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Effects of Boron-Containing Lewis Acids on Olefin Metathesis

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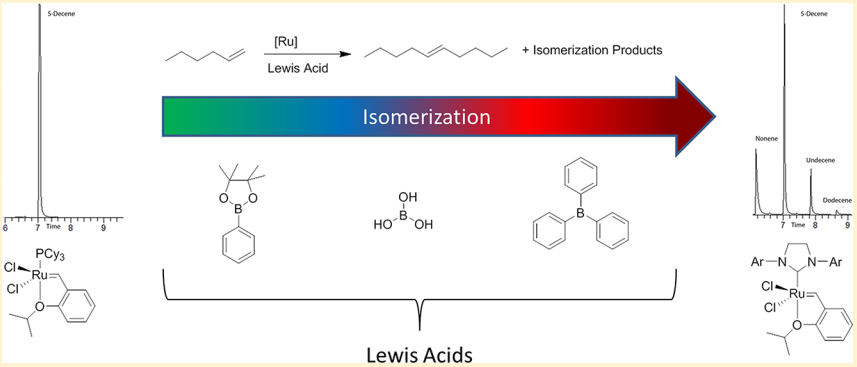
Supporting Information



ABSTRACT: Boron-containing Lewis acids have shown a profound effect on the cross-metathesis reaction of 1-hexene. Grubbs first-generation catalyst shows over 100% improvement in conversion in some cases, while the yields increase by up to 50% with Grubbs second-generation catalyst. With the inclusion of boron-containing Lewis acids, compounds prepared using Grubbs second-generation-type catalysts display significantly reduced levels of isomerization.

Thus far, there has been no systematic study of the effects of boron-containing Lewis acids on isomerization and resulting cross-metathesis conversion using a variety of Grubbs-type catalysts.

Increasing the yields and decreasing the isomerization of olefin metathesis reactions is important in the fields of organic synthesis, polymer chemistry, and pharmaceuticals. Herein, we use a model system to prove that boron-containing Lewis acids increase the yields of olefin metathesis reactions containing Grubbs first- and second-generation catalysts. By use of GC-MS we demonstrate that olefin isomerization is nearly eliminated in the presence of boron-containing Lewis acids.

Olefin metathesis has opened many new avenues for the synthesis of carbon−carbon double bonds and has proven invaluable for many fields of chemistry.[1] Ring-closing metathesis (RCM) and cross metathesis (CM) have revolutionized the synthesis of pharmaceuticals and large total synthesis targets.[2−4] Ring-opening metathesis polymerization (ROMP) and acyclic diene metathesis (ADMET) polymerization have provided ways to synthesize new materials, often with unique morphologies.[5−8] As knowledge of these techniques increases, researchers are continuing to expand the range of olefin metathesis applications.

Numerous Grubbs-type olefin metathesis catalysts have been developed over the past 15 years.[9] Each catalyst has specific strengths and weaknesses, generally in reference to stability, activity, and tendency for isomerization of the olefin.[10] Grubbs first-generation catalyst (G1) is less active and less stable than second-generation Grubbs catalyst, but G1 does not display a propensity toward isomerization.[11] Hoveyda−Grubbs first-generation catalyst (HG1) has a higher stability and is slightly more active than G1, although still less active than the second-generation catalysts.[12] Grubbs second-generation catalyst (G2) is quite active and stable, but it can lead to significant isomerization of the double bond.[11,13,14] Hoveyda−Grubbs second generation catalyst (HG2) scores highest in all of the metrics above, being the most stable and active, but also having the greatest tendency for isomerization.[15−17]

Isomerization of the double bond in olefin metathesis has been attributed to the formation of ruthenium hydride.[18,19] Metal-centered Lewis acids and protic acids reduce isomerization in reactions involving Grubbs second-generation type catalysts.[20−23] Lewis acids have been shown to activate molybdenum nitride catalysts, leading to increased yields and rates of alkyne metathesis.[24,25] Vedrenne et al. studied how Lewis acids, including some containing boron, facilitate the CM of certain olefins having functional groups that interfere with the catalyst or undergo some other side reaction. In these cases, the Lewis acids are thought to coordinate with the functional group, leaving the metathesis catalyst unencumbered.[26]

