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Site- and Regioselective Silaborative C−C Cleavage of 1-Alkyl-2-Methylenecyclopropanes Using a Platinum Catalyst with a Sterically Demanding Silylboronic Ester

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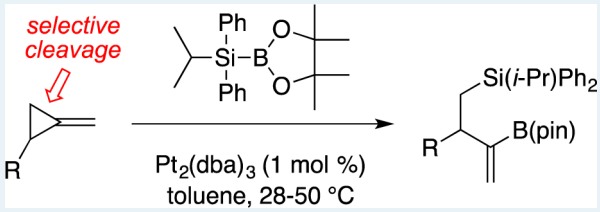
Supporting Information

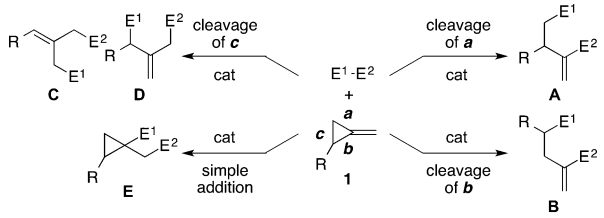
ABSTRACT: 1-Alkyl-2-methylenecyclopropanes react with silylboronic esters under mild conditions in the presence of a phosphine-free platinum catalyst, giving 3-substituted 2-boryl-4-silyl-1-butenes through selective cleavage of the less hindered proximal C−C bond of the cyclopropane ring. The steric bulk of the silyl group of the silylboronic esters was critical for efficient formation of the silaboration products, and *i*-PrPh$_2$Si−B(pin) was developed as a silylboronic ester of choice.



KEYWORDS: *homogeneous catalysis, platinum catalyst, C−C bond cleavage, silaboration, methylenecyclopropane, organoboron compound, organosilicon compound, selectivity*

The use of transition-metal-catalyzed reactions of methylenecyclopropanes (MCPs) to conduct organic transformations has received much attention recently because of the unique, multifarious reactivities of such systems.[1] Among the MCPs that bear substituents on the double bond or on the cyclopropane ring, the reactions of unsymmetrical MCPs such as 1-substituted 2-methylenecyclopropanes **1** are especially complex and difficult to control (Scheme 1). The addition of a reagent having an E^1−E^2 bond, for example, B−B, C−H, and H−N bonds, often accompanies cleavage of one of the three nonequivalent C−C bonds (bonds ***a***−***c***) of the cyclopropane ring to give 1,3-difunctionalized alkenes **A**−**D**.[2−4] Simple 1,2-addition to the double bond may also take place to give a cyclopropane derivative **E**.[5] The course of the reaction depends on the reagents and catalysts used, as well as on the steric and electronic properties of the substituent R. Reactions of 1-substituted MCPs **1** often suffer from low selectivity, as exemplified by platinum-catalyzed diboration,[2b] nickel-catalyzed hydroacylation,[2e] and titanium- and zirconium-catalyzed hydroamination,[3b] which give a mixture of **A** and **B** (Scheme 1, bottom). Considering the ready availability of **1**,[6] the development of new catalyst systems with suitable reagents is highly desirable for further utilization of this key compound in organic synthesis.

Scheme 1. Transition-Metal-Catalyzed Addition of E^1−E^2 to 1-Substituted 2-Methylenecyclopropanes 1



Reaction examples that result in a mixture of isomers:

reagent	E^1−E^2	cat	selectivity	ref.
(pin)B−B(pin)	B−B	Pt	**A**:**B** = 57:43–79:21	2b
PhCHO	C−H	Ni	**A**:**B** = 91:9	2e
H$_2$NR'	H−N	Ti, Zr	**A**:**B** = 29:71–0:100	3b

