
Table II. Exposed Surface Area and Average Atomic Electrostatic Potentials of the Metal Center in Alkylmagnesium and Titanium Reagents

reagent	surface area of contained metal,[a] Å	average atomic potential of contained metal[b,c]
CH_3MgCl	46.2	107.2
$(CH_3MgCl)_2$	33.8	111.3
$CH_3MgCl{\cdot}H_2O$	32.0	98.6
$CH_3MgCl{\cdot}2H_2O$	18.6	31.4
$(CH_3)_2Mg$	43.6	91.4
$(CH_3)_2Mg{\cdot}H_2O$	29.5	81.5
$(CH_3)_2Mg{\cdot}2H_2O$	16.9	4.2
$(CH_3O)_3TiCH_3$	12.5	

[a] See text for definitions. [b] Atomic averages computed by using previously reported methods.[5a,10] [c] In kcal mol^{-1}.

alkoxy ligands, consistent with the monomeric solution structure of the reagent.[20] Therefore, methyltitanium triisopropoxide is a type B nucleophile, i.e., one in which the nucleophilic "center" is "associated" with an electrophilic site that is not readily accessible for external interactions.[21]

In analogy to type A nucleophiles, electrostatic considerations indicate that nucleophilic reagents of type B will add preferentially anti to the more electron rich olefin face. Thus, addition of alkyltitanium species to vinyl sulfoxides should occur anti to the sulfur lone pair, or alternatively syn to the "bulky" tolyl group, with the vinyl sulfoxide reacting from the *S*-cis conformer,[4,15] i.e.,



(15) Unless otherwise noted, interpretation of the experimental data is based on the assumption that vinyl sulfoxides react from a conformer in which the SO and CC double bonds are syn copolanar.[4] 3-21G*//3-21G* calculations on 2-(methylsulfinyl)acrolein, a more appropriate model for the cyclopentenone sulfoxides used experimentally, show no evidence for alternative forms. Kahn, S. D.; Hehre, W. J., unpublished results.

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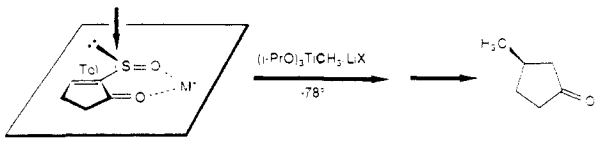
(21) This contrasts to the interpretation of rate accelerations reported for the addition of $(i\text{-}PrO)_3TiMe$ to electrophilic groups flanked by α-heteroatom functionality. See: Reetz, M. T.; Maus, S. *Tetrahedron* **1987**, *43*, 101.

The experimental data[17b,19] are in accord, although it should be noted that these results have also previously been rationalized by using a "chelate" model,[17] i.e.,

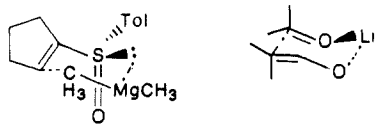


Clearly, further experimental work, directed at the effect of added cryptands or crown ethers on addition selectivity, is needed to distinguish between the differing interpretations.

(Dimethylcopper)lithium exhibits the same diastereochemical preferences (with a selectivity of 91:9) as methyltitanium triisopropoxde,[17b] although it is not clear at this time whether these reagents ("cuprates") are best categorized as type A or type B nucleophiles. Research is under way to provide clarification.

Finally, the experimental data (Table I) show that dialkylmagnesium[22] and alkali-metal enolates,[23] in the absence of added chelating metals, add to the more electron rich olefin face of chiral vinylic sulfoxides,[24] opposite to the preferences established for additions of type A and B nucleophiles.[25] Notably, both of these reagents possess accessible electrophilic sites (Table II), and thus are type C nucleophiles, consistent with the aggregation and solvation of alkyllithium and Grignard reagents.

In contrast to the preference of "nucleophiles" to avoid electron-rich allylic functionality,[4] theoretical studies[5b,c,e,f] as well as numerous experimental investigations[26] attest to the preferred association of electrophiles with electron-rich olefin faces. It is postulated here that the *accessible* electrophilic site (the metal) of type C reagents is responsible for the noted stereochemical preferences, overwhelming the "normal" preference[4] of nucleophilic reagents to avoid electron-rich functionality. This is exemplified by the addition of dimethylmagnesium to (*S*)-(+)-2-(*p*-tolylsulfinyl)-2-cyclopentenone, wherein the favored approach of the reagent results from the interaction of the central magnesium with the sulfur lone pair (in addition to interaction with the sulfoxide oxygen). The seemingly direct analogy of additions of type C nucleophiles to the putative transition structure of enolate additions to carbonyl compounds[27] is quite striking, i.e.,



