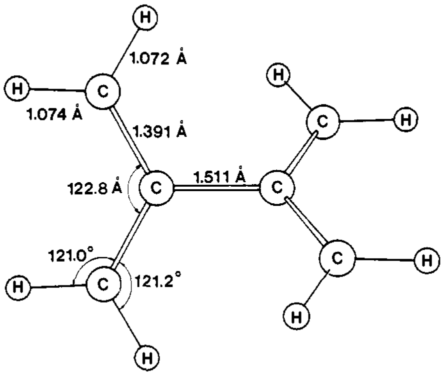

Figure 1. Triplet UHF optimized geometry for TME. The dihedral angle between the planes of the allyl groups is 44.9°.

Table I. Calculated Singlet and Triplet Energies for TME

geometry	calcn	$E(^1A_1)^a$	$E(^3B_3)^a$	ΔE^b
planar (D_{2h})	TCSCF/RHF	−231.7575	−231.7546	1.8
planar (D_{2h})	SD-CI	−232.0447	−232.0403	2.8
triplet minimum (D_2)	TCSCF/RHF	−231.7599	−231.7600	−0.1
triplet minimum (D_2)	SD-CI	−232.0443	−232.0437	0.4
perpendicular (D_{2d})	TCSCF/RHF	−231.7634	−231.7594	2.5
perpendicular (D_{2d})	SD-CI	−232.0464	−231.0428	2.2

[a] Energies in hartrees. [b] $E(^3B_3) - E(^1A_1)$ in kcal/mol.

lowest singlet and triplet state of TME prefer nonplanar geometries. However, our calculations find the singlet to lie below the triplet at all the geometries investigated. Thus, the computational results reported here stand in direct conflict with the experimental finding of a triplet ground state.[7]

The lowest triplet state of planar (D_{2h}) and perpendicular (D_{2d}) TME was optimized with UHF calculations. These calculations were performed with Gaussian 82,[10] with use of the 3-21G basis set.[11] However, the UHF triplet geometry of lowest energy, shown in Figure 1, was found to have only D_2 symmetry with a dihedral angle of 44.9° between the planes of the allyl groups. A vibrational analysis showed this geometry to be a true energy minimum.

CI calculations were performed at all three geometries, using the Dunning split-valence basis set, augmented by a set of polarization functions on carbon.[12] The calculations were carried out with MELD,[13] starting from an RHF wave function for the triplet and a two-configuration (TC) SCF wave function for the singlet. The CIs involved all single and double excitations within the conceptual minimal basis set of valence orbitals. In D_2 symmetry this generated 32 561 spin-adapted configurations for $^3B_3$ and 16 570 for $^1A_1$. In order to provide the maximum amount of electron correlation with the virtual orbitals used, the virtual space was transformed to K orbitals.[14]

The TCSCF/RHF and CI energies are given in Table I. The calculations at the TCSCF/RHF level do not include the effects of dynamic spin polarization,[2] since spin polarization requires intraallylic electron correlation. Dynamic spin polarization, which is included at the CI level, results in enhanced π bonding in the lowest singlet state between the central carbons of the allylic moieties[2,3] and, hence, is largest at planar geometries.

Despite this fact, the singlet is found to prefer the perpendicular to the planar geometry. However, this preference is reduced from 3.7 kcal/mol at the TCSCF level to 1.1 kcal/mol at the CI level of theory. Since the triplet also has a lower energy at the perpendicular than at the planar geometry, it is likely that in both states this energetic preference is due to the smaller interallylic, steric repulsion at the former geometry.

The UHF triplet minimum occurs near the geometry of minimum electronic interaction between the allyl NBMOs. At this geometry, the singlet and triplet are essentially degenerate in energy at the TCSCF/RHF level of theory. When CI is included, dynamic spin polarization causes the singlet to fall 0.4 kcal/mol below the triplet, since at this geometry there is still appreciable overlap between the π orbitals on the central carbons.

The CI energy of the singlet at its optimal geometry (D_{2d}) is 1.3 kcal/mol lower than that at the optimal UHF triplet geometry (D_2), so that the adiabatic singlet–triplet energy separation is computed to be 1.7 kcal/mol.[15] The calculated energy separation allows the possibility that a thermally populated triplet might be observable by EPR, but the singlet is unequivocally predicted to be the ground state.