Lewis acids that contain boron were chosen for this study, due to the wide range of acid strengths that are available. Recently boron-containing moieties have been used in organic synthesis,[30−32] pharmaceuticals,[33−35] and polymers.[36−38] Understanding boron's effect on common synthetic and

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polymerization techniques can open many doors in these fields. The calculated values for fluorine affinities were used as a measure of Lewis acidity ,as shown in Figure 1: triphenylborane

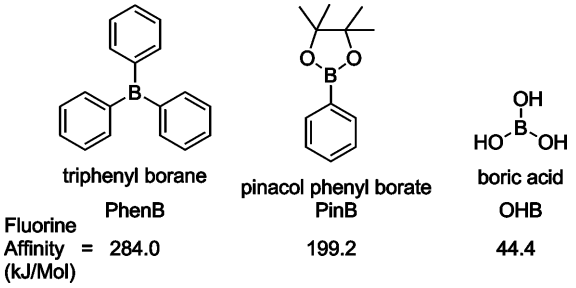


Figure 1. Boron-containing Lewis acids which exhibit a range of Lewis acidities. Fluorine affinity is used as a metric of Lewis acidity, PhenB being the strongest Lewis acid and OHB being the weakest.[27−29].

(PhenB) displays the highest Lewis acidity, boric acid (OHB) is the weakest, and pinacolphenylborate (PinB) is in the middle.[27−29]These Lewis acids were studied for their impact on yield and olefin isomerization tendency of a variety of Hoveyda- and Grubbs-type metathesis catalysts (Figure 2). As

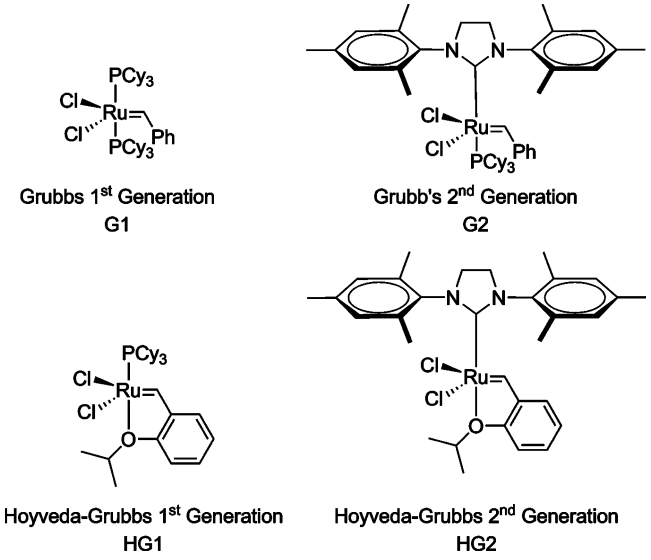


Figure 2. Hoveyda- and Grubbs-type catalysts used in this study.

the model system, we used the cross metathesis (CM) of 1-hexene (Scheme 1) monitored by GC and NMR. Deuterated chloroform was chosen as the solvent to aid in NMR analysis and to solvate the Lewis acid. Chlorinated solvents have been shown to facilitate olefin metathesis.[39−41]

The yields were studied for all four catalysts with each of the boron-containing Lewis acids. As shown in Table 1, HG1 provided similar yields when used with PhenB, PinB, and OHB.

