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Catalytic Activity of Phosphine−Copper Complexes for Hydroboration of Styrene with Pinacolborane: Experiment and Theory

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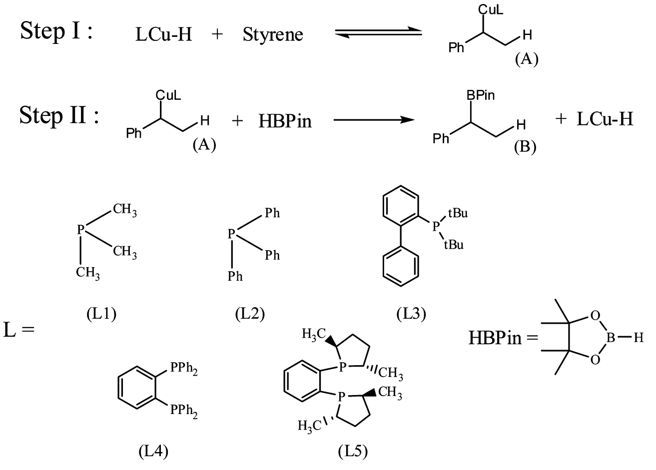
We have carried out density functional theory calculations as well as experiments to rationalize the catalytic activity of various phosphine-copper complexes for the hydroboration of styrene with pinacolborane. The experimentally obtained catalytic efficiency was explained on the basis of activation barriers for consecutive reaction mechanism steps as well as by molecular orbitals and charges in the transition state. Bidentate ligands were found to be more efficient than monodentate ligands for catalytic activity. Bidentate ligands make the reactant complexes less stable than monodentate ligands due to steric hindrance. This information could be usefully utilized for new catalysts design. The calculated kinetic data were consistent with the experimental conversion efficiency in a process that was hypothesizd to undergo the addition of Cu−H to styrene as the rate-limiting step. From the electronic distribution of the HOMO and the charge of the copper atom in the transition state, it was found that styrenes substituted with electron withdrawing groups would give higher conversions, and the catalytic efficiency could be increased with properly designed electron-donating ligands for the copper catalyst complex.

Introduction

Regio- and enantioselective hydroboration reactions of alkenes[1,2] are of great importance because the resultant C−B bond can be converted to C−N, C−O, or C−C bonds with retention of chirality.[3−6] Consequently, stereoselective hydroboration reactions that generate easily handled, stable organoboranes (C−B bonds) are highly desirable,[7−11] as the boron intermediates can be utilized in such stereoselective transformations. Many catalysts have been utilized for enantioselective hydroborations. In particular, copper(I) complexes with phosphine ligands have very recently been found to catalyze the hydroboration of styrenes with pinacolborane with excellent regio- and enantioselectivity.[12] The hydroboration of styrene catalyzed by copper(I) catalysts with phosphine ligands has been proposed to take place in two steps: (i) addition of Cu−H to the styrene and (ii) transmetalation (of the copper) with pinacolborane.

Previously, it was presumed that in the first catalytic step, the Cu−H catalyst adds regioselectively to styrene with the copper bound to the α-carbon and the hydride (H) bound to the more electron deficient *β*-carbon of the olefin; however, this process needed to be investigated in more detail. Thus, in this study, we focused our investigation on the reaction intermediates and transition states to elucidate the addition mechanism in detail and also the effect of phosphine ligands on the catalytic activity of the hydroboration. Herein, we report the use of density functional theory calculations as well as experimental data to rationalize the catalytic activity of various phosphine−copper complexes for the hydroboration of styrene with pinacolborane. To shed light on the origin of the catalytic activity for several selected catalysts shown in Scheme 1, we compared the experimental conversion percentages for the catalytic reactions with theoretically obtained thermodynamic (enthalphies) and kinetic (activation barriers) factors. The ligands **L1**, **L2**, and **L3** are monodentate phosphines, whereas **L4** and **L5** are bidentate bisphosphines. For these ligand−metal complexes, we attempted to explain the experimentally obtained catalytic activity (conversion efficiency) based on kinetic theory for two possible mechanisms: a pre-equilibrium process and a simple consecutive step process.