It is, of course, conceivable that higher level calculations could reverse the energy ordering of these two states. However, there is a simple physical argument in favor of a singlet ground state. If TME is regarded as two allyl radicals, any long-range bonding between the allyl NBMOs will selectively stabilize the singlet. Moreover, even at geometries where there is no long-range bonding, dynamic spin polarization in the singlet will still stabilize it with respect to the triplet.[3]

Although there are several possible explanations for the apparent conflict between the theoretical prediction of a singlet ground state for TME and the experimental finding of a linear Curie–Weiss plot for this diradical, the correct resolution remains to be determined.

Acknowledgment. We thank the National Science Foundation for support of this research. Some of the calculations were performed on a Convex C-1 computer, whose purchase was made possible by Grant CHE-85501 from the National Science Foundation.

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(9) For experimental studies of singlet TME, see: Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic: New York, 1981; pp 138–149.

(10) Binkley, J.; Frisch, S.; Raghavachari, M.; Fluder, E.; Seeger, R.; Pople, J. A., Carnegie-Mellon University.

(11) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939.

(12) Dunning, T. H.; Hay, P. J. In *Methods of Electronic Structure Theory*; Schafer, H. F., III, Ed.; Plenum: New York, 1977; Vol. 2.

(13) Developed by E. R. Davidson and co-workers at the University of Washington.

(14) Feller, D.; Davidson, E. R. *J. Chem. Phys.* **1981**, *74*, 3977.

(15) With both the RHF and CI calculations, the triplet minimum, found by rigid rotation of the allyl groups in Figure 1, occurs at a dihedral angle of 53.2° between the planes of the allyl groups. At this geometry the $^3B_1$ CI energy of −232.0440 hartrees is 0.5 kcal/mol above that of $^1A_1$ and gives an adiabatic singlet–triplet splitting of 1.5 kcal/mol.

Nucleophilic Addition Reactions of Hindered Unsaturated Boranes. A New Synthesis of Organoboranes

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Received August 8, 1986

Olefin activation to nucleophilic addition by virtue of the presence of polarizing substituents is of fundamental importance. Conspicuously absent are examples of such activation by boron-containing groups owing to their normally facile formation of ate complexes with nucleophiles.[1] We wish to report the first examples of boron-activated nucleophilic additions to olefins made possible by the steric suppression of ate complex formation.

It has been shown previously that ate complex formation can be sterically retarded in appropriately substituted arylboranes.[2]

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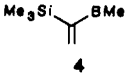
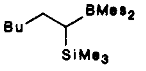
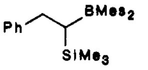
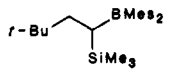
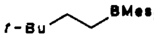
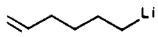
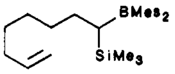
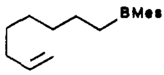
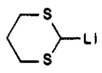
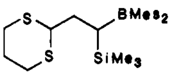
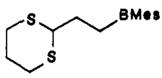
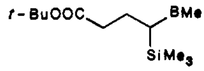
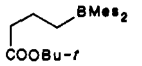
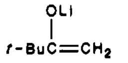
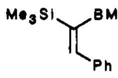
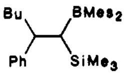
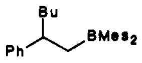
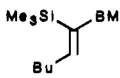
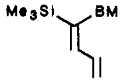
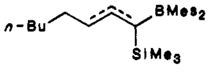
(1) Pelter, A.; Smith, K. In *Comprehensive Organic Chemistry*; Jones, D. N., Ed.; Pergamon: New York, 1979; Vol. 3, Section 14.

(2) Brown, H. C.; Dodson, V. H. *J. Am. Chem. Soc.* **1957**, *79*, 2304. Blount, J. F.; Finocchiaro, P.; Gust, D.; Mislow, K. *Ibid.* **1973**, *95*, 7019. Glogwski, M. E.; Zumbulyadis, N.; Williams, J. L. R. *J. Organomet. Chem.* **1982**, *231*, 97.

