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Bu_2SnIH-Promoted Proximal Bond Cleavage of Methylenecyclopropanes and Successive Radical Cyclization and/or Pd-Catalyzed Coupling Reaction

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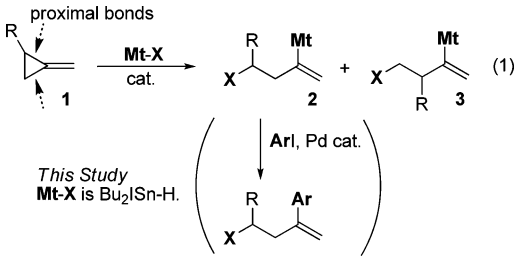
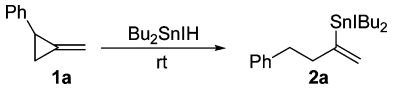
Methylenecyclopropanes (MCPs, **1**) are useful building blocks in organic synthesis due to their high level of reactivity derived from ring-strain, and easy availablity.[1] MCPs can be transformed into various organometallic species depend on the reaction positions by metal reagents (such as Sn-H,[2a] Si-H,[2b−d] B-B,[2e] Si-B[2f,g]).[2,3] Although some reports have attributed the cleavage of proximal bonds, almost the reported examples are limited to the cleavage of less-substituted bond to give a vinylic metal **3** (eq 1).[2] From this point of view, the selective cleavage at the hindered proximal bond is significant to generate alternate vinylic metals **2**. Preparation of a wide range of vinylic metals is strongly required as a valuable coupling partner in the formation of a π-conjugated system. We report here on the selective formation of vinyltins **2** from MCPs **1** by using di-*n*-butyliodotin hydride (Bu_2SnIH).[4] Furthermore, applications to intramolecular cyclization and one-pot Pd-catalyzed coupling between the resulting vinyltins and aryl iodide are presented.



Initially, reaction conditions were optimized by using the reaction of 1-methylene-2-phenylcyclopropane (**1a**) and Bu_2SnIH prepared in situ from the redistribution of Bu_2SnI_2 and Bu_2SnH_2 (Table 1).[5] The reaction proceeded well at room temperature in several solvents, including hexane, acetonitrile and THF, to produce an α-substituted vinyltin **2a** in moderate yields (entries 1−3). It should be noted that no regioisomers were generated in all runs. Selective cleavage at the substituted proximal bond in MCPs with metallic species has scarcely been reported, in particular, the reaction of MCPs **1** having terminally unsubstituted alkene is unprecedented.[6] This reaction was completely suppressed by the addition of a small amount of a radical inhibitor, galvinoxyl (entry 4). In contrast, the addition of a radical initiator Et_3B increased the yield up to 81% (entry 5). These facts indicate that a radical step is included in the reaction. Consequently, the addition of Et_3B at room temperature in THF solvent was employed as optimized conditions.

Next, the generality of MCPs **1** was investigated. The resulting reaction mixture including vinyltins **2** was directly treated with aryl iodide in the presence of a Pd catalyst, because the isolation treatment caused the loss of **2** (Table 2).[7] The high yield (92%) of **4a** strongly indicated a quantitative formation of **2a** and successive

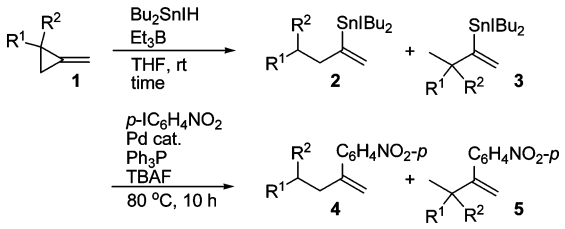
Table 1. Hydrostannation of Methylenecyclopropane **1a** by Bu_2SnIH[a]



entry	solvent	time (h)	yield of **2a** (%)
1	hexane	20	45
2	MeCN	20	33
3	THF	20	53
4[b]	THF	20	2
5[c]	THF	14	81

[a] **1a** (1.0 mmol), Bu_2SnIH (1.0 mmol), solvent (1 mL). [b] Galvinoxyl (0.1 mmol) was added. **1a** was recovered in 88%. [c] Et_3B (0.1 mmol) was added.

Table 2. Regioselective Hydrostannation of MCPs **1** and Successive Coupling with Aromatic Iodide[a]



	MCPs **1**				yield (%)			
entry		R^1	R^2	time (h)	**4**		**5**	
1	**1a**	Ph	H	14	**4a**	92	**5a**	0
2	**1b**	*n*-C_8H_{17}	H	10	**4b**	77	**5b**	13
3	**1c**	CH_2OBn	H	10	**4c**	66	**5c**	20
4	**1d**	Ph	Ph	138	**4d**	75	**5d**	0
5	**1e**	-$(CH_2)_5$-		16	**4e**	98	**5e**	0

[a] MCPs (1.0 mmol), Bu_2SnIH (1.0 mmol), THF (1 mL), Et_3B (0.1 mmol), *p*-$IC_6H_4NO_2$ (1.0 mmol), $Pd_2(dba)_3$-$CHCl_3$ (0.015 mmol), Ph_3P (0.08 mmol), 1 M TBAF solution in THF (3 mL).

Pd-catalyzed effective coupling with 4-iodonitrobenzene in the one-pot treatment (entry 1). Alkyl-substituted substrates, **1b** and **1c**, also gave the desired products, **4b** and **4c**, in moderate yields, but in which respective isomers **5b** and **5c** were produced (entries 2 and 3). The *gem*-disubstituted MCPs, **1d** and **1e**, effected the formation of vinyltins **4d** and **4e**, respectively, in high yields (entries 4 and 5). In the case of *vic*-disubstituted and trisubstituted MCPs **1f** and **1g**, disubstituted alkenes **4f** and **4g** were obtained with unidentified byproducts, however, in which no regioisomer **5** was observed (eqs 2 and 3). The lower yield of **4g** might depend on the steric demanding of highly substituted **1g**.

