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Origin of Thermodynamic versus Kinetic Control of Allene Hydroboration with 9-Borabicyclo[3.3.1]nonane and 10(R)-Trimethylsilyl-9-Borabicyclo[3.3.2]decane

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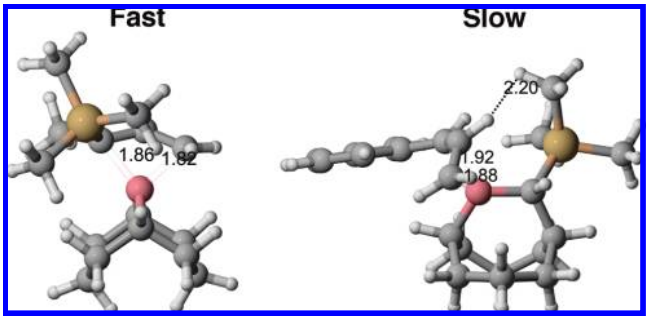
ABSTRACT

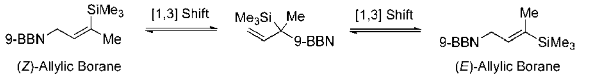


Density functional theory was used to locate transition states for hydroboration reactions of allenes with 9-borabicyclo[3.3.1]nonane and 10-R-9-borabicyclo[3.3.2]decane, as well as transition states for [1,3]-boratropic shift and aldehyde addition reactions of the derived allylboranes. The origin of kinetic versus thermodynamic control in the allene hydroboration step is described.

The reaction of 1-substituted allenes with dialkylboranes typically gives (*E*)-allylic boranes.[1] Studies by Wang on the reaction of allenylsilanes with 9-borabicyclo[3.3.1]nonane (9-BBN) and dicyclohexylborane (Chx_2BH) suggest that hydroboration initially gives (*Z*)-allylic boranes, which then undergo rapid thermodynamically controlled Z to E isomerization via two [1,3]-boratropic shifts (Scheme 1).[2] Because of this facile equilibration, hydroboration of allenes with common dialkylborane reagents such as 9-BBN, Chx_2BH, and $(Ipc)_2BH$ generally give γ-substituted (*E*)-allylic boranes.

Soderquist has shown that (*Z*)-crotyl-10-TMS-9-borabicyclo[3.3.2]decanes are thermally stable against Z to E isomerization.[3a] On the basis of this unique thermal stability, Roush and co-workers have recently developed a general methodology for generating γ-substituted (*Z*)-allylic boranes via the hydroboration of monosubstituted allenes with 10-TMS-9-borabicyclo[3.3.2]decane (**1a**).[4] Scheme 2 shows the scope of this methodology. Hydroboration of the indicated allenes with **1a** followed by addition of an aldehyde to the

Scheme 1. Example of Proposed Isomerization Mechanism for (Z)-Allylic Boranes[2]



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(1) (a) Brown, H. C.; Narla, G. *J. Org. Chem.* **1995**, *60*, 4686. (b) Narla, G.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 219.

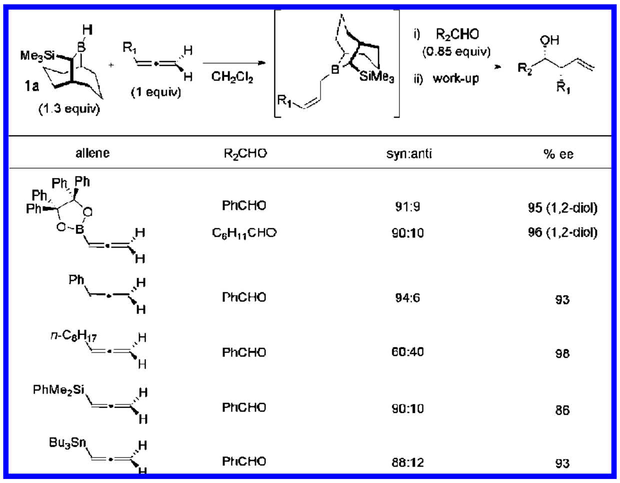
(2) (a) Wang, K. K.; Gu, Y. G.; Liu, C. *J. Am. Chem. Soc.* **1990**, *112*, 4424. (b) Gu, Y. G.; Wang, K. K. *Tetrahedron Lett.* **1991**, *32*, 3029.

(3) (a) Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044. (b) González, A. Z.; Román, J. G.; Alicea, E.; Canales, E.; Soderquist, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 1269.

