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A convenient method for the synthesis of 4,4-diarylbut-1-enes via the successive allylation of aromatic aldehydes and the Friedel–Crafts alkylation reaction of aromatic nucleophiles with the intermediary benzyl silyl ethers using $HfCl_4$ or $Cl_2Si(OTf)_2$

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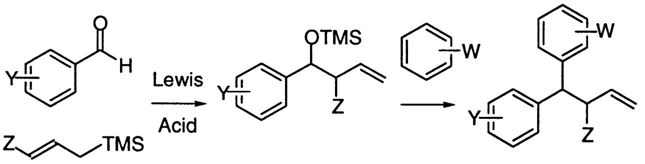
Abstract—The three-component coupling reaction among aromatic aldehydes, allyltrimethylsilane and aromatic nucleophiles is efficiently performed by the promotion of $HfCl_4$. A similar reaction occurs using allyltributyltin as the first nucleophile to aromatic aldehydes with a catalytic amount of $Cl_2Si(OTf)_2$ generated in situ from $SiCl_4$ and AgOTf. © 2002 Elsevier Science Ltd. All rights reserved.

In the preceding communication,[1] the Friedel–Crafts alkylation of aromatic compounds with benzyl or allyl silyl ethers as versatile electrophiles to produce various diarylmethanes was reported. As an application of the novel reaction for the convenient synthesis of more complex molecules, we planned to use homoallyl silyl ethers **A** having a benzyl silyl ether moiety because **A** are easily generated by the addition of allyltrimethylsilanes to aromatic aldehydes (Scheme 1).[2] Since both the allylation forming **A** and successive Friedel–Crafts alkylation of aromatic nucleophiles with **A** could be promoted under acidic conditions,[1] a one-pot synthetic method for the preparation of a variety of 4,4-diarylbut-1-enes **B** might be established by the successive allylation and Friedel–Crafts alkylation reaction. We would now like to report a new sequential reaction that forms various substituted butenes **B** via the three-component coupling reaction among aromatic aldehydes, allylmetal reagents and aromatic compounds.

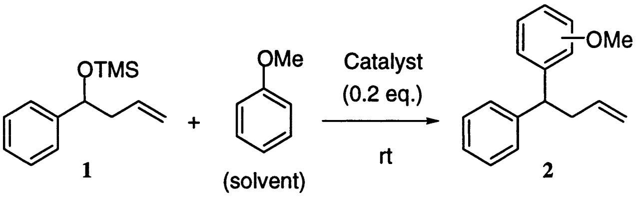


A **B**

Scheme 1. Three-component coupling among aromatic aldehydes, allyltrimethylsilanes and aromatic nucleophiles.

First, the isolated trimethylsilyl ether **1** was chosen as a model substrate to examine the Friedel–Crafts alkylation (Table 1). Similar to results in the preceding communication, the reaction of anisole with **1** smoothly proceeded to give the desired disubstituted butenes **2** in high yields when $Cl_2Si(OTf)_2$ or $Hf(OTf)_4$ was used as the catalyst. The reaction of anisole with **1** or the corresponding free alcohol (1-phenylbut-3-en-1-ol) in the presence of $Sc(OTf)_3$ afforded the coupling products in moderate or low yields (50 or 23%).

Table 1. Isolated yields of 4-methoxyphenyl-4-phenylbut-1-enes



1 **2**

Entry	Catalyst	Time (h)	Yield (%)	(*o*-/*p*-)[a]
1	$Cl_2Si(OTf)_2$	1	93	20/80
2	$Hf(OTf)_4$	1	Quant.	19/81
3	$Sc(OTf)_3$	12	50	20/80

[a] Determined by ^1H NMR.