Addition of silylboronic esters to unsaturated hydrocarbons (i.e., silaboration) has provided new synthetic pathways to structurally defined organoboron and organosilicon compounds.[7] Transition-metal-catalyzed silaborative C−C cleavage of MCPs has been developed as a unique 1,3-silaboration method that allows regioselective introduction of boryl and silyl groups with site-selective opening of the cyclopropane ring.[8] Our studies on silaborative C−C cleavage of MCPs have made clear the limitations of this reaction: the reaction of unsymmetrical **1** suffers from low site selectivity as observed in the previous study on the phosphoramidite/Pd catalyst systems,[8d] in which the products were obtained as a mixture of **A** and **B** (**A**/**B** ratio of 54:46 to 86:14, Scheme 2). Herein, we describe a new catalyst system that accomplishes complete site selectivity in silaborative C−C cleavage of **1** (Scheme 2). A phosphine-free platinum catalyst with a sterically demanding silylboronic ester has been found to be effective for the reaction, which proceeds through selective cleavage of bond ***a***.

We started our study by screening a range of palladium catalysts for silaborative C−C cleavage of 1-cyclohexyl-2-

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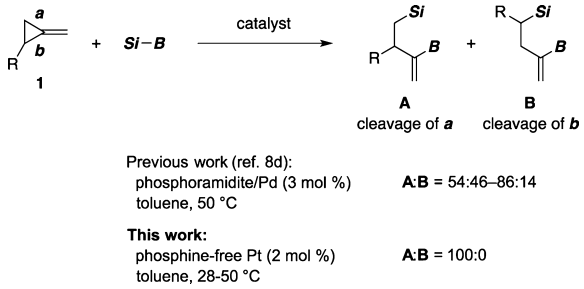
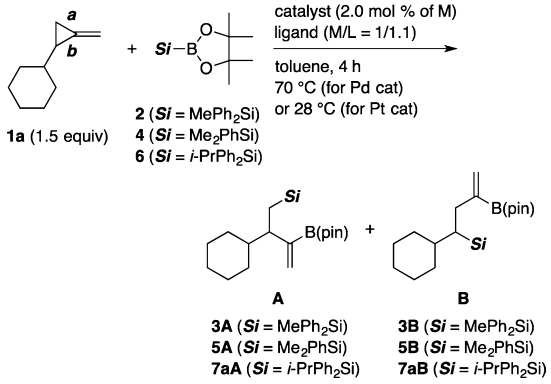
Scheme 2. Silaborative C−C Cleavage of 1



methylenecyclopropane (**1a**) (entries 1−7, Table 1). Compound **1a** (1.5 equiv) reacted with $MePh_2Si$−B(pin) (**2**) at 70 °C in toluene in the presence of palladium catalysts. Catalysts generated in situ from $Pd(dba)_2$ (2.0 mol %) and phosphorus ligands (2.2 mol %) promoted the silaborative C−C cleavage (entries 2−5), whereas no reaction took place with a phosphine-free palladium(0) complex (entry 1). The palladium-catalyzed reaction gave **3B** through cleavage of bond ***b*** as the major product; compound **3A** was formed as a minor product through cleavage of bond ***a*** (**3A**/**3B** ratio of 19:81 to 29:71, entries 2−5). Palladium catalysts bearing $PCyPh_2$ and PCy_3 showed high catalyst efficiencies (entries 3 and 5). The $Pd/PCyPh_2$-catalyzed reaction of **1a** with Me_2PhSi−B(pin) (**4**) resulted in formation of **5A** and **5B** with lower site selectivity (**5A**/**5B** ratio of 32:68, entry 6). We also conducted the reaction with the new silylboronic ester *i*-$PrPh_2Si$−B(pin) (**6**),[9] but this reagent did not participate in the reaction with **1a** under the reaction conditions, probably because of the steric hindrance of **6** (entry 7).

Table 1. Reaction Conditions for Silaborative C−C Cleavage of 1a[a]



