Ruthenium-Catalyzed Regiospecific Borylation of Methyl C–H Bonds

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We report a family of ruthenium complexes that catalyzes the regiospecific terminal functionalization of alkanes. Many examples of the functionalization of alkanes catalyzed by rhenium, rhodium, iridium, palladium, and platinum complexes have been reported,[1] but few examples catalyzed by ruthenium have been published since the original dehydrogenations disclosed by Felkin.[2,3] Considering that ruthenium complexes are now common as catalysts for many transformations in organic synthesis,[4] it is surprising that so little catalytic functionalization of alkanes with organometallic ruthenium complexes has been reported. Even stoichiometric transformations of alkanes via organometallic ruthenium complexes are rare.[3,5] Transformations of alkanes by ruthenium that are comparable to those by other group 8 metals would be valuable because of the low cost of this metal[6] and the ability to exploit the different electron count to create catalysts with distinct coordination spheres.

A series of metal complexes has been reported to catalyze the thermal borylation of aromatic[7] and benzylic C–H bonds,[8,9] but the catalytic borylation of alkanes has been conducted only with rhodium.[10,11] No borylation of alkanes has been reported with metals of the closely related iron triad. We now disclose a series of ruthenium complexes that act as precatalysts for the selective borylation of alkanes. One of these precatalysts contains a new binding mode for a boryl group, and all complexes show an unusual propensity to form higher yields of organoboronate esters from reactions of alkanes than from arenes. The functionalization of aliphatic C–H bonds occurs with high regioselectivity for terminal C–H bonds and tolerates the presence of heteroatoms.

(1)
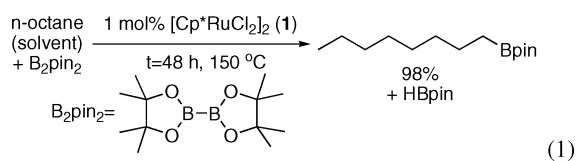
The finding that $[Cp*RhCl_2]_2$[12] catalyzes the borylation of alkanes[8,13] led us to test reactions catalyzed by a series of $Cp*MCl_n$ complexes. Among these complexes, 1 mol % of $[Cp*RuCl_2]_2$ (1) (2 mol % of Ru) catalyzed the reaction of B_2pin_2 (pin = pinacolate, eq 1) with octane to form HBpin and 1-octylBpin in quantitative yield after 48 h. With this result in hand, we studied reactions catalyzed by ruthenium complexes possessing structures and oxidation states that are likely to be closer to those of an active catalyst for alkane functionalization.

Table 1 summarizes the results of reactions of B_2pin_2 with octane catalyzed by $(Cp*RuCl)_4$ (2), $Cp*Ru(H)(COD)$ (3),[12] $Cp*Ru(Cl)$-(TMEDA) (4), $[Cp*Ru(OMe)]_2$ (5),[12] $(COD)Ru(2-methylallyl)_2$ (6), and $Ru(acac)_3$ (7). Several of these complexes catalyzed the borylation process to form alkylboronate esters in substantial yields. Of them, the Ru(III) dichloride dimer 1 was most active. The related borylation of octane by pinacolborane (HBpin) in the presence of these catalysts did not yield octylBpin.

Table 1. Effect of Catalyst Structure on the Ru-Catalyzed Borylation of Alkanes

catalyst	yield[a]	conversion[a]
$(Cp*RuCl_2)_2$ (1)	98% (75%)[b]	99%
$(Cp*RuCl)_4$ (2)[c]	65%	99%
$Cp*Ru(H)(COD)$ (3)	58%	80%
$Cp*Ru(Cl)(TMEDA)$ (4)	95%	98%
$[Cp*Ru(OMe)]_2$ (5)	7%	65%
$(COD)Ru(2-methylallyl)_2$ (6)	7%	59%
$Ru(acac)_3$ (7)	4%	76%

[a] Determined by GC. [b] Isolated yield in parentheses. [c] 5 mol % of Ru used.

Studies on the selectivities of the various catalyst precursors imply that all of the complexes generate a common active catalyst. Reactions of B_2pin_2 with butyl ethyl ether and 2-methylheptane are shown in Scheme 1. The reactions occurred preferentially at the less hindered methyl group and preferentially at the methyl group closer to the oxygen atom. The borylation of butyl ethyl ether by 1, 2, 3, and 5 generated a similar ratio of the two possible reaction products. The borylation of 2-methylheptane would be more discriminating of the steric properties of the ancillary ligands. Reactions of this alkane catalyzed by 1, 2, 3, and 5 occurred to give the same ratio of the two regioisomeric products (although in variable yields). The observed selectivities are similar to those observed with the rhodium complex $Cp*Rh(\eta^6-C_6Me_6)$.[7b]

The vast majority of organometallic C–H activation occurs more rapidly and in higher yield with arenes than with alkanes. However, studies on the borylation of arenes and alkanes by dichloro dimer 1 showed that the reactions with alkanes occurred in much higher yield than those with arenes. In contrast to the nearly quantitative yield of alkylboronate ester from reactions of B_2pin_2 in alkanes catalyzed by dichloride dimer 1, only 20% yield of PhBpin was formed from the reaction of B_2pin_2 with benzene; reactions of B_2pin_2 with benzene catalyzed by complexes 2, 4, and 5 also formed less than 20% yield of PhBpin.

Further studies imply that the catalyst is inhibited by the presence of arene. B_2pin_2 and a 35:1 mixture of octane and benzene were heated with 2.5 mol % of 1 (5.0 mol % of Ru). After 24 h, a mixture of 4% octylBpin and 25% PhBpin was observed. To determine if the catalyst was poisoned by formation of $[Cp*Ru(\eta^6-C_6H_6)]^+$,[14] an ESI/MS of the reaction mixture and NMR spectroscopic data were obtained. These data did not provide evidence for the formation of $[Cp*Ru(\eta^6-C_6H_6)]^+$. However, an ESI/MS of the reaction mixture formed from the reaction of a 35:1 mixture of octane and mesitylene revealed the formation of the known[15] $[Cp*Ru(\eta^6-C_6H_3Me_3)]^+$.