SCHEME 1: Ligands for the Copper(I) Catalysts



Computational Details

The hydroboration of styrene by copper(I) catalysts ligated (or coordinated) with phosphine ligands takes place in two steps: (i) addition of Cu−H to the styrene and (ii) transmetalation (of the copper) with pinacolborane. It has been accepted that in the first step, the copper catalyst adds to the double bond of the styrene with a regioselective addition of the hydrogen atom due to electronic effects. Thus, we focused only on the syn addition of the copper catalyst with the styrene in the first step, and a successive hydroboration with pinacolborane in the second step. For these two consecutive catalytic steps, we obtained all of the intermediates

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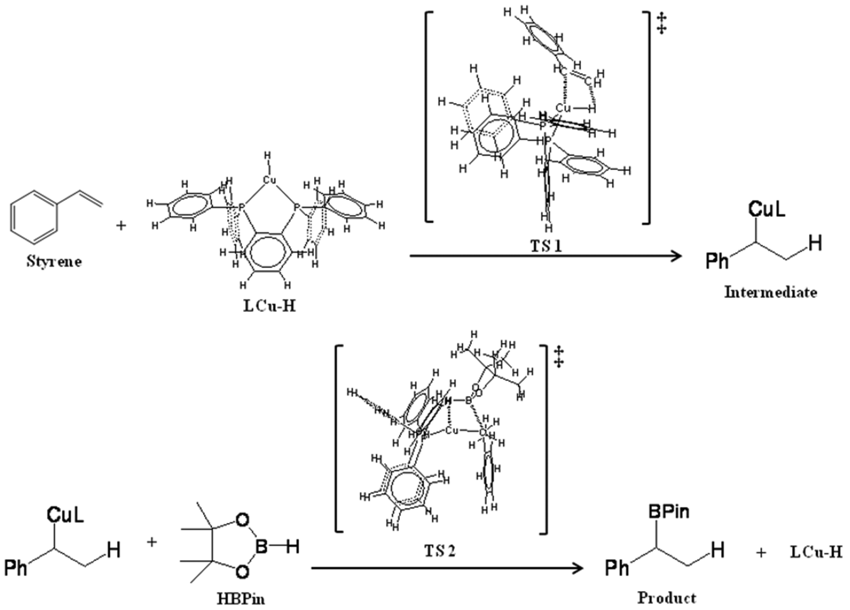


Figure 1. A representative reaction pathway showing the reactants, transition states, intermediates, and products for **L** = **L4**.

and transition states for the catalytic reactions with each of the phosphine ligands. The geometries for all of the reactants, transition states, intermediates, and products were optimized by density functional theory (DFT) calculations with 6-311G* basis sets using Becke's three parameters employing the Lee−Yang−Parr functional (B3LYP). The B3LYP functional has been successfully applied[13−17] to similar metal complex containing systems, although B3LYP was reported to be inaccurate in the interacting systems with large dispersive forces.[18,19] For example, although the barriers tend to be slightly lower than the experimental values, the relative values for similar systems are realiable.[20−23] However, in comparing catalytic activities, relative energy differences are more important than the accuracy of the absolute energy. Thus, we hoped that the DFT calculations with the B3LYP functional could be used to obtain the desired mechanistic information. All calculations were performed using a suite of Gaussian 03 programs.[24] All transition states were confirmed by a single imaginary vibrational frequency as well as by vibrational motions.

Experimental Procedure for the Hydroboration with Phosphine Ligands

A mixture of CuCl (0.025 mmol, 2.5 mg), NaO*t*-Bu (0.03 mmol, 3.0 mg), and phosphine (**L**) (0.025 mmol) in anhydrous toluene (0.2 mL) was stirred for 10 min in a Schlenk tube under an atmosphere of nitrogen. Pinacolborane (0.6 mmol, 90 μL) was added to the reaction mixture and stirred for 10 min at room temperature. Styrene (0.5 mmol) and tetradecane (0.25 mmol) as an internal standard were added in toluene (0.1 mL), and the reaction tube was washed with further toluene (0.2 mL) and sealed. The reaction was stirred for 24 h, and then the reaction conversion was determined on the basis of the consumed styrene by GC analysis with an internal standard. In particular, with **L5**, the reaction time for complete conversion could be reduced to 5 h in the presence of 3 mol % copper catalyst.