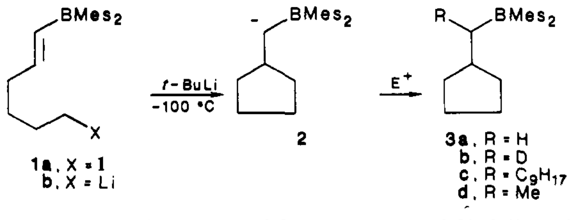
0002-7863/87/1509-0931$01.50/0

Table I. Organoboranes from Nucleophilic Additions to Unsaturated Dimesitylboranes[a]

entry	acceptor	RM	adduct **2**[b]	yield, %	borane **3**	yield, %
1	 **4**	n-BuLi		96		100
2		BuMgCl		0, 51[c]		
3		$Bu_2Cu(CN)Li_2$		66[d]		
4		PhLi		95[e]		96
5		t-BuLi		86[f]		94[g]
6				91		90
7				97		96
8		$LiCH_2COOBu$-t		96[h]		93
9		$PhC\equiv CLi$		0[i]		
10		 $t\text{-BuC(OLi)}\!=\!CH_2$		0		
11	 **8**	n-BuLi		91		100
12	 **9**	n-BuLi		0[j]		
13	 **10**	n-BuLi		95[k]		

[a] Addition reactions were typically conducted by adding nucleophilic reagents to the acceptor in THF at −78 °C followed by warming to 20 °C and quenching with HOAc. Products were purified by PTLC (silica gel, hexane) or recrystallization (MeOH). Desilylations were performed by stirring **6** with 3–5 equiv of Bu_4NF in moist THF (0.5 M) at 25 °C for 0.25–2.0 h. [b] All structures reported are supported by ^1H and ^{13}C NMR data; all crystalline compounds gave satisfactory elemental analyses. [c] $CuBr\cdot Me_2S$ present. [d] Et_2O as solvent. [e] Mp 120.5–121.5 °C. [f] Mp 118.0–119.5 °C. [g] Mp 104–106 °C. [h] Mp 133.0–134.5 °C. [i] Reference 15. [j] A mixture (82%) of starting material and its (*E*)-allylic isomer (1:1.6) was obtained from allylic proton abstraction and reprotonation. [k] A 1:1.75 mixture of α,β- and (*E*)-β,γ-double-bond isomers.

Pelter and co-workers[3] have reported that ate complex retardation in dimesitylboranes enables the formation of useful α-boryl carbanions through deprotonation reactions. Our initial attempts to add alkyllithium reagents to vinyldimesitylborane,[4] $Mes_2BCH{=}CH_2$ (Mes = mesityl), resulted in complex mixtures in which ate complex formation was implicated. An intramolecular metal–halogen exchange-initiated addition reaction[5] where (*E*)-olefin geometry precludes intramolecular ate formation has been successful, however (eq 1). Treating **1a**[6] with t-BuLi (2



(1)

equiv, THF, 1 min at −100 °C, 10 min at 0 °C) followed by quenching with HOAc gives **3a** in 92% yield, and DOAc gives **3b** (77% d_1). The intermediacy of anion **2** was further demonstrated through alkylation with n-nonyl bromide and methyl iodide giving **3c** and **3d** in 60% and 55% yield, respectively.

The persistent presence of 5–34% of **3a** in alkylation reactions, the incomplete deuterium incorporation cited above, the recent controversy over the contribution of a SET pathway in iodine–lithium exchange reactions,[8] and the presumed susceptibility of vinylboranes to radical addition reactions[9] owing to the stability of α-boryl radicals[10] leave open the possibility that this reaction proceeds to some extent by a pathway involving radical intermediates, however. Indeed, when **1a** is heated in benzene with Bu_3SnH and AIBN, **3a** is obtained in 80% yield, demonstrating that such vinylboranes are good terminators in radical cyclization processes.[11]

Molecular models suggested that the increased protection of boron needed for intermolecular addition reactions might be present in α-substituted vinyldimesitylboranes. To our delight, **4**[12] has proven to be an excellent acceptor and provides a new route

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(3) (a) Pelter, A.; Singaram, B.; Williams, L.; Wilson, J. W. *Tetrahedron Lett.* **1983**, *24*, 623. (b) Pelter, A.; Williams, L.; Wilson, J. W. *Ibid.* **1983**, *24*, 627. (c) Pelter, A.; Singaram, B.; Wilson, J. W. *Ibid.* **1983**, *24*, 631.