Considering the ability of arenes to affect the C–H activation of alkanes, one might expect basic heteroatoms to also influence the catalytic process. However, the reactions of these ruthenium

Scheme 1

1 32:68	**3** 29:71
2 29:71	**5** 27:73

1 30:70	**3** 29:71
2 29:71	**5** 30:70
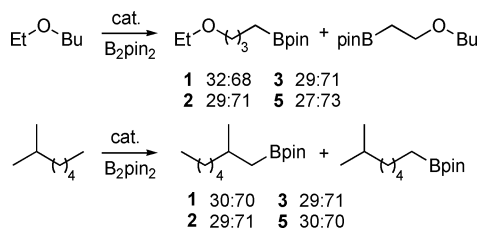
Chart 1. Products from Ru-Catalyzed Terminal Borylation of Heteroatom-Containing Substrates[a]
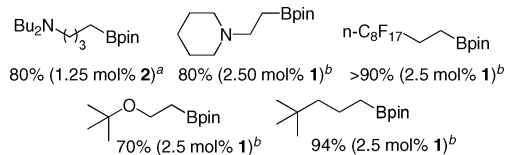
^{a} Conditions: neat, 150 °C, 24 h, yield determined by GC. ^{b}Neat, 150 °C, 48 h, yield determined by GC.
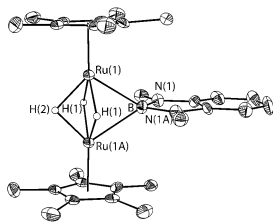
Figure 1. ORTEP diagram of Cp*$_2$Ru$_2$H$_3$[B(*N*,*N*-dimethylphenylenediamine)] (**8a**).

complexes occurred with ethers (vide supra), fluoroalkanes, and amines in yields that were comparable to those of the reactions of alkanes (Chart 1). Moreover, these reactions were selective for functionalization at the less hindered methyl group regardless of the identity or presence of a heteroatom. The optimal ruthenium catalyst for these reactions depended on substrate, but either **1** or **2** catalyzed these reactions in good to excellent yields.

The borylation of hydrocarbons catalyzed by Cp*−Rh complexes occurs by the reaction of transition metal−boryl complexes with C−H bonds to form boronic esters and metal hydrides. We therefore sought to generate Ru−boryl species from each of the ruthenium catalyst precursors. Details of these studies will be reported separately. However, the reaction of **3** with the diaminoborane HBX$_2$ in which X$_2$ = *N*,*N*′-dimethyl-1,2-benzenediamide and *N*,*N*′-4,5-tetramethyl-1,2-benzenediamide formed Cp*$_2$Ru$_2$(μ-BX$_2$)(μ-H)$_3$ (**8a** and **8b**, respectively, eq 2). These are the first complexes with symmetrically bridging boryl groups.

R = H (**8a**) 23%
R = Me (**8b**) 30%   (2)
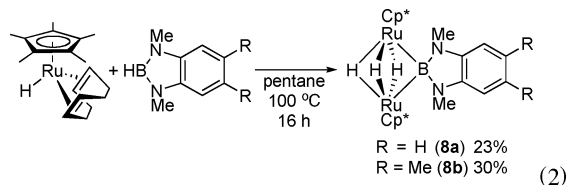
The solid-state structure of **8a**, determined by X-ray crystallography, is shown in Figure 1; the boryl ligand of **8b** lies on a crystallographic mirror plane and, therefore, symmetrically bridges the two metal centers. The only other complexes with bridging boryl groups include three with a semi-bridging structure[16] and one with an unsymmetrical heterodinuclear structure.[17] The ^{1}H NMR spectra of **8a** and **8b** at room temperature exhibit only one hydride signal. However, ^{1}H NMR spectra at −40 °C contain two singlet resonances in a 2:1 ratio of intensities.

Bridging diazaborolanyl complexes **8a** and **8b** cannot be exact intermediates in the catalytic functionalization of alkanes by alkoxy-substituted B$_2$pin$_2$, and no C−H bond functionalization has been reported by any diazaboryl complex or aminoborane reagent. Nevertheless, **8a** and **8b** were precatalysts for the functionalization of alkanes with B$_2$pin$_2$ and 2 mol % of **8b** after 48 h at 150 °C, yielding 20% octylBpin.

Considering the higher reactivity of pinacolborane reagents than of diaminoborane reagents, one would expect the pinacolboryl analogues of **8a** and **8b** to be more reactive than the isolated diazaboryl complexes, and possibly to be the species that react with alkanes. Such a complex could react directly with alkanes, in line with the reactions of alkanes with trinuclear ruthenium polyhydrides,[5,18] or after cleavage to monomeric boryl complexes that would be related to Cp*Rh−boryl intermediates in the Rh-catalyzed borylation of alkanes.[11] Studies to prepare the pinacolboryl analogues of **8a** and **8b** are ongoing.

In summary, we have shown that several ruthenium compounds serve as precatalysts for the terminal borylation of alkanes, that high yields can be obtained from reactions catalyzed by complexes of this metal, that the catalyst is tolerant of heteroatoms, and that these catalysts display an unusual trend of higher yields for reactions of alkanes than for reactions of arenes. This work presents the opportunity to develop catalysts with ligands and geometries distinct from those of the existing rhodium catalysts for alkane functionalization, and this work will be part of future studies.

Supporting Information Available: Procedures for synthesis and characterization of reaction products (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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