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Selective Intermolecular [2 + 2] Cycloaddition Reaction Using Platinum(II) Catalyst with Hollow-shaped Triethynylphosphine

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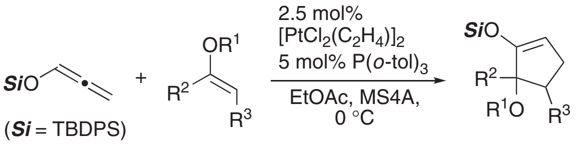
Intermolecular [2 + 2] cycloaddition reaction of an allenyl silyl ether with vinyl ethers was realized on the basis of electrophilic activation of the allene by the platinum–phosphine catalyst, affording the corresponding methylenecyclobutanes in good yield. The use of the bulky trialkynylphosphine as a ligand was indispensable to achieve highly selective [2 + 2] cycloaddition.

Use of allenes as a component of [2 + 2] cycloaddition reactions has been extensively studied, such as photochemical or thermal reactions with alkenes and alkynes, Lewis acid-promoted reactions of electron-rich allenes with electron-deficient alkenes, etc.[1] In these reactions, combination of substrates is restricted depending on the kind of the reaction. For example, standard photochemical reactions usually employ the combination of simple allenes and cyclic enones,[1,2] and most of the thermal reactions are restricted to intramolecular reaction.[1,3] More recently, transition-metal-catalyzed [2 + 2] cycloaddition reactions of allenes have become a topic of interest of many research groups, and several novel reactions have been reported.[1] These reactions are mostly carried out with simple allenes, and use of electron-rich substrates is still rare in spite of its utility for the preparation of highly functionalized cyclobutane derivatives.[1,4] Quite recently, another combination of substrates, that is, the combination of electron-rich allenes and electron-rich alkenes,[5] has attracted attention with the rapidly expanding chemistry of the electrophilic activation of carbon–carbon multiple bonds.[1a,6]

We previously reported the first example of the transition-metal-catalyzed intermolecular [3 + 2] cycloaddition reaction of an allenyl silyl ether with vinyl ethers utilizing electrophilic activation of the allenyl ether by a platinum(II) catalyst.[7] The reaction showed wide generality and afforded synthetically useful oxygenated cyclopentene derivatives in high yield (eq 1).

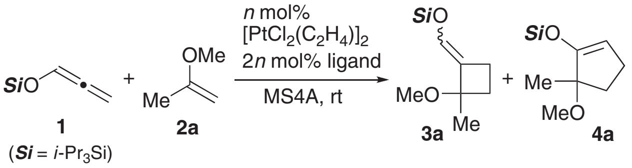


(1)

In the present study, we focused our attention on the development of platinum(II)-catalyzed intermolecular [2 + 2] cycloaddition reaction of electron-rich allenes and electron-rich alkenes. It should be noted that there are several precedents for the intramolecular [2 + 2] cycloaddition of the same concept using gold(I) catalysts,[5a,8] and quite recently, the first example of the intermolecular [2 + 2] cycloaddition was reported by Chen et al.,[9] however, the combination of substrates is still limited and expansion of this reaction is highly desirable in view of the high synthetic utility of the reaction for the preparation of functionalized cyclobutane derivatives.