(4) Brown, N. M. D.; Davidson, F.; Wilson, S. W. *J. Organomet. Chem.* **1981**, *209*, 1.

(5) Cooke, M. P., Jr. *J. Org. Chem.* **1984**, *49*, 1144.

(6) Prepared by the hydroboration of 6-iodo-1-hexyne with Mes_2BH.[7]

(7) Pelter, A.; Singaram, S.; Brown, H. *Tetrahedron Lett.* **1983**, *24*, 1433.

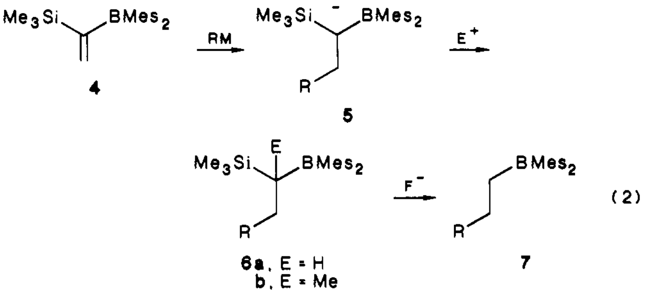
(8) (a) Bailey, W. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* **1984**, 2098. (b) Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarrett, R. M.; Okarma, P. J. *Ibid.* **1985**, *50*, 1999. (c) Newcomb, M.; Williams, W. G.; Crumpacker, E. L. *Tetrahedraon Lett.* **1985**, *25*, 1183. (d) Ashby, E. C.; Pham, T. N.; Park, B. *Ibid.* **1985**, *26*, 4691.

(9) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.

(10) Lane, C. F.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212. Lane, C. F.; Brown, H. C. *Ibid.* **1971**, *93*, 1025. Brown, H. C.; Lane, C. F. *Synthesis* **1972**, 303.

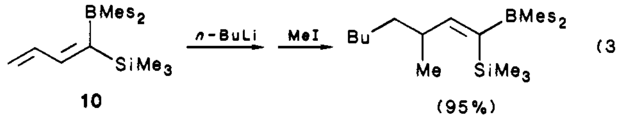
(11) Hart, D. J. *Science (Washington, D.C.)* **1984**, *223*, 883. Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553.

to useful organoboranes (eq 2, Table I).[14]



Additions proceed readily with a variety of nucleophiles, giving air-stable adducts **6**. Adducts were not obtained either with the lithium enolate of pinacolone or with lithium phenylacetylide, although in the latter case an ate complex derived product was obtained.[15] While not definitive, it is noteworthy that the use of 5-hexenyllithium (Table I, entry 6) as a probe for possible SET involvement[8] gives no cyclic product. Cuprate reagents[16] do undergo addition reactions (Table I, entries 2, 3), however.

β-Substitution is tolerated in the absence of allylic hydrogens (Table I, entry 11); in their presence (Table I, entry 12), allyl anion formation occurs with the more basic organolithium reagents. Interestingly, the addition to diene acceptor **10** occurs at the terminal carbon and protonation of the intermediate allylic anion gives rise to a mixture of isomers, while reaction of the intermediate with MeI results in exclusive γ-alkylation[3c] (eq 3). Attempts to alkylate the highly hindered α-carbon of addition intermediates **5** have been successful only with MeI, where **6b** (R = Bu, Ph) were obtained in 96% and 93% yield, respectively.



Functionalized silylated boranes **6a** are rapidly desilylated by Bu_4NF in moist THF in nearly quantitative yield (Table I) giving boranes **7** of a type which has been shown to be convertible to alcohols,[3] alkylatable carbanions,[3b] diols,[17] and olefins.[18] Interestingly, more highly substituted silylated borane **6b** (R = Ph) is deboronated by fluoride ion under the same conditions, giving (1-phenyl-2-propyl)trimethylsilane in 74% yield. The direct oxidation of **6a** (R = Ph) with alkaline hydrogen peroxide gives a 1.6:1 mixture of 1-(trimethylsilyl)phenethyl alcohol and phenethyl alcohol while prior treatment with Bu_4NF followed by oxidation in a one-pot procedure gives only phenethyl alcohol in 95% yield.