(4) (a) Kister, J.; DeBaillie, A. C.; Lira, R.; Roush, W. A. *J. Am. Chem. Soc.* **2009**, *131*, 14174. (b) The S-configuration of **1a** was used in all calculations.

10.1021/ol902364d CCC: $40.75

Scheme 2. Scope of Kinetically Controlled Allene Hydroboration



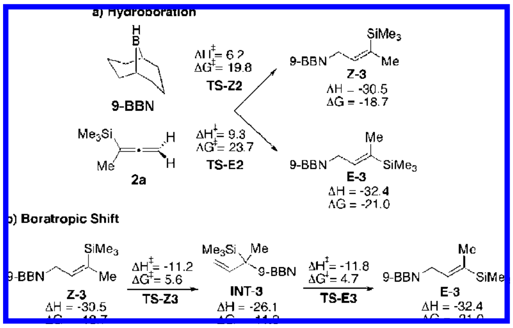
allene	R$_2$CHO	syn:anti	% ee
Ph, Ph, Ph, Ph, O–B	PhCHO C$_6$H$_{11}$CHO	91:9 90:10	95 (1,2-diol) 96 (1,2-diol)
Ph	PhCHO	94:6	93
n-C$_8$H$_{17}$	PhCHO	60:40	98
PhMe$_2$Si	PhCHO	90:10	86
Bu$_3$Sn	PhCHO	88:12	93

derived allyboranes followed by oxidative work up generally gives greater than 90% enantiomeric excess and close to a 9:1 ratio of syn to anti products.[4] In contrast, Soderquist has reported that the use of 10-Ph-9-borabicyclo[3.3.2]decane (**1b**) for similar reactions gives essentially no kinetic diastereochemical control.[3b]

The novelty that stable (*Z*)-allylboranes can only be generated from reaction with **1a** and not by using **1b** or other known dialkylborane reagents has prompted us to use B3LYP/6-31G(d,p)[5] density functional theory (DFT) to study the allene hydroboration, and subsequent [1,3]-boratropic shift and aldehyde addition transition states (TSs).[6]

To start, we explored the reaction of 9-BBN with allene **2a** (Scheme 3). In accord with Wang's speculation,[2] the computed TS energetics reveal that formation of **Z-3** is kinetically favored by 3.1 kcal/mol over **E-3** (Scheme 3a). The bulky TMS group that is directed toward the borabicyclo unit disfavors **TS-E2** compared to **TS-Z2** (Figure 1a). The alternative regiosiomeric TSs is ~6 kcal/mol higher in energy. The ΔH_{rxn} values for 9-BBN addition to **2a** are −30.5 and −32.4 kcal/mol for **Z-3** and **E-3**.

Scheme 3. (a) 9-BBN Hydroboration of Allene **2a** and (b) [1,3]-Boratropic Shift Energetics Relative to Separated Reactants



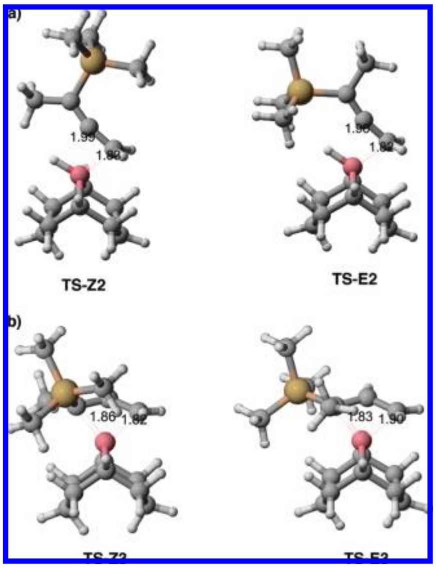


Figure 1. (a) Hydroboration and (b) [1,3]-boratropic shift TSs for 9-BBN addition to allene **2a**.

Two concerted [1,3]-boratropic shift TSs are required to convert **Z-3** into **E-3**. This general type of TS consists of a boron atom interacting with a π-allyl carbon fragment.[7] The first transition state, **TS-Z3**, gives intermediate **INT-3** with a $\Delta H^{\ddagger}$ of 19.3 kcal/mol relative to **Z-3** (Scheme 3b, Figure 1b). Rotation of the alkene group sets up a second [1,3]-boratropic shift to give **E-3** via **TS-E3** with a lower $\Delta H^{\ddagger}$ of 14.3 kcal/mol. **TS-Z3** and **TS-E3** have similar forming and breaking B−C bond lengths of ~1.9 and ~1.8 Å for the unsubstituted and substituted carbon centers, respectively. To show that there is no unique steric or electronic feature in these TSs caused by the borabicyclo[3.3.1]nonane structure, we have also computed the activation enthalpy for dimethylallylborane rearrangement. The $\Delta H^{\ddagger}$ for this [1,3]-boratropic shift is 20.1 kcal/mol, which is very close to the 19.3 kcal/mol for **TS-Z3**.