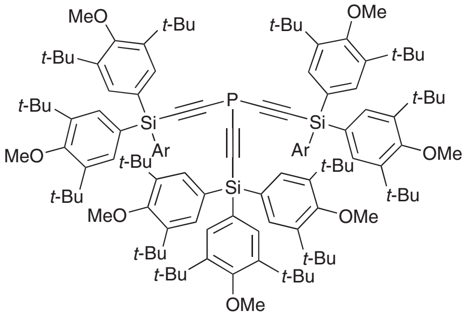
In the previous study, it was found that use of triisopropylsilyl allenyl ether (**1**) instead of *tert*-butyldiphenylsilyl (TBDPS) allenyl ether favored the formation of a methylenecyclobutane derivative, although the selectivity was not high. Thus, when 2.5 mol % of $[PtCl_2(C_2H_4)]_2$ was added to a mixture of the allenyl ether **1** and 2-methoxypropene (**2a**) in CH_2Cl_2 at room temperature, the reaction proceeded smoothly to give a mixture of methylenecyclobutane **3a** and cyclopentene **4a** in the combined yield of 73% in a ratio of 56:44. Then we first examined the effect of phosphine ligand on this reaction to realize the selective [2 + 2] cycloaddition reaction. The reaction was examined as follows. To a CH_2Cl_2 solution of **1** and **2a** was added a CH_2Cl_2 solution of 2.5 mol % of $[PtCl_2(C_2H_4)]_2$ (5 mol % based on Pt) and 5 mol % of a phosphine or phosphite ligand at room temperature. After appropriate reaction time, the reaction was quenched with *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), and the results are summarized in Table 1. As shown here, most of the standard ligands gave the products in moderate selectivity (Entries 2–5). But when the reaction was carried out in the presence of Sawamura's phosphine **5** (bulky trialkynylphosphine) (Figure 1),[10] the selectivity was improved in favor of the formation of the cyclobutane derivative **3a** without lowering the yield (66% yield, **3a**:**4a** = 83:17)

Table 1. Screening of reaction conditions



Entry	*n*	Ligand	Solvent	Time /h	Yield /%[a]	Ratio **3a**:**4a**
1	2.5	—	CH_2Cl_2	3	73	56:44
2		PPh_3		0.5	79	62:38
3		P(*o*-tol)$_3$		1	80	43:57
4		P(2-furyl)$_3$		1	72	64:36
5		$P(OEt)_3$		2	72	59:41
6		$P(CCSiMe_3)_3$		0.5	89	64:36
7		**5**		0.25	66	83:17
8			toluene	0.25	89	91:9
9			hexane	0.25	85	95:5
10			EtOAc	0.25	74	74:26
11			toluene/hexane[b]	0.25	86	93:7
12	0.5		toluene/hexane[c]	0.5	90	95:5
13	0.05		toluene/hexane[d]	3	95[e]	95:5

[a]Yield and ratio of the products were determined by ^1H NMR analyses using 1,1,2,2-tetrachloroethane as an internal standard. [b]Toluene:hexane = 1:2. [c]Toluene:hexane = 1:14. [d]Toluene:hexane = 1:149. [e]Isolated yield.



5 (Ar = 3,5-(t-Bu)$_2$-4-MeO-C$_6$H$_2$-)

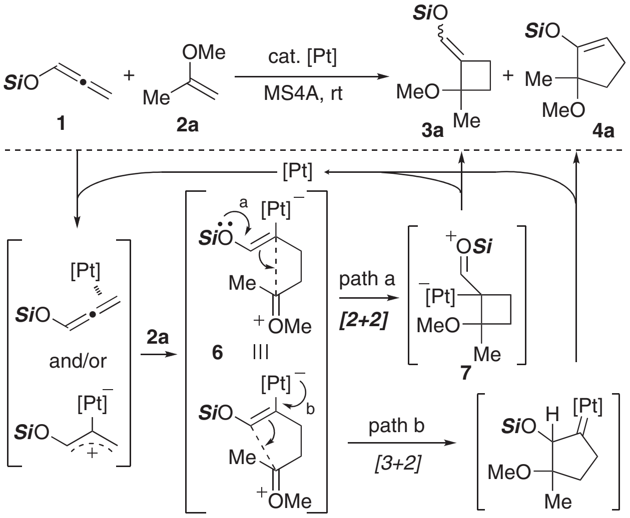
Figure 1. Structure of the Sawamura's phosphine **5**.

(Entry 7). As the use of tris(trimethylsilylethynyl)phosphine gave nearly the same ratio as the reaction using other typical ligands (Entry 6), the bulkiness of the ligand should play an important role in the selective preparation of the cyclobutane derivative **3a**.