The importance of the interaction between the electropositive metal in several type C nucleophiles and basic sites on achiral substrates has been alluded to previously.[28,29] In the case of reductions of carbonyl compounds with lithium borohydride, interaction of the carbonyl oxygen with the tightly ion paired lithium cation has been suggested as the major attractive force along the reaction coordinate.[28c,d] Subsequent efforts to explore the mechanistic details of model Grignard additions[28b] and methyllithium alkylations of carbonyl compounds[28e] have concluded that the interaction between the metal of these type C reagents and the carbonyl oxygen dictates the preferred attack trajectory. The "electrophilic" nature of the nucleophilic species has been stressed[28e] and is supported by analysis of the energetic composiiton of the transition structures.[28b]

Thus far, no mention has been made of the role that solvation might play in altering the reagent's electrostatic discriminations of substrate asymmetry. While it is obvious that both nucleophile and substrate must desolvate for reaction to occur[28e] (even if only at the sites involved in the bond-forming process), the calculations presented here suggest that solvation will not fundamentally change the sense of the electrostatic biases controlling addition stereochemistry. Specifically, calculated electrostatic potentials for representative type C nucleophiles (Table II), i.e., reagents most likely to be affected by interactions with solvent, are all qualitatively similar, irrespective of reagent aggregation and local solvation. *It can be inferred that while differential solvation of chiral substrates, and solvation and aggregation of nucleophilic agents, may be reponsible for the subtle variances in experimental selectivities seen upon changes in reaction conditions, e.g., solvent and temperature,*[34] *these effects are likely to be of relatively minor concern when addressing inherent reaction asymmetries, at least in the nucleophilic additions discussed here.*[30]

Lastly, asymmetric biases imposed by steric interactions can also influence overall reaction stereoselectivity. Note, however, that these biases will vary with nucleophile type. Type A and B nucleophiles, as a consequence of their inherent preference to avoid electron-rich functionality, approach the double bond in vinylic sulfoxides from the side of the carbon substituent on sulfur (in a contrasteric fashion). On the other hand, type C nucleophiles, in an effort to maximize favorable electrostatic interactions between the electrophilic metal and the sulfur lone pair, approach from the opposite (sterically favored) side. Thus, attempts at steric control, i.e., use of bulky substituents at sulfur, should attenuate or even reverse reaction stereochemistry in additions involving A and B nucleophiles, while substitution should accentuate the stereochemical preferences of additions involving nucleophiles of type C species.[32]

Conclusion

The stereochemistry of nucleophilic additions to chiral vinylic sulfoxides, and to electronically asymmetric substrates in general, follows predictable patterns depending on whether or not an *accessible* electrophilic site, e.g., an incorporated metal or tightly ion paired cation, is present. Nucleophiles that either do not incorporate electropositive metals (type A nucleophiles), or alternatively, organometallic reagents in which the central metal is prohibited from interacting with the substrate by its ancillary ligands (type B nucleophiles), will act to avoid areas of high electron density such as lone pairs or lone-pair-containing substituents. The stereochemistry of addition of nucleophiles incorporating an *accessible* electron-deficient metal, or having a

(22) Posner, G. H.; Hulce, M. *Tetrahedron Lett.* **1984**, *25*, 379.

(23) "Sodium enolates": (a) Tsuchihashi, G.; Mitamura, S. M.; Inouye, S. Oguro, K. *Tetrahedron Lett.* **1973**, 323. "Lithio enolates": (b) Posner, G. H.; Asirvatham, E. *J. Org. Chem.* **1985**, *50*, 2589. (c) Posner, G. H.; Switzer, C. *J. Am. Chem. Soc.* **1986**, *108*, 1239.

(24) Highly stabilized enolate anons, e.g., bis α-silyl or α-bromo substituted (cf. ref 23c) react via ion-separated species, i.e., they are type A nucleophiles.

(25) This reversal in addition selectivity upon changing from a type B ($MeTi(i\text{-}PrO)_3$) to a type C ($MgMe_2$) nucleophile extends beyond conjugate additions to vinyl sulfoxides. For an example of additions to α-alkoxy ketones, see: Reitstøen, B.; Kilaas, L.; Anthonsen, T. *Acta Chem. Scand., Ser. B* **1986**, *B40*, 440.

(26) For example: (a) Giese, b.; Bartman, D. *Tetrahedron Lett.* **1985**, *26*, 1197. (b) Chamberlin, A. R.; Mulholland, R. L., Jr. *Tetrahedron* **1984**, *40*, 2297. (c) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487. (d) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733. (e) Raiter, M.; Castaing, M.; Godet, J.; Peryre, M. *J. Chem. Res. (S)* **1978**, 179. (f) Bellucci, G.; Bianchini, R.; Ingrosso, G.; Mastrorilli, E. *Gazz. Chim. Ital.* **1978**, *108*, 643.

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(29) Kauffman, T.; Abel, K.; Bourath, W.; Kolb, M.; Moller, T.; Pahde, C.; Raedeker, S.; Robert, M.; Wensing, M.; Wichman, B. *Tetrahedron Lett.* **1986**, *27*, 5351.

(30) In one careful study,[31] changes in solvent have been documented to alter selectivities in conjugate additions to chiral vinylic sulfoxides. The selectivity of additions involving type C nucleophiles (Grignard reagents) is greatly affected by solvent, whereas the selectivity of additions of type B nucleophiles ($RTi(i\text{-}PrO)_3$) is less sensitive to the nature of the solvent.