The reaction course is supposed as follows (Scheme 1). The dibutyliodotin radical ($Bu_2ISn^{\bullet}$) adds to the central carbon of MCPs **1** to give cyclopropylmethyl radical **A**, which is followed by the selective proximal bond cleavage at a hindered site. It is well-known that the rate of ring-opening of the cyclopropylmethyl radical is very fast ($>10^8\ s^{-1}$).[8] Hence, as the stability of the resulting carbon radical determined the regioselectivity of the ring-opening, phenyl

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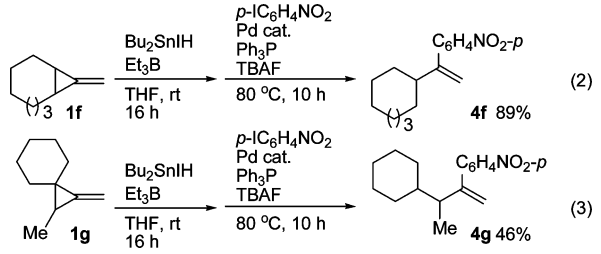
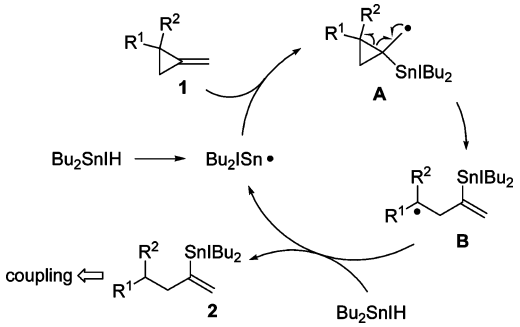
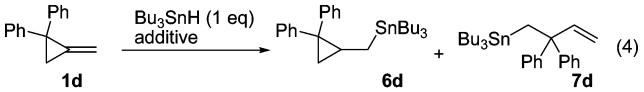


or dialkyl substituents gave high selectivity because of the generation of stable benzyl or tertiary alkyl radicals **B**. In the case of mono alkyl-substituted MCPs **1b** and **1c**, the mixtures of regioisomeric products were obtained due to the small difference in the stability between primary and secondary radicals (see Table 2, entries 2 and 3). Finally, homoallyl radical **B** was hydrogenated by Bu_2SnIH to give vinyltin **2** with regeneration of a tin radical.

Scheme 1. Plausible Mechanism



This highly selective metalation to the central carbon is a characteristic feature of Bu_2SnIH. In contrast, when MCP **1d** was treated with Bu_3SnH in the presence of Et_3B, cyclopropylmethyltin **6d** was obtained in 85% yield without ring-opening products such as **2** or **3**, in which the addition to terminal olefin carbon is exclusive.[9] In addition, $Pd(Ph_3P)_4$-catalyzed hydrostannation produced only homoallyltin **7d** in 79% yield,[2a] and the reaction promoted by Lewis acid such as $AlCl_3$ or $B(C_6F_5)_3$ resulted in a complicated mixture.[10] Although a credible reason why the tin radical $Bu_2ISn^•$ selectively adds to the internal carbon of MCPs **1** is not clear yet and the mechanism is only tentative, a interaction between the π-bond and/or σ-bond of MCPs and the tin center of Bu_2SnIH, whose Lewis acidity is increased by an iodine substituent, might affect this regioselectivity.

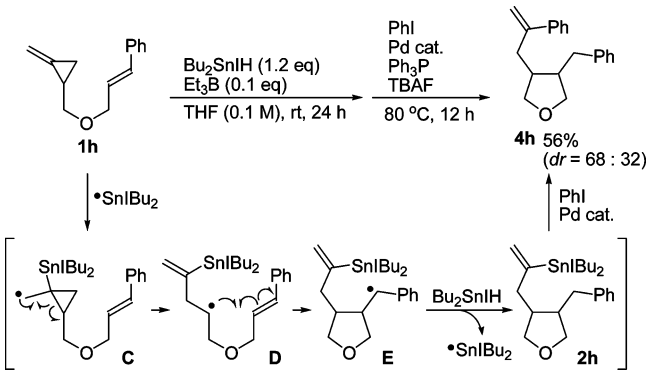


in hexane, Et_3B (0.1 eq), rt, 30 h	85%	0%
in THF, $Pd(Ph_3P)_4$ (0.04 eq), 65 °C, 10 h	trace	79%
in THF, $AlCl_3$ or $B(C_6F_5)_3$ (0.1 eq), rt, 10 h	complicated mixture	

In the next stage, we applied this radical cleavage to a transformation from the MCP **1h** bearing allylic ether moiety into cyclized vinyltin **2h** (Scheme 2).[11] After the reaction at room temperature for 20 h, a subsequent coupling reaction with iodobenzene was performed to produce cyclic ether **4h** in moderate yield. In this reaction the generated cyclopropylmethyl radical **C** quickly isomerizes to radical **D**, which cyclizes to intermediate **E**. The following hydrogenation and coupling gave the desired product **4h**.

In conclusion, the hydrostannation of MCPs using Bu_2SnIH to produce α-substituted vinyltins was presented, which showed unprecedented regioselectivity. The generated vinyltins could be

Scheme 2. Radical Cyclization



applied to a one-pot coupling reaction without isolation or change of solvent. Moreover, a radical cyclization initiated from the reduction of MCPs was accomplished. Mechanistic consideration and reactivity of more substituted MCPs are under investigation.

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Supporting Information Available: Experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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