Further examination of the reaction solvent revealed that use of less polar solvent favored the formation of the cyclobutane derivative. Thus when the reaction was carried out in toluene, the reaction completed within 15 min at room temperature and the selectivity of the reaction was improved to 91:9 in the combined yield of 89% (Entry 8). Use of hexane as solvent further improved the selectivity up to 95:5 (Entry 9), but the reproducibility of the product yield is not very good probably due to the low solubility of the platinum catalyst. In order to solve this problem, a small amount of toluene was employed as a solvent to prepare the platinum–phosphine complex, which was added to a hexane solution of the two reactants. By this protocol high yield was achieved with good reproducibility without lowering the selectivity (Entry 11). Furthermore, the catalyst loading could be reduced even to 0.05 mol % (0.1 mol % based on Pt) without lowering the yield of the products (Entry 13).

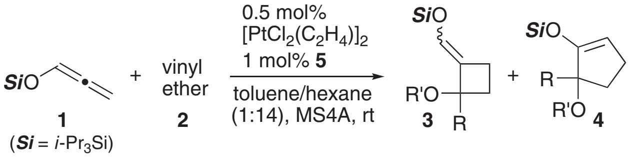
The reaction was thought to proceed in a similar manner as in the previous [3 + 2] cycloaddition reaction (Scheme 1). Thus, zwitterionic intermediate **6** was generated by the attack of 2-methoxypropene on the platinum-activated allenyl ether and then the silyl enol ether attacked the oxonium carbon to give the cyclobutylplatinum intermediate **7** (path a), which finally gave the product **3** with regeneration of the platinum catalyst. The Sawamura's bulky tris(triarylsilylethynyl)phosphine **5** would make the conformation of the zwitterionic intermediate **6** favorable for the cyclobutane formation.

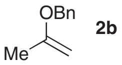
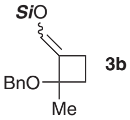
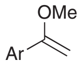
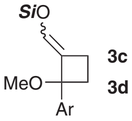
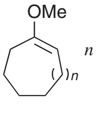
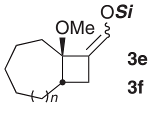
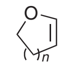
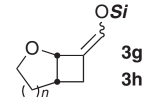
The generality of the reaction concerning the vinyl ethers is summarized in Table 2.[11] Several 1,1-disubstituted alkenyl ethers **2b**–**2d** reacted to give the cyclobutane derivatives **3b**–**3d** in good yield with high selectivity (Entries 1–3). Cyclic alkenyl ethers **2e** and **2f** could also be employed without problem to give bicyclic cyclobutanes **3e** and **3f** in good yield (Entries 4 and 5). Dihydrofuran **2g** and dihydropyran **2h** also reacted to give the products **3g** and **3h** in highly selective manner (Entries 6 and 7).



Scheme 1. Proposed reaction mechanisms.

Table 2. Generality of the intermolecular [2 + 2] cycloaddition reaction



Entry	Vinyl ether[a]	Major product	Yield/%[b]	Ratio (**3**:**4**)[c]
1			86	>97:<3
2	 Ar = p-BrC$_6$H$_4$ **2c**	 **3c**	94	96:4
3[d]	p-NO$_2$C$_6$H$_4$ **2d**	**3d**	77	>97:<3
4	 n = 1 **2e**	 **3e**	98	94:6
5	2 **2f**	**3f**	99	>97:<3
6	 n = 1 **2g**	 **3g**	76	>97:<3
7	2 **2h**	**3h**	69	>97:<3

[a] 1.1–5 equiv. [b] Combined yield of **3** and **4**. [c] The ratio was determined by ^{1}H NMR analysis. [d] Toluene:hexane = 1:6.5.

In conclusion, we have developed the platinum-catalyzed intermolecular [2 + 2] cycloaddition reaction of triisopropylsilyl allenyl ether and vinyl ethers. This reaction affords a concise method for the preparation of functionalized methylenecyclobutane derivatives in high yields. Combined with our previous report,[7] either of the [2 + 2] or [3 + 2] cycloaddition products could be selectively prepared mainly by choosing the appropriate phosphine ligand.[12]

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11 In all the cases, the [2 + 2] cycloadducts **3** were mainly obtained as *E*-isomer concerning the geometry of the silyl enol ether moiety (E:Z = between 72:28 and >97:<3). See Supporting Information for details.[12]

12 Supporting Information is also available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.