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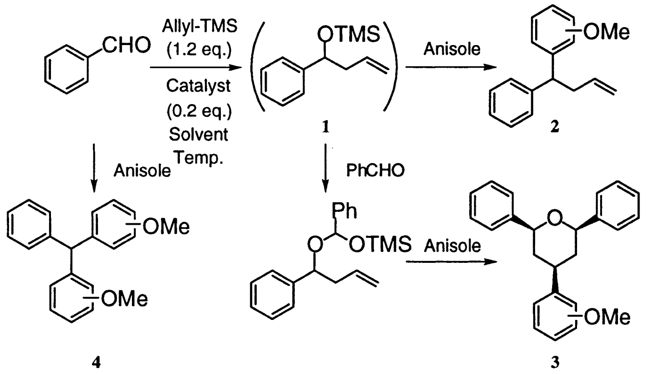
Next, we tried to develop the three-component coupling reaction using aromatic aldehydes, allyltrimethylsilanes and aromatic nucleophiles in order to directly produce **2** by the one-pot operation; that is, after generation of the benzyl silyl ether **1** in situ from benzaldehyde (1.0 equiv.) and allyltrimethylsilane (1.2 equiv.) using a catalytic amount of $Cl_2Si(OTf)_2$ (20 mol%) in CH_2Cl_2, anisole (5 equiv.) was added to the reaction mixture. However, a regioisomeric mixture of the corresponding cyclic ethers **3** was mainly obtained by the sequential coupling of **1** with benzaldehyde followed by cyclization and alkylation with anisole (Table 2, entry 1).[3] The reactions using $Hf(OTf)_4$ and $Sc(OTf)_3$ gave complex mixtures of several by-products, and TMSOTf did not promote the desired successive reactions. Furthermore, anisole was used as a solvent for the first step in order to prevent the side reaction of **1** with an excess amount of benzaldehyde; nevertheless, the selectivities were not improved and undesirable results occurred as shown by entries 2–5.

It was postulated that a Lewis acid, which has a weaker acidity, is more suitable for the above synthesis since metal triflates have a sufficient activity to promote the undesired reaction of **1** with benzaldehyde. Based on this hypothesis, various metal chlorides were reexamined for the one-pot reaction, and it was found that the stoichiometric use of $HfCl_4$ is the most effective for the selective formation of **2** (Table 3). It is quite remarkable that the side reaction of the produced intermediate, the benzyl silyl ether **1**, with the benzaldehyde to produce **3** does not take place at all when $HfCl_4$ is used as the catalyst in the above sequential reactions (entries 6–8).

Table 4 shows examples of the three-component coupling reaction forming several disubstituted butenes. 4-Tolualdehyde and 4-halogenated benzaldehydes were successfully employed for the generation of benzyl silyl ethers, and the sequential addition of anisole to the intermediates afforded the desired compounds in high yields (entries 2–6). Although 4-anisaldehyde has a low reactivity for the reaction with allyltrimethylsilane and the total yield is not satisfactory (entry 7), the desired 4,4-diarylbut-1-enes were obtained in good yields using 4-pivaloxybenzaldehyde as an electrophile for the reaction (entry 8). Furthermore, when toluene was used as the solvent in the above reaction, a mixture of the desired disubstituted butenes was produced in moderate yield by a one-pot operation with benzaldehyde, allyltrimethylsilane and $HfCl_4$ (entry 10).

A typical experimental procedure is described for the reaction of benzaldehyde with allyltrimethylsilane in anisole: to a suspension of hafnium tetrachloride (80.1 mg, 0.250 mmol) in anisole (3.8 mL) at 0°C were successively added a mixture of allyltrimethylsilane (34.2 mg, 0.300 mmol) and benzaldehyde (26.5 mg, 0.250 mmol) in anisole (1.2 mL). The reaction mixture was stirred for 45 min at room temperature and then saturated aqueous sodium hydrogencarbonate was added. The mixture was extracted with diethyl ether, and the organic layer was washed with brine, dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography to afford a mixture of 4-methoxyphenyl-4-phenybut-1-enes (58.7 mg, 99%, (*o*-)/(*p*-) = 16/84) as a colorless oil.