Table 1. CM Conversions of 1-Hexene

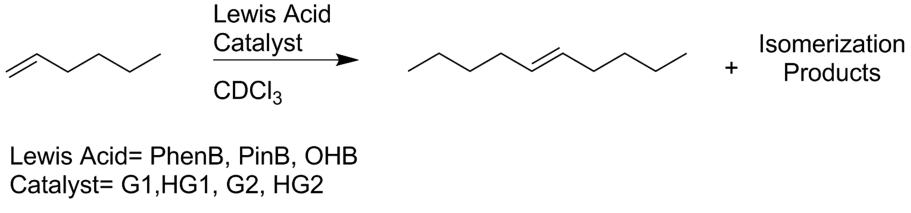
	yield[a](%)			
Lewis acid	HG1	G1	HG2	G2
control[b]	84	29	99+	63
OHB	78	71	24	60
PinB	74	62	33	69
PhenB	81	5	50	5

[a]Yields determined by NMR. [b]Control reactions were performed without Lewis acids. Reaction conditions: 100 mg of 1-hexene, 20 mol % of Lewis acid, and 1 mol % of catalyst reacted at 45 °C in $CDCl_3$ for 15 h. The standard deviation was found to be 7.9%.

For Grubbs first-generation (G1) catalyst the control reaction yielded 29% CM, but addition of OHB and PinB significantly increased the yields to 71% and 62%, respectively (Table 1). In these cases, the Lewis acid behaves as a phosphine sponge. It removes the tricyclohexylphosphine ligand from the catalyst and increases the rate of the initiation step. This capture of phosphine ligands has been shown with a variety of boron-containing and metal-containing Lewis acids; these include triphenylborane,[42] tris(pentafluorophenyl)borane,[43] 9-borabicyclo[3.3.1]nonane,[44] and copper iodide.[45] Furthermore, metal-containing Lewis acids such as tin(III) chloride[20] and copper iodide[46] have displayed yield and rate increases in metathesis reactions, presumably from the phosphine sponge effect. This is supported by a shift in the ^{31}P NMR of G1 in the presence of PinB, presumably caused by the complexation of the phosphine ligand with the Lewis acid. This effect was not observed for the HG1 catalyst because the dissociative ligand is the isopropylphenyl group, not the tricyclohexylphosphine. The PhenB Lewis acid surprisingly led to only about 5% conversion. Similar results with PhenB were found with Grubbs second-generation catalyst (G2) and will be discussed in more detail below.

The trend in yields for Hoveyda−Grubbs second-generation catalyst (HG2) was expected to be similar to that of HG1, but this was not the case. As seen in Table 1, the control reaction achieved nearly quantitative conversion, but the addition of a Lewis acid dramatically decreased the yields in the order PhenB at 50%, PinB at 33%, and OHB at 24%,. This is contrary to current thought, since the HG2 catalyst is expected to show increased stability in comparison to G1 and G2. The yields follow the trend in acid strength; the stronger Lewis acids cause the catalyst to decay more slowly. When studying the effects of Lewis acids on olefins that were hard to metathesize, Vedrenne et al. showed that chlorocatacholborane at 10 mol % enhanced

Scheme 1. Model Reaction Used To Study the Effects of Lewis Acids on Olefin Metathesis[a]



[a]Reaction conditions: 100 mg (1.2 mmol) of 1-hexene, 20 mol % of Lewis acid, 1 mol % of catalyst reacted at 45 °C in $CDCl_3$ for 15 h.

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the cross-metathesis reaction using HG2 of methyl vinyl ketone and BOC-protected 2-propene-1-amine, but at 40 mol % borane the reaction was retarded.[26] These results indicate that there is an optimal concentration of Lewis acid before it causes decomposition of HG2 catalyst.

The results for HG2 were not entirely negative. When the isomerization was studied by GC-MS, it was found that the addition of any of the Lewis acids led to an almost complete reduction in isomerization. In comparison to the GC traces from the HG1 reactions, which show only very minimal isomerization, the traces with Lewis acids and HG2 are almost identical (Figure 3). The boron-containing Lewis acid presumably reacts with any hydride formed to shut down that isomerization path.