entry	Si−B	catalyst	yield (%)[b]	A/B[c]
1	**2**	$Pd(dba)_2$	no reaction	-
2	**2**	$Pd(dba)_2/PPh_3$	13 (**3**)	29:71
3	**2**	$Pd(dba)_2/PCyPh_2$	83 (**3**)	19:81
4	**2**	$Pd(dba)_2/PCy_2Ph$	35 (**3**)	29:71
5	**2**	$Pd(dba)_2/PCy_3$	97 (**3**)	25:75
6	**4**	$Pd(dba)_2/PCyPh_2$	58[d] (**5**)	32:68
7	**6**	$Pd(dba)_2/PCyPh_2$	no reaction	-
8	**2**	$Pt_2(dba)_3$	45 (**3**)	100:0
9	**2**	$Pt_2(dba)_3/2PPh_3$	3 (**3**)	100:0
10	**2**	$Pt_2(dba)_3/2PCyPh_2$	15 (**3**)	100:0
11	**2**	$Pt_2(dba)_3/2PCy_2Ph$	6 (**3**)	100:0
12	**2**	$Pt_2(dba)_3/2PCy_3$	4 (**3**)	100:0
13	**4**	$Pt_2(dba)_3$	35[d] (**5**)	100:0
14	**6**	$Pt_2(dba)_3$	81[d] (**7a**)	100:0
15[e]	**6**	$Pt_2(dba)_3$	90[f] (**7a**)	100:0

[a]$Pd(dba)_2$ (2.0 mol %) or $Pt_2(dba)_3$ (1.0 mol %), phosphine ligand (0 or 1.0 mmol), silylboronic ester (0.10 mmol), **1a** (0.15 mmol), and toluene (0.1 mL) were stirred at 70 °C (for Pd) or 28 °C (for Pt). [b]GC yield. [c]Determined by GC. [d]^1H NMR yield. [e]2.0 equiv of **1a** was used. [f]Isolated yield.

We then turned our attention to the use of platinum catalysts (entries 8−15, Table 1). In contrast to the palladium catalysts, phosphine-free $Pt_2(dba)_3$ (1.0 mol %)[10] was found to be effective for the reaction of **1a** with **2**, allowing the reaction to proceed even at 28 °C (entry 8). The reaction took place selectively through cleavage of bond ***a*** to give **3A** as a single isomer (**A**/**B** ratio of 100:0), albeit in moderate yield. Use of phosphine ligands resulted in a significant decrease in the rate of reaction (entries 9−12). We found that sterically demanding silylboronic ester **6** reacted cleanly with **1a** to afford **7aA** in high yield in the presence of $Pt_2(dba)_3$ catalyst (**A**/**B** ratio of 100:0, entry 14). The yield of **7aA** was improved to 90% when the reaction was carried out with an increased amount of **1a** (2 equiv, entry 15).

A range of MCPs **1** were subjected to the reaction with **6** by using $Pt_2(dba)_3$ as catalyst (Table 2).[11] Silaborative C−C cleavage of MCPs having 2-phenylethyl and *n*-hexyl groups (**1b** and **1c**) took place smoothly at 28 °C to give the corresponding alkenylboronic esters **7b** and **7c**, respectively, in high yields (entries 1 and 2). Silyloxyalkyl-substituted **1d** and **1e** also reacted with **6** at 28 °C (entries 3 and 4). In contrast, silaborative C−C cleavage of **1f**, bearing a siloxymethyl group, was relatively slow, resulting in faster consumption of **1f** through a side reaction. Elevation of reaction temperature (50 °C) improved the relative reaction rate of silaboration over that of the side reaction of **1f**, giving **7f** with reasonable yield after 16 h (entry 5). Silaborative C−C cleavage of 3-chloropropyl-substituted **1g** and a phthalimide derivative **1h** also took place efficiently at 50 °C to give **7g** and **7h** in 79 and 81% yields, respectively (entries 6 and 7). On the other hand, the reaction of phenyl-substituted **1i** resulted in the formation of a complex mixture containing a small amount of desired product **7i** (entry 8).

The reaction profile for the platinum-catalyzed reaction of **1b** with **6** (2 equiv) at 28 °C is shown in Scheme 3. The profile indicates that silaborative C−C cleavage competes with isomerization of **1b** to give 2-(2-phenylethyl)-1,3-butadiene (**8**) under the reaction conditions employed.[12] Notably, isomerization of **1b** to **8** was suppressed when **6** was consumed, indicating that a complex formed from **6** and $Pt_2(dba)_3$ may be involved in the isomerization.