The reaction of **1a** with methylallene (**2b**) and phenylallene (**2c**) also show a kinetic preference for giving (*Z*)-allylic boranes **Z-5** and **Z-7** (Scheme 4a). Figure 2a shows the lowest energy boat/chair ring borabicyclo[3.3.2]decane conformation TS for hydroboration of phenylallene with **1a**, **TS-Z6**, to give **Z-7**. **TS-Z6** is 3.3 kcal/mol lower than **TS-E6**, which gives **E-7**. In **TS-E6**, repulsion with the borabicyclo ring causes the phenyl group to twist by 38°.[8] Although phenylallene shows a large *Z-E* hydroboration selectivity, the $\Delta\Delta H^{\ddagger}_{(E\text{-}Z)}$ for methylallene is only 0.4 kcal/mol, but does

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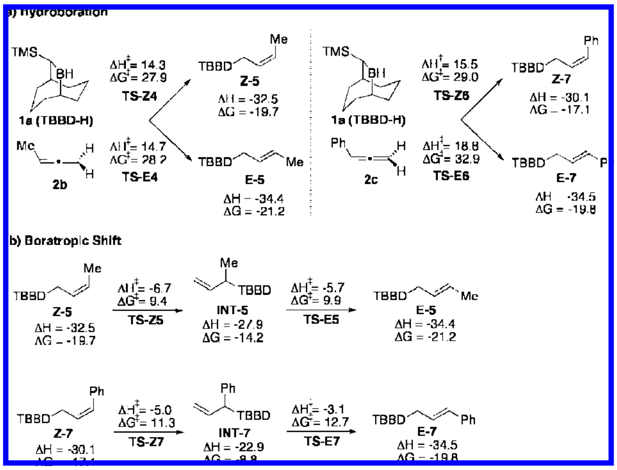
(5) *Jaguar*, version 7.5; Schrodinger, LLC: New York, 2008. All stationary points were verified as minima or first-order saddle points by calculation of the full Hessian. Enthalpy and free energy corrections were applied at 298 K and all energies are reported in kcal/mol.

(6) This level of theory gives energetics in agreement with CCSD(T) theory for [1,3]-boratropic shifts. See:Choi, J. Y.; Kim, C. K.; Kim, C. K.; Lee, I. *J. Phys. Chem. A* **2002**, *106*, 5709.

(7) The other extreme on a closed-shell More O'Ferrall-Jencks diagram would be a charge-separated boracyclobutane. Between the ground state and TS, the NBO charges change most significantly at the boron center, which loses positive charge.

Scheme 4. (a) Allene Hyroboration by **1a** and (b) [1,3]-Boratropic Shift Energetics Relative to Separated Reactants



favor the (*Z*)-crotyl borane **Z-5**. This predicted decrease in hydroboration selectivity is in agreement with the 60:40 ratio of syn to anti 1,2-diols formed from the reaction of **1a** with $n\text{-}C_8H_{17}{-}CH{=}C{=}CH_2$ (Scheme 2).

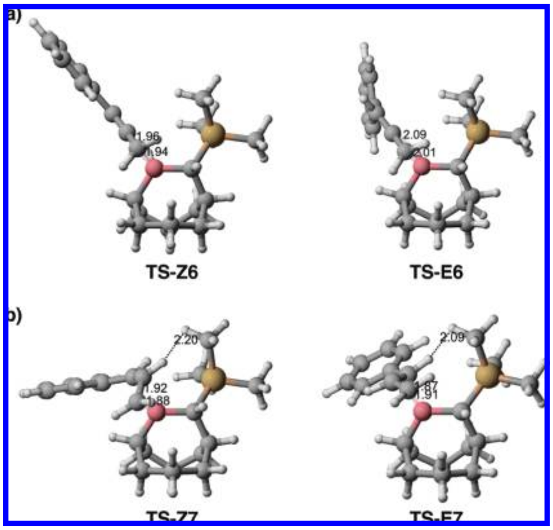


Figure 2. (a) Hydroboration and (b) [1,3]-boratropic rearrangement TSs for reaction of **1a** with allene **2c**.

