

Synthetic Methods

Gallium Tribromide Catalyzed Coupling Reaction