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Origin of Thermodynamic versus Kinetic Control of Allene Hydroboration with 9-Borabicyclo[3.3.1]nonane and 10-R-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 (Chx₂BH) 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, Chx₂BH, and (Ipc)₂BH only 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} Based on 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 derived allylboranes 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}

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Supporting Information Available. Cartesian coordinates and absolute energies.

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 two other regioisomeric TSs are ~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**.

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 Å 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°. Although phenylallene shows a large *Z-E* hydroboration selectivity, the $\Delta\Delta H^\ddagger_{(E-Z)}$ for methylallene is only 0.4 kcal/mol, but does 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*-C₈H₁₇-CH=C=CH₂ (Scheme 2).

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 compared 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 methylene 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 pinacolborane 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. Both **TS-Z8** and **TS-E8** show a large intramolecular distance between the π -allyl methine and methylene 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 C-Si bond of the TMS group into the empty boron p-orbital of **Z-7**. The Si-C bond is angled at $\sim 70^\circ$ 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, SnMe₃, 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.

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 methine and methylene C-H bonds in the boratropic isomerization TS. This raises the barrier for [1,3]-boratropic rearrangement thus allowing kinetic control of the allene hydroboration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. (a) Brown HC, Narla G. J. Org. Chem 1995;60:4686. (b) Narla G, Brown HC. Tetrahedron Lett 1997;38:219.
2. (a) Wang KK, Gu YG, Liu C. J. Am. Chem. Soc 1990;112:4424. (b) Gu YG, Wang KK. Tetrahedron Lett 1991;32:3029.
3. (a) Burgos CH, Canales E, Matos K, Soderquist JA. J. Am. Chem. Soc 2005;127:8044. [PubMed: 15926828] (b) González AZ, Román JG, Alicea E, Canales E, Soderquist JA. J. Am. Chem. Soc 2009;131:1269. [PubMed: 19117388]
4. Kister J, DeBaillie AC, Lira R, Roush WA. J. Am. Chem. Soc 2009;131:14174. [PubMed: 19775159] (b) The S-configuration of **1a** was used in all calculations
5. Jaguar. version 7.5. New York, NY: Schrodinger, LLC; 2009. 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 JY, Kim CK, Kim CK, 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.
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 DH, Kister J, Chen M, Roush WA. J. Org. Chem. 2009 DOI: 10.1021/jo901737d.
9. This prediction is in accord with the experimental observation that Ipc₂BH hydroboration of 1,1-disubstituted allenes shows high kinetic control. See:Chen M, Handa M, Roush WR. J. Am. Chem. Soc. 2009 DOI: 10.1021/ja904599h.
10. Substituent effects on the barrier for the [1,3]-boratropic shift of dimethyl borane is given in the SI.
11. Glendening, ED.; Badenhoop, JK.; Reed, AE.; Carpenter, JE.; Bohmann, JA.; Morales, CM.; Weinhold, F. NBO 5.0. Madison, WI: Theoretical Chemistry Institute, University of Wisconsin; 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 SiH₃ the barrier is intermediate between TMS and hydrogen because there is both a small hyperconjugative effect and reduced steric interactions.
13. Sarotti AM, Pellegrinet SC. J. Org. Chem 2009;74:3562. [PubMed: 19348492]

Figure 1.

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

Figure 2.

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

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

Figure 4.
Lowest energy MeCHO addition transition state.

Scheme 1.

Example of proposed isomerization mechanism for (Z)-allylic boranes.²

allene	R_2CHO	syn:anti	% ee
	PhCHO	91:9	95 (1,2-diol)
	$\text{C}_6\text{H}_{11}\text{CHO}$	90:10	96 (1,2-diol)
	PhCHO	94:6	93
	PhCHO	60:40	98
	PhCHO	90:10	86
	PhCHO	88:12	93

Scheme 2.
Scope of kinetically controlled allene hydroboration.

a) Hydroboration

b) Boratropic Shift

Scheme 3.

a) 9-BBN Hydroboration of allene **2a** and b) [1,3]-boratropic shift energetics relative to separated reactants.

a) Hydroboration

b) Boratropic Shift

Scheme 4.

a) Allene hydroboration by **1a** and b) [1,3]-boratropic shift energetics relative to separated reactants.