Table 2. Isolated yields of 4-methoxyphenyl-4-phenylbut-1-enes and 2,6-diphenyl-4-methoxyphenyl(2*H*-3,4,5,6-tetrahydropyrans)

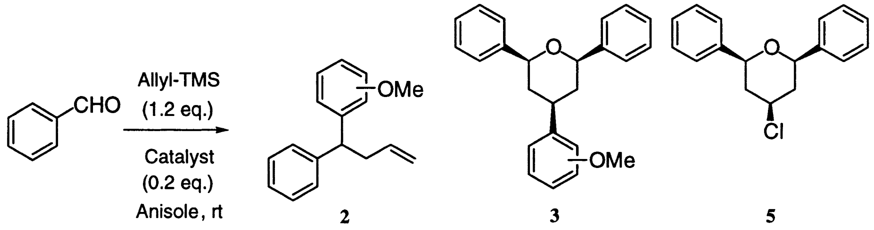


Entry	Catalyst	Solvent	Temp. (°C)	Yield	
				2 (*o*-/*p*-)[b]	**3** (*o*-/*p*-)[b]
1	$Cl_2Si(OTf)_2$	CH_2Cl_2	0	25 (19/81)	25 (38/62)
2	$Cl_2Si(OTf)_2$	Anisole	rt	0	41 (38/62)
3	$Hf(OTf)_4$	Anisole	rt	5 (20/80)	38 (40/60)
4	$Sc(OTf)_3$	Anisole	rt	6 (19/81)	30 (38/62)
5[a]	TMSOTf	Anisole	rt	0	0

[a] A mixture of triarylmethanes **4** was obtained in 20% yield.

[b] The ratio was determined by ^1H NMR.

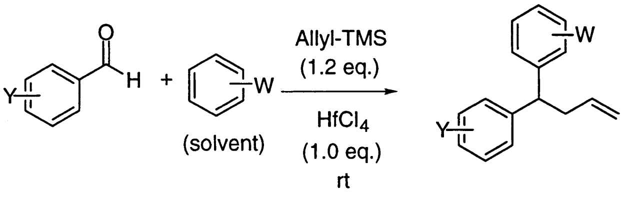
Table 3. Isolated yields of 4-methoxyphenyl-4-phenylbut-1-enes, 2,6-diphenyl-4-methoxyphenyl(2*H*-3,4,5,6-tetrahydropyrans) and 4-chloro-2,6-diphenyl(2*H*-3,4,5,6-tetrahydropyran)



Entry	Catalyst (amount)	Conc. (M)	Yield (%)		
			2 (*o*-/*p*-)[a]	**3** (*o*-/*p*-)[a]	**5**
1	$AlCl_3$ (0.2)	0.1	0	24 (39/61)	2
2	$GaCl_3$ (0.2)	0.1	26 (20/80)	14 (40/60)	3
3	$SiCl_4$ (0.2)	0.1	6 (20/80)	1 (ND)	2
4	$SnCl_4$ (0.2)	0.1	2 (19/81)	9 (40/60)	3
5	$TiCl_4$ (0.2)	0.1	3 (20/80)	10 (41/59)	10
6	$HfCl_4$ (0.2)	0.1	53 (15/85)	0	0
7	$HfCl_4$ (1.0)	0.1	87 (16/84)	0	0
8	$HfCl_4$ (1.0)	0.05	99 (14/86)	0	0

[a] The ratio was determined by ^1H NMR.

Table 4. Isolated yields of several 4,4-diarylbut-1-enes



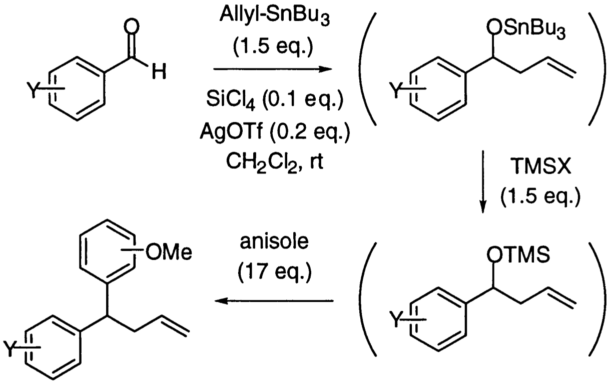
Entry	Y	W	Yield (%)	(*o*-W)/(*p*-W)[a]
1	H	MeO	99	16/84
2	4-Me	MeO	79	9/91
3	4-F	MeO	80	14/86
4	4-Cl	MeO	87	15/85
5	4-Br	MeO	86	13/87
6	4-I	MeO	81	10/90
7	4-OMe	MeO	31	0/100
8	4-OPiv	MeO	86	8/92
9	3-OPiv	MeO	88	22/78
10	H	Me	51	15/85

[a] Determined by ^1H NMR.