After **Z-7** is formed there is only one boratropic shift TS, **TS-Z7**, that converts **Z-7** into **INT-7** (Scheme 4b, Figure 2b). Location of **TS-Z7** and no alternative TS reveals that the allene R (phenyl or for **TS-Z5** methyl) group is oriented away from the 10-TMS group and that it *is not involved in steric interactions and does not* slow down the [1,3]-boratropic rearrangement. Rather, it is the interaction between the π-allyl methine C−H bond with the 10-TMS group (2.20 Å) that results in a steric repulsion and raises the barrier for rearrangement. This steric interaction raises the $\Delta H^{\ddagger}$ for **TS-Z7** to 25.1 kcal/mol. This is 5.8 kcal/mol larger than the $\Delta H^{\ddagger}$ for **TS-Z3** and accounts for the unusually large stability of **Z-7** compared to **Z-3**. In addition, the $\Delta H^{\ddagger}$ for rearrangement of **Z-5**, via **TS-Z5**, is 25.8 kcal/mol, indicating that the steric bulk of the allene R group does not influence the (*Z*)-allylic borane stability.

INT-7 is less exothermic by 7.2 kcal/mol compard to **Z-7** and a second rearrangement TS, **TS-E7**, leads to the (*E*)-allylic borane **E-7**. Although the allene phenyl group is directed away from the TMS group, the terminal π-allyl C−H bond is now in close contact with the 10-R group and raises the barrier for rearrangement.

For a direct comparison of **1a** versus 9-BBN for slowing down the [1,3]-boratropic shift, we have also computed the barrier for rearrangement for reaction of 9-BBN with phenylallene. In this rearrangement the $\Delta H^{\ddagger}$ is only 17.1 kcal/mol. This is an 8 kcal/mol lower barrier than **TS-Z7**.

Although the R-group of 1-substituted allenes does not directly interact with the 10-TMS group of **1a**, these TS geometries indicate that in 1,1-disubstituted allenes a second methyl group would be in close proximity to the 10-TMS group. To probe this possible interaction, the rearrangement barrier for 1,1-dimethylallene was computed. The $\Delta H^{\ddagger}$ increases to 33.0 kcal/mol because of the close interaction of the second methyl group with the 10-TMS group.[9]

Although 1-substituted phenyl and methyl allenes have similar rearrangement barriers, the allene R group can have a substantial impact on the electronic nature of the TS and lower the barrier. For example, the $\Delta H^{\ddagger}$ for rearrangement of the pinacol borate substituted (*Z*)-allylic borane is only 20.0 kcal/mol.[10]

To probe the 1-substituted allene steric model we have also computed the activation enthalpies for rearrangement with **1b** and 10-*t*-Bu-9-borabicyclo[3.3.2]decane (**1c**). When R = Ph, $\Delta H^{\ddagger}$ for the rearrangement of the (*Z*)-allylic borane derived from phenylallene is only 19.3 kcal/mol via **TS-Z8** (Figure 3a). The second rearrangement TS, **TS-E8**, has a $\Delta H^{\ddagger}$ value of 20.8 kcal/mol. These barriers are 5−6 kcal/mol lower than the rearrangement barriers when R = TMS.

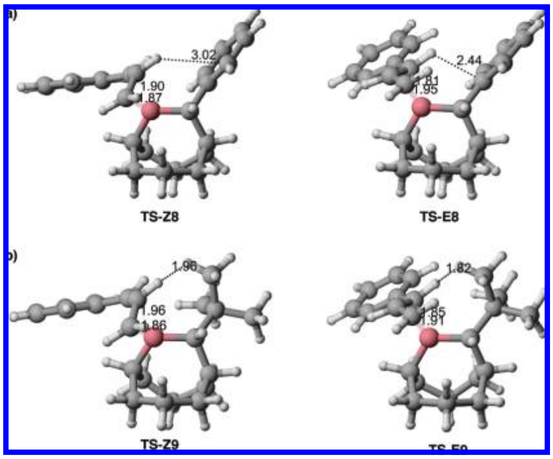


Figure 3. Comparison of 10-R [1,3]-boratropoic transition states for (a) R = Ph and (b) R = *t*-Bu.

Both **TS-Z8** and **TS-E8** show a large intramolecular distance between the π-allyl C−H bonds and the 10-Ph group. For R = *t*-Bu, the $\Delta H^{\ddagger}$ for both [1,3]-boratropic rearrangements are 26.1 kcal/mol (**TS-Z9** and **TS-E9**, Figure 3b), which is larger than **TS-Z7** and **TS-E7**. Again, these large barriers for rearrangement are due to the steric congestion between the 10-*t*-Bu group and the π-allyl C−H bonds (1.96 Å and 1.82 Å).