A possible mechanism for the platinum-catalyzed silaborative C−C cleavage of MCPs is shown in Scheme 4. Oxidative addition of the Si−B bond to Pt(0) is followed by coordination of MCP to give complex **F**.[13] Insertion of the C−C double bond of MCP to the Pt−B bond takes place to afford cyclopropylmethyl complex **G**.[14] The latter complex undergoes *β*-carbon elimination through cleavage of the less sterically hindered C−C bond (bond ***a***) of the cyclopropane ring to give **H**, which finally affords product **A** through reductive elimination. An alternative pathway for the ring opening is oxidative addition of the less hindered C−C bond of the cyclopropane ring to Pt(II) to form metalacycle **I**.[15] Subsequent reductive elimination to form the C−B bond results in the formation of **H**. *β*-Elimination from **I** may proceed competitively, leading to isomerization of MCP to 1,3-diene via **J**.

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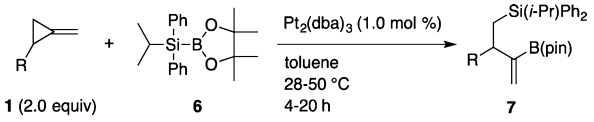
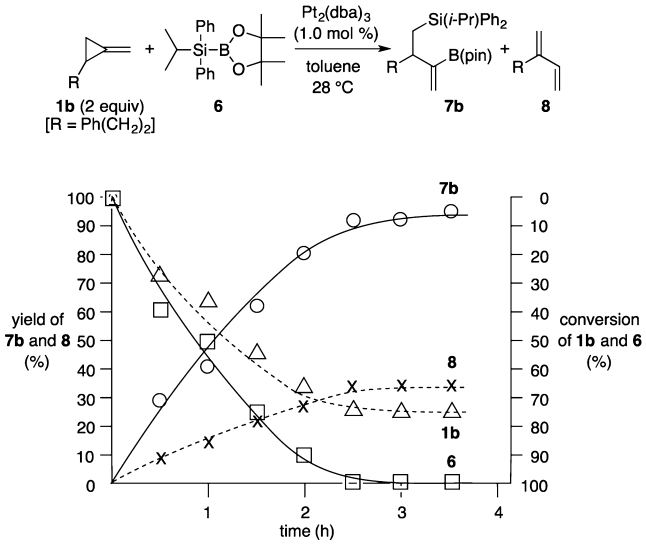
Table 2. Platinum-Catalyzed Site- and Regioselective Silaborative C−C Cleavage of 1[a]



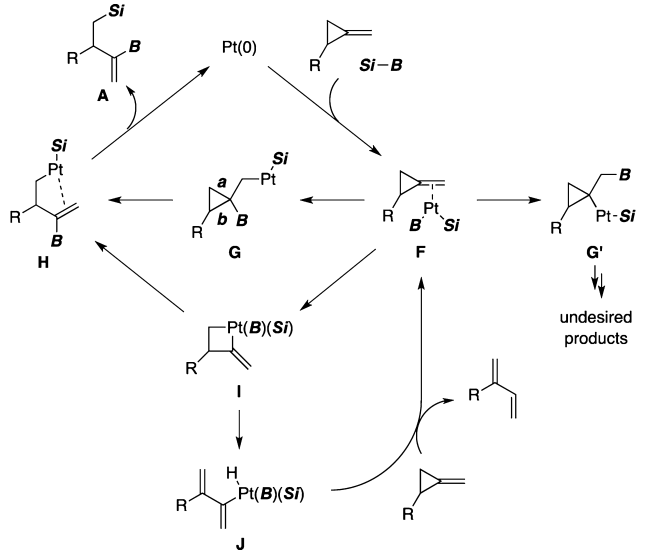
entry	MCP	temp (°C)	time (h)	yield (%)[b]
1	**1b** [R = $Ph(CH_2)_2$]	28	4	92 (**7b**)
2	**1c** (R = *n*-C_6H_{13})	28	4	84 (**7c**)
3	**1d** [R = *t*-$BuMe_2SiO(CH_2)_3$]	28	4	85 (**7d**)
4	**1e** [R = *t*-$BuMe_2SiO(CH_2)_2$]	28	4	88 (**7e**)
5[c]	**1f** (R = *t*-$BuMe_2SiOCH_2$)	50	16	74 (**7f**)
6	**1g** [R = $Cl(CH_2)_3$]	50	10	79 (**7g**)
7	**1h** [R = (phthaloyl)$N(CH_2)_2$]	50	5	81 (**7h**)
8	**1i** (R = Ph)	50	20	<10 (**7i**)