Next, allyltributyltin[2] was used as the nucleophile instead of allyltrimethylsilane for the three-component coupling reaction with benzaldehyde and anisole. After screening several catalysts, it was proved that $HfCl_4$ (1 equiv.) does not have enough activity for the promotion of the allylation of benzaldehyde with allyltributyltin and the desired 4,4-diarylbut-1-enes **2** and the undesired triarylmethanes **4** were produced in 30 and 62% yields, respectively. On the other hand, it was found that the allylation was efficiently promoted using the combined catalyst generated in situ from 10 mol% $SiCl_4$ and 20 mol% AgOTf, and the successive treatment of the formed tin alkoxide with TMSCl and anisole gave the desired **2** in 90% yield (see Table 5, entry 1). In this protocol, the intermediate, a tin alkoxide, is too stable for the second electrophilic substitution with anisole. Therefore, transmetallation of tin to silicon was performed by adding TMSCl, and the instantly generated trimethylsilyl ether **1** might work as a reactive electrophile to anisole for producing the desired three-component coupling products. According to this one-pot but stepwise method, it is not necessary to use the second nucleophile as a solvent for the first allylation reaction. Furthermore, this protocol prevents forming several by-products in principle since aromatic aldehydes do not contact the anisole or benzyl silyl ether **1** if the allylation completely proceeds. Other examples are listed in Table 5. Similar results were obtained to that of the three-component coupling reaction of aromatic aldehydes, allyltrimethylsilane and anisole using a stoichiometric amount of $HfCl_4$. It is noteworthy that a catalytic amount of the Lewis acid is required in this alternative strategy employing allyltributyltin and silylation reagents.

A typical experimental procedure is described for the reaction of benzaldehyde with allyltributyltin and anisole: to a suspension of silver trifluoromethanesulfonate (25.7 mg, 0.100 mmol) in dichloromethane (1.85 mL) at room temperature was added silicon tetrachloride (8.5 mg, 0.050 mmol) in dichloromethane (0.15 mL). After the reaction mixture had been stirred for 1 h, a mixture of allyltributyltin (248.3 mg, 0.750 mmol) in dichloromethane (1.0 mL) and benzaldehyde (53.1 mg, 0.500 mmol) in dichloromethane (1.0 mL) were successively added. The reaction mixture was stirred for 1 min and then a solution of chlorotrimethylsilane (81.5 mg, 0.750 mmol) in dichloromethane (1.0 mL) was added. After the reaction mixture had been stirred for 10 min, anisole (1.0 mL, 8.6 mmol) was added. The reaction mixture was stirred for 2 h and then saturated

Table 5. Isolated yields of several 4,4-diarylbut-1-enes



Entry	Y	X	Yield (%)	(o-MeO)/(p-MeO)[a]
1	H	Cl	90	15/85
2	4-Me	Cl	68	9/91
3	4-Cl	OTf	80	14/86
4	4-Br	OTf	86	13/87
5	4-I	OTf	87	9/91
6	3-OPiv	OTf	63	23/77

[a] Determined by ^{1}H NMR.

aqueous sodium hydrogencarbonate was added. The mixture was extracted with dichloromethane, and the organic layer was washed with brine, dried over sodium sulfate. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin layer chromatography to afford a mixture of 4-methoxyphenyl-4-phenybut-1-enes (107.3 mg, 90%, (o-)/(p-) = 15/85) as a colorless oil.

Thus, we developed a new method for the one-pot synthesis of 4,4-diarylbut-1-enes via the successive allylation of aromatic aldehydes and the Friedel–Crafts alkylation reaction of aromatic nucleophiles with the intermediary benzyl silyl ethers using $HfCl_4$ or $Cl_2Si(OTf)_2$. Other applications of the present protocol and syntheses of useful derivatives from 4,4-diarylbut-1-enes are now in progress.

Acknowledgements

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