An alternative possibility that we have considered for explaining the high barrier of **TS-Z7** is σ-p type hyperconjugative stabilization from the Si−C bond of the TMS group into the empty boron p-orbital of **Z-7**. The Si−C bond is angled at ~70° relative to the B−C bond. Natural orbital populations of the boron p-orbital were computed for the ground states of the (*Z*)-allylic boranes with 10-R groups = *t*-Bu, TMS, $SnMe_3$, and Ph.[11] The relative populations are 0.16, 0.20, 0.24, and 0.20e, respectively. This indicates that σ-p orbital hyperconjugation occurs but the 10-phenyl group induces roughly the same orbital population as the 10-TMS group.[12]

For the benefits of the kinetic hydroboration of allenes with **1a** to be realized, the $\Delta G^{\ddagger}$ for the reaction of the derived (*Z*)-allylic borane with aldehydes must be lower in energy than the $\Delta G^{\ddagger}$ for [1,3]-rearrangement. To probe this question, the TSs for **Z-7** addition to MeCHO were explored. There are four distinct TSs resulting from approach of the aldehyde to the allylic borane on the same or opposite side of the 10-TMS group and whether the acetaldehyde methyl group is oriented in an axial or equatorial position. In addition, there are four boat/chair conformations of the borabicyclo auxiliary. **TS-10** (Figure 4) is the lowest-energy structure.[13] Indeed, the free energy barriers for **TS-Z7** and **TS-E7**, 28.4 and 29.8 kcal/mol, are higher than that for allylboration of MeCHO, $\Delta G^{\ddagger}$ = 21.2 kcal/mol. Consequently, the *syn*-homoallylic alcohol is the major product of this reaction sequence.

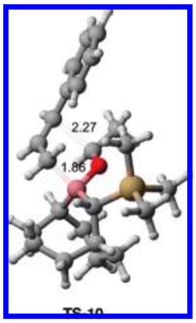


Figure 4. Lowest-energy MeCHO addition transition state.

In conclusion, exploration of allene hydroboration, [1,3]-boratropic shift, and aldehyde addition TSs has revealed that reagent **1a** gives unusually stable (*Z*)-allylic boranes because the 10-TMS group interacts with the π-allyl C−H bonds in the [1,3]-sigmatropic shift TS. This raises the barrier for rearrangement, thus allowing kinetic control of the allene hydroboration.

Acknowledgment. This work was supported by the NIH (GM038436 and GM026782) and a postdoctoral fellowship to J.K. from the Ministère des Affaires Etrangères et Europèennes (France).

Supporting Information Available: Cartesian coordinates and abolute energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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[8] In both **TS-Z6** and **TS-E6**, allene **2c** approaches the borane face opposite of the 10-TMS group. Hydroboration from the side nearest the 10-TMS group is disfavored by ~3 kcal/mol. Also see: Ess, D. H.; Kister, J.; Chen, M.; Roush, W. R. *J. Org. Chem*. **2009**; DOI: 10.1021/jo901737d.

[9] This prediction is in accord with the experimental observation that Ipc_2BH hydroboration of 1,1-disubstituted allenes shows high kinetic control. See: Chen, M.; Handa, M.; Roush, W. R. *J. Am. Chem. Soc*. **2009**, *131*, 14602.

[10] Substituent effects on the barrier for the [1,3]-boratropic shift of dimethyl borane is given in the Supporting Information.

[11] *NBO 5.0*; Glendening, E. D., Badenhoop, J. K., Reed, A. E., Carpenter, J. E., Bohmann, J. A., Morales, C. M., Weinhold, F., Eds.; Theoretical Chemistry Institute, University of Wisconsin: Madison, WI, 2001; http://www.chem.wisc.edu/~nbo5.

[12] The C−Si bond length decreases by only 0.004 Å between **Z-7** (1.930 Å) and **TS-Z7** (1.934 Å). The barrier for rearrangement of **TS-Z7** decreases by 6.4 kcal/mol when the 10-TMS group is deleted and replaced with hydrogen. When the 10-TMS is is deleted and replaced with SiH_3, the barrier is intermediate between TMS and hydrogen because there is both a small hyperconjugative effect and reduced steric interactions.

[13] Sarotti, A. M.; Pellegrinet, S. C. *J. Org. Chem*. **2009**, *74*, 3562.