In summary, we have demonstrated the feasibility of using hindered boryl substituents to activate olefins to nucleophilic addition reactions. Preliminary experiments suggest that other α-substituted vinyldimesitylboranes also undergo addition reactions, and work is in progress on this new class of acceptors.

Acknowledgment. We thank the National Science Foundation for support of this work.

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(12) Prepared[4] in 60% yield from (1-(trimethylsilyl)vinyl)lithium[13] and Mes_2BF^{3a} in Et_2O at −78 °C. Acceptors **8**, **9**, and **10** were similarly prepared.

(13) Boeckman, R. K., Jr.; Bruza, K. S. *Tetrahedron Lett.* **1974**, 3365.

(14) Vinylsilanes undergo addition reactions with reactive alkyllithium reagents: Mulvaney, J. E.; Gardlund, Z. G. *J. Org. Chem.* **1965**, *30*, 917. Hudrlik, P. F.; Peterson, D. *Tetrahedron Lett.* **1974**, 1133. Cason, L. F.; Brooks, H. G. *J. Org. Chem.* **1954**, *19*, 1278. Chan, T. H.; Chang, E. *Ibid.* **1974**, *39*, 3264.

(15) $(PhCH{=}C(Mes))B(Mes)(CH_2{=}CSiMe_3)$, mp 139–140 °C, 87% yield.

(16) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. H. *Ibid.* **1984**, *40*, 5005.

(17) Pelter, A.; Buss, D.; Pitchford, A. *Tetrahedron Lett.* **1985**, *26*, 5093. Pelter, A.; Bugden, G.; Rosser, R. *Ibid.* **1985**, *26*, 5097.

(18) Pelter, A.; Singaram, B.; Wilson, J. W. *Tetrahedron Lett.* **1983**, *24*, 635.

Avermectin Chemistry: Problems of Conjugation, Deconjugation, and Epimerization

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Received September 25, 1986

The able studies of Merck scientists[1,2] have shown that the remarkable biological activity[3] of the avermectins **1**[4] is strongly structure-dependent. With the oxahydrindene moiety, for example, the isomers obtained by epimerization and conjugation (i.e., **2** and **3**, Chart I) show much reduced biological activities, as also does the aromatized product **4**. Thus, the most daunting challenges confronting any synthesis of these molecules come from (a) control of configuration and (b) suppression of lability at the C2 stereocenter. Our laboratory[5] recently described a synthesis of chiron[6] (**5a**) for the "southern" half of **1**, in which these isomerizations could be examined. In subsequent studies (Scheme I), we have discovered (a) that the regioisomeric olefin **6a** was frequently easier to obtain than **5a** and (b) that the carboxylic derivative **5b** underwent conjugation to **6b**, even on standing at room temperature. It therefore seemed to us, given the conditions for the isolation of the natural product,[4] that the intact avermectins are more stable than might have been expected from the partial structure **5b**. This increased stability could conceivably be attributed to the constraints of the macrolactone, as we have surmized elsewhere.[5]

We were, therefore, intrigued by the recent report of a synthesis of avermectin B_{1a} (i.e., **1Aa**) in which a deconjugative transformation was executed as the "last major hurdle".[7] This achievement promised to simplify the synthetic challenge enormously, particularly in view of the easier formation of **6a** and **6b** (vide supra). However, rather than confront this hurdle at late stages of such a monumental undertaking, we decided to examine the comparable transformations in the Ivermectin series **1B**, since much of the groundwork had already been laid securely by Merck scientists.[2] Thus, 2-*epi*-ivermectin **2Ba** and Δ^2-ivermectin **3Ba** were prepared from Ivermectin and were converted into disilylated (**1Bb**, **2Bb**, and **3Bb**) and trisilylated (**1Bc** and **3Bc**) derivatives under standard conditions. Deconjugation of **3Bc** with LDA followed by acetic acid quench under a variety of conditions (Table I, entries a–c) gave either the 2-epi product **2Bb**, or caused the simple loss of the trimethylsilyl group (i.e., **3Bb**).

It was conceivable that the C22–C23 double bond, which is present in avermectin B_{1a} (**1A**), but not in Ivermectin (**1B**), could so alter the shape of the molecule as to change the stereochemical course of deconjugation.[8] Accordingly, the Pivnichny procedure[2]

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