Results and Discussions

Experimentally, **L2**, **L3**, **L4**, and **L5** gave 29, 18, 71, and 100% conversion, respectively, with catalytic activity in the order **L5** > **L4** > **L2** > **L3**. Representative structures along the reaction coordinate for step I and step II are shown in Figure 1 for the case of **L4**. In step I, the copper(I) catalyst and styrene form a four-membered ring transition state as they approach. The most striking structural features from the reactants along the reaction coordinate to the transition state are the lengthening of the L−Cu, Cu−H, and C═C bond lengths and the decrease of the L−Cu−H bond angle. For example, in the case of **L4**, the L−Cu, Cu−H, and C═C bond lengths were calculated to be 2.273, 1.550, and 1.335 Å for the reactants and 2.293/2.303, 1.634, and 1.447 Å for the transition state, respectively. For monodentate ligands (**L1**−**L3**), the L−Cu−H bond angle varies tremendously from linear (~180.0°) in the reactants to 126.3−129.6° in the transition states. For bidentate ligands (**L4** and **L5**), however, the L−Cu−H angle changes by about 21−24°, from 134.6/135.1° to 113.5/111.7°. The Cu···C and H···C distances in the transition states were about 2.04 and 1.60 Å, which are quite similar to the distances obtained from a previous calculation[13−17] in a similar system.

Similarly, in the boration step (step II), the H−B and Cu−C bond lengths increase along the reaction coordinate as the transition state is approached, and the L−Cu−C bond angle decreases by a large amount for monodentate ligands (**L1**−**L3**), while it decreases by a small amount for bidentate ligands (**L4** and **L5**).

Figure 2 shows the energy profiles for the catalytic reactions with **L1**−**L5**, and Table 1 lists the enthalphy changes and activation barriers for the two steps. As seen in Figure 2, the reactant complexes with **L1**, **L2**, **L3**, **L4**, and **L5** were stabilized by −19.65, −14.71, −12.41, −11.27, and −9.24 kcal/mol, respectively, which is similar to previous calculations with similar systems in which the reactant complexes were 10−11 kcal/mol more stable than the isolated reactant species.[13−16] To better understand the catalytic activity, we compared the kinetic rates considering the following mechanism:

$$\text{reactant complex (RC)} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{intermediate (I)} \xrightarrow{k_2} \text{product (P)}$$

where the conversion between RC and I is step 1; the coverstion from I to P is step 2; k_1, k_2, and k_{-1} are the rate constants for

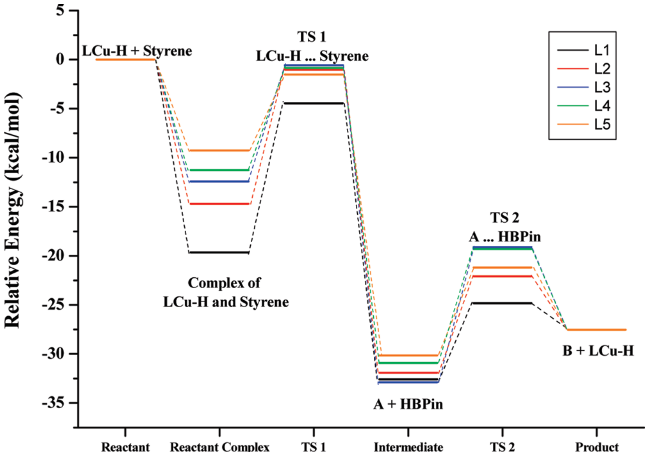


Figure 2. Energy profiles for step I and step II with **L1**−**L5**.

TABLE 1: Calculated Activation Barriers ($\Delta E^{\ddagger}$) and Enthalpy Changes (ΔH) in Steps I and II

ligands	step I			step II		
$\Delta E_1^{\ddagger}$	$\Delta E_{-1}^{\ddagger}$	ΔH_1	$\Delta E_2^{\ddagger}$	ΔH_2		conversion[a]
L1	15.19	28.12	−12.93	7.77	5.04	
L2	13.69	30.89	−17.20	9.82	4.36	29
L3	11.85	32.33	−20.48	13.79	5.35	18
L4	10.43	30.06	−19.63	11.61	3.37	71
L5	7.73	28.62	−20.89	8.95	2.60	100

[a] Reactions were run using 5 mol % CuCl, 6 mol % NaO*t*-Bu, and 5 mol % ligand at room temperature. Conversions were measured by GC analysis with an internal standard after 24 h. Energies are in kcal/mol. $\Delta E_1^{\ddagger}$, $\Delta E_{-1}^{\ddagger}$, and $\Delta E_2^{\ddagger}$ denote the activation barriers for the forward and backward reactions in step I and the forward reaction in step II, respectively. ΔH_1 and ΔH_2 denote the enthalpy changes in steps I and II, respectively.

the forward reactions of step I and step II and the reverse reaction of step I, respectively; and the corresponding activation barriers are denoted by $\Delta E_1^{\ddagger}$, $\Delta E_2^{\ddagger}$, and $\Delta E_{-1}^{\ddagger}$. In the case when k_1 and k_{-1} are much larger than k_2, the reaction is considered to proceed via a pre-equilibrium mechanism. However, from our calculations, as seen in Figure 2, the values of $\Delta E_2^{\ddagger}$ are smaller than those of $\Delta E_1^{\ddagger}$ and $\Delta E_{-1}^{\ddagger}$ for **L1** and **L2** and are comparable for **L3**, **L4**, and **L5**; hence, k_2 should be larger than or comparable to k_1 and k_{-1}. Thus, a pre-equilibrium mechanism for the process is discounted. Instead, a higher barrier step I (the addition of Cu−H to the styrene) could be the rate-limiting step in some cases. In step I, the reverse reaction, a beta-hydride elimination, was proposed to occur; however, this reaction was found to be difficult based on the calculations.

Step I is exothermic, and step II is endothermic. The activation barriers for step I ($\Delta E_1^{\ddagger}$) were calculated to be 15.19, 13.69, 11.85, 10.43, and 7.73 kcal/mol for the ligands **L1**, **L2**, **L3**, **L4**, and **L5**, respectively; and the enthalpy changes (ΔH_1) were calculated to be −12.93, −17.20, −20.48, −19.63, and −20.89 kcal/mol. In step II, the barriers ($\Delta E_2^{\ddagger}$) were 7.77, 9.82, 13.80, 11.61, and 8.95 kcal/mol, respectively; and the enthalpy changes (ΔH_2) were 5.04, 4.36, 5.35, 3.37, and 2.60 kcal/mol. Considering step I to be the rate-limiting step, catalytic activity is given in the following order: **L5** > **L4** > **L3** > **L2**, which is in agreement with the experimental results, except for **L2** and **L3**. Experimentally, the catalytic activity was in the order, **L5** > **L4** > **L2** > **L3**. This discrepancy may be the result of step I not always being the rate-limiting step due to the comparable barriers $\Delta E_1^{\ddagger}$ and $\Delta E_2^{\ddagger}$. The experimental results can be rationalized as successive reaction steps with the restriction that intermediates rarely revert to reactants by the reverse reaction due to the much higher barrier of $\Delta E_{-1}^{\ddagger}$ than $\Delta E_2^{\ddagger}$, that is, once intermediates are formed, they proceed to products. Thus, the amount of products should be proportional to the amount of generated intermediates and inversely proportional to the exponentional of the activation barrier of step II ($\exp(-\Delta E_2^{\ddagger}/RT)$). Similarly, the amount of intermediates is inversely proportional to the exponentional of the activation barrier of step I ($\exp(-\Delta E_1^{\ddagger}/RT)$). Therefore the amount of the products would be proportional to $\exp(-(\Delta E_1^{\ddagger} + \Delta E_2^{\ddagger})/RT)$. Using this rationale, the product ratio was calculated to be 8.5:1:37:2831, which is in agreement with the experimental results.

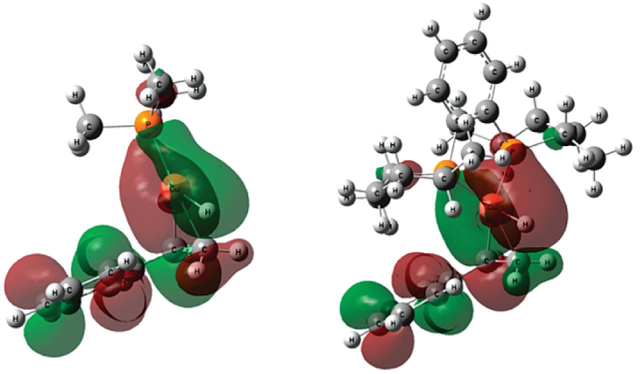
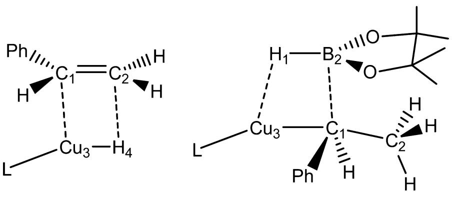


Figure 3. HOMOs of TS1 in **L1** and **L4**.

On the basis of this successive step mechanism, in order to increase catalytic activity, it is obvious that both activation barriers ΔE_1‡ and ΔE_2‡ would need to be lowered. In particular, as seen in Figure 2, the activation barrier ΔE_1‡ was mainly lowered by less stabilization of the reactant complex. In other words, when the reactant complex is more stabilized, catalytic activity will decrease. The reactant complexes with **L4** and **L5** were less stabilized compared to **L1**, **L2**, and **L3**. It should also be noted from Figure 2 that the energy differences between the different catalytic systems in the reactant−catalyst complexes and in TS2 are much larger than the energy differences in TS1 and the intermediates. This implies that it is easier to control the energies of the reactant complexes and TS2 than the intermediates and TS1 and suggests that new powerful catalysts could be developed through the proper design of less stabilized reactant complexes and/or by stabilizing the transition state in step II.

Figure 3 shows the highest occupied molecular orbitals (HOMOs) of the transition states in step I (TS1) for **L1** and **L4** as representative of monodentate and bidentate ligands for the copper catalysts. The most striking feature of the transition states is that the Cu−H of the catalysts interacts with the C═C of styrene, with the copper donating electrons to the carbon atom. Thus, it is expected that the catalyst would be more effective in the styrene insertion when the styrene has an electron withdrawing group at the meta or para position, which is consistent with our previous experimental data.[12] Furthermore, the catalytic efficiency would increase with a properly designed electron-donating ligand for the catalytic copper complex, as can be seen from the electronic population of the copper atom in the transition states. A natural bond orbital (NBO)[25] population analysis was performed to obtain more reliable charges for copper in the transition states. The charge of the copper in the transition states for step I were calculated to be 0.831, 0.905, 0.938, 1.003, and 1.007 for **L1**, **L2**, **L3**, **L4**, and **L5**, respectively, and for step II were 0.888, 0.924, 0.968, 1.008, and 1.007, respectively. Although the electronic population of the copper

SCHEME 2: Transition States for L = L4



TS1 TS2

atom in the various ligands does not deviate much, careful scrutiny indicates that the electron density of the copper with bidentate ligands (**L4** and **L5**) is more positive than with monodentate ligands (**L1**−**L3**). Thus, more electron density is transferred to the styrene with bidentate ligands than with monodentate ligands, resulting in higher catalytic activity, which is in good agreement with experimental results.

From the NBO population analysis and based on valence bond theory, the σ-bond between C_1 and C_2 for TS1 of **L4** is formed from the $sp^{1.90}$ orbital of C_1 and the $sp^{1.71}$ orbital of C_2. In other words, the p character is slightly reduced as the reactants approach to form TS1. $C_2 \cdots H_4$ has an orbital interaction between the $sp^{9.31}$ (almost a p orbital) orbital of C_2 and the s orbital of H_4. Thus, in TS1, the σ-bond between C_1 and C_2 is mostly retained while the π-bond between C_1 and C_2 is mostly broken, with the p orbital used to interact with the s orbitals of Cu_3 and H_4. Similarly, in TS2, the σ-bond between H_1 and B_2 is formed by an overlap between the s orbital of H_1 and the $sp^{2.64}$ orbital of B_2. In contrast to TS1, the p character of the boron increases as the reactants approach to form TS2. $B_2 \cdots C_1$ has an overlap between the $sp^{4.86}$ orbital of B_2 and the $sp^{4.37}$ orbital of C_1, where both the boron and carbon have some s character.

Conclusions

In conclusion, we investigated the catalytic reaction mechanism of the hydroboration of styrene using copper(I) catalysts coordinated with monodentate and bidentate phosphine ligands. Copper catalysts with bidentate ligands were found to give higher catalytic activity than those with monodentate ligands. The experimental conversion efficiency in the catalytic hydroboration was thoroughly rationalized based on kinetic theory with a two-step mechanism. In particular, the catalytic activity could be increased by lowering the activation barriers for steps I and II. In our case, the activation barrier for step I was found to be lower in the case of bidentate ligands (**L4** and **L5**) due to less stabilization of the reactant complexes. Bidentate ligands make the reactant complexes less stable than monodentate ligands due to steric hindrance. From the electronic distribution of the HOMO and the charge of the copper atom in the transition states, it was found that styrenes with an electron withdrawing group would have a higher conversion, and the catalytic efficiency could be increased with a properly designed electron-donating ligand for the catalytic copper complex. The NBO charges of the copper atom clearly demonstrate that bidentate ligands give a higher catalytic efficiency than monodentate ligands. These results provide useful information for the development of new metal catalysts for the copper-catalyzed hydroboration reaction.

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Supporting Information Available: Absolute and relative energies, atomic coordinates, and geometrical parameters of the reactants, intermediates, transition states, and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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