(31) Posner, G. H.; Frye, L. L. *Isr. J. Chem.* **1984**, *24*, 88.

(32) Changing from *p*-tolyl to 1-naphthyl[33] does not alter reaction stereochemistry in Et_2Mg additions (type C) to arylsulfinylcycloalkenones,[22] whereas additions of (dimethylcopper)lithium, a type A or B nucleophile, have a reversed sense of stereoselectivity when *p*-tolyl is changed to 1-naphthyl.[17b]

(33) See: Hulce, M. Ph.D. Thesis, Johns Hopkins University, 1983, p 93.

(34) There are presently insufficient data with which to address the relative contributions of enthalpic and entropic effects on reaction asymmetry.

tightly ion paired cation (type C nucleophiles), is also controlled by electrostatics, although here it is the electrophilic metal that exerts the dominant influence. The preferred attack trajectory is, therefore, syn to electron-rich functionality on the substrate.

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Registry No. CH_3MgCl, 676-58-4; $(CH_3MgCl)_2$, 113669-22-0; $CH_3MgCl{\cdot}H_2O$, 113669-23-1; $CH_3MgCl{\cdot}2H_2O$, 113669-24-2; $(CH_3)_2Mg$, 2999-74-8; $(CH_3)_2Mg{\cdot}H_2O$, 113669-25-3; $(CH_3)_2Mg{\cdot}2H_2O$, 113669-26-4; $(CH_3O)_3TiCH_3$, 64516-18-3.

Intramolecular Hypervalent Sn–O Interaction. The Origin for Fixation of Six-Membered Carbocycles to the 1,3-Diaxial Conformer and for Stereoselective Osmylations

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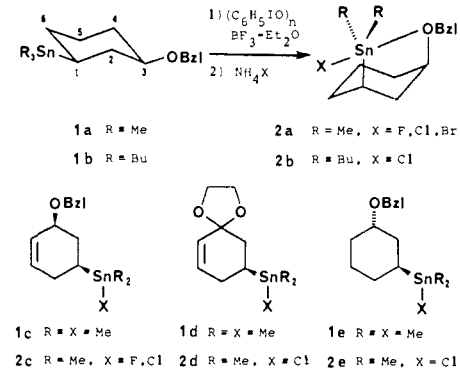
Abstract: Reported for the first time are the synthesis and characterization of 1,3-diaxial six-membered carbocycles, in which intramolecular Sn–O hypervalent interaction is essential for the conformational preference. When one of the methyl groups of (*cis*-3-(benzyloxy)cyclohexyl)trimethylstannane (**1a**), which exists predominantly as a 1,3-diequatorial conformer, is replaced by a highly electronegative substituent such as halogen by utilizing BF_3-activated iodosylbenzene, the resulting (*cis*-3-(benzyloxy)cyclohexyl)halogenodimethylstannane **2a** (X = Cl), both in solution and the solid state, adopts a 1,3-diaxial conformation as a result of an intramolecular hypervalent interaction between the tin and etheric oxygen atoms. This is termed the "stabilizing 1,3-diaxial interaction". The tin atom of **2a** (X = Cl) has a distorted trigonal-bipyramidal configuration with the oxygen and chlorine atoms in apical positions. The stabilizing 1,3-diaxial interaction makes possible a highly stereoselective osmylation of (5,5-(ethylenedioxy)cyclohex-3-enyl)chlorodimethylstannane (**2d**). Dimethylhalogenostannyl groups were converted into the corresponding hydroxyl groups with retention of configuration.

Diaxial conformation of cis-1,3-disubstituted cyclohexanes is particularly unfavorable in terms of 1,3-diaxial interactions.[2] The destabilizing interaction caused by van der Waals repulsion biases the zwitterion structure of *cis*-3-aminocyclohexanecarboxylic acid toward the diequatorial conformation, even though strong electrostatic attraction between both axial substituents would be expected to occur in the diaxial structure of the zwitterion.[3] We report herein the synthesis and characterization of the first examples of 1,3-diaxial six-membered carbocycles, in which a "stabilizing 1,3-diaxial interaction" between tin and oxygen atoms plays an essential role in determining the conformational preference.

Tetraalkyltins, because of their low Lewis acidity, produce hypervalent pentacoordinated complexes only in reactions with strong nucleophiles such as alkyllithiums.[4] Thus, *cis*-cyclohexylstannane **1a** shows no evidence of any intramolecular donor–acceptor interaction and both substituents are equatorial.[5]

Scheme I



On replacement of one of the methyl groups of **1a** with a highly electronegative ligand such as halogen, the tin atom of **2a** becomes sufficiently acidic that the intramolecular hypervalent Sn–O interaction[6,7] can be expected to become important. We therefore

(1) (a) Kyoto University. (b) Osaka University. (c) Shionogi & Co. Ltd.

(2) (a) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley-Interscience: New York, 1965; Chapter 2. (b) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; Chapter 8.

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