[a] $Pt_2(dba)_3$ (1.0 mol %), **6** (0.10 mmol), **1** (0.20 mmol), and toluene (0.1 mL) were stirred at 28 or 50 °C. [b] Isolated yield. [c] 3.0 equiv of **1f** was used.

Scheme 3. Reaction Profile



Scheme 4. Possible Mechanism



The mechanism involving **I** can be reasonably use to explain the experimental result that isomerization proceeded only in the presence of the silylboronic ester (Scheme 3). We also found that the isomerization of MCP to 1,3-diene took place to a similar extent regardless of the steric bulk of the silyl groups. Thus, we assume that the two ring-opening pathways (**F−G−H** and **F−I−H**) proceed in parallel, and the former pathway may also give **G′**, which does not afford the desired product.[16] The regioselectivity in the formation of **G** and **G′** may be controlled by the steric bulk of the silyl group,[17] and selective formation of **G** may be a reason for the high yield of **7** in the reaction of **6**.

In conclusion, we have established a site- and regioselective silaborative C−C cleavage of 1-alkyl-2-methylenecyclopropanes **1**. A phosphine-free platinum catalyst was effective for the selective silaborative cleavage of the less sterically hindered proximal C−C bond of the cyclopropane ring. Use of the new silaboration reagent *i*-$PrPh_2Si$−B(pin) (**6**) was critical for the production of 3-substituted 2-boryl-4-silyl-1-butenes in high yield.

■ ASSOCIATED CONTENT

Supporting Information

The following file is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b00513.

Experimental details and characterization data of the products (PDF)

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Notes

The authors declare no competing financial interest.

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(11) Typical procedure is given for the reaction of **1b** with **6** (entry 1). $Pt_2(dba)_3$ (1.1 mg, 1.0 mmol), **6** (35 mg, 0.10 mmol) and **1b** (32 mg, 0.20 mmol) were dissolved in 100 mL of toluene in a screw-capped vial and the mixture was stirred at 28 °C for 4 h. The reaction was monitored by GC. After removal of the volatile materials, the reaction mixture was purified by silica gel chromatography (hexane:Et_2O = 19:1) to give **7b** (47 mg, 92%).

(12) For transition-metal-catalyzed isomerization of MCPs to 1,3-dienes, see: (a) Osakada, K.; Takimoto, H.; Yamamoto, T. *Organometallics* **1998**, *17*, 4532−4534. (b) Nishihara, Y.; Yoda, C.; Osakada, K. *Organometallics* **2001**, *20*, 2124−2126. (c) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 270−275. (d) Itazaki, M.; Nishihara, Y.; Takimoto, H.; Yoda, M.; Osakada, K. *J. Mol. Catal. A: Chem.* **2005**, *241*, 65−71. (e) Shi, M.; Wang, B.-Y.; Huang, J.-W. *J. Org. Chem.* **2005**, *70*, 5606−5610. (f) Shao, L.-X.; Li, J.; Wang, B.-Y.; Shi, M. *Eur. J. Org. Chem.* **2010**, 6448−6453. See also refs 5b and 5g.

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(14) For insertion of C−C triple bond into the Pt−B bond, see ref 13a.

(15) The pathway involving oxidative addition of the proximal C−C bond of MCP has been proposed in refs 2g, 8a, and 12a.

(16) One of the possible undesired pathways via **G′** is the pathway involving cleavage of the distal C−C bond to form π-allylplatinum. See refs 4d, 4e, and 12c.

(17) The steric effect of the silyl group on isomer selectivity has been discussed in the study on silaboration of 1-alkene. Suginome, M.; Nakamura, H.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2516−2518.

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