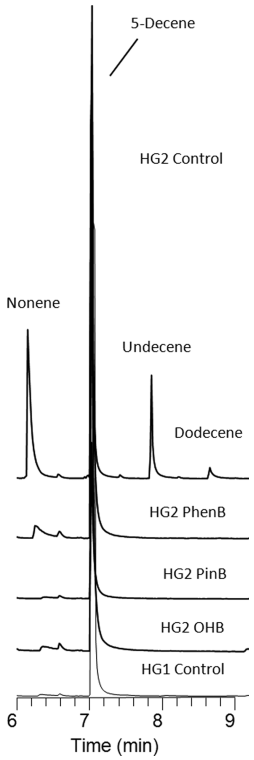

Figure 3. GC traces showing a reduction in isomerization with the addition of Lewis acids.

Grubbs second-generation catalyst (G2) behaves as a hybrid of HG2 and G1. The control reaction yielded 63% conversion. With OHB and PinB added to the reaction, the yields were 61% and 69%, respectively, indicating that there was a competition between the decomposition tendency of HG2 and the phosphine sponge effect observed with G1. This competition was also observed when the concentration of the Lewis acid was varied. Figure 4 displays the CM yields as a function of Lewis acid concentration. PinB was used for this study because it displayed the greatest effect in terms of yield enhancement and isomerization reduction. When PinB was added at 5 mol %, the yield increased to 97%, a dramatic change from the 63% control experiment. When the concentration of PinB was increased to 10−20%, the yields dropped to about 68%. At 30−50% Lewis acid the yields further decreased to about 50−55%. These results demonstrate a competition between the increase in the rate of initiation and the decomposition of the catalyst. At low concentrations the PinB only removes the phosphine

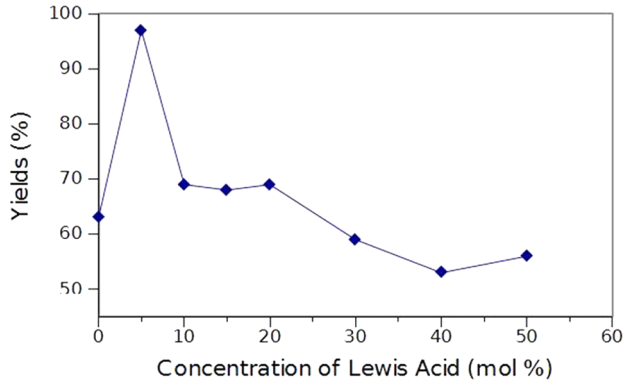

Figure 4. Concentration effects of PinB Lewis acid on CM reactions using G2. The standard deviation was found to be 7.9%.

from the catalyst, causing an increase in yield. However, once the concentration of PinB is increased, the catalyst begins to decompose.

With PhenB and either G1 or G2, small amounts of the CM product were observed. However, with HG1 or HG2, PhenB was one of the better Lewis acids. To further investigate this behavior, the reaction was run neat. The control experiments for G1 and G2 resulted in yields of 76% and 55%, respectively. However, in the experiments containing BPhen, the G1 and G2 yields were 93% and 68%, respectively, an increase in converstion of 122% and 124% for G1 and G2, respectively, from the control reactions. These results lead to the conclusion that BPhen is a good Lewis acid choice, but it is sensitive to the solvent choice when using Grubbs first- and second-generation catalysts. In comparison to the increases in conversion from control experiments observed with OHB and PinB for G1, 245% and 214%, respectively, PhenB is not as effective at increasing the yield of the CM reaction.

This work has demonstrated the effect of boron-containing Lewis acids on olefin metathesis yield and isomerization tendency. The Grubbs series of catalysts show improvements in both yield and isomerization tendency in the presence of boron-containing Lewis acids, while the Hoveyda-type catalysts show no change in yield for HG1 and a decrease in both yield and isomerization with HG2. These results have implications for olefin metathesis reactions in chemistry, polymer synthesis and polymerization, and pharmaceutical science.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text and figures giving detailed reaction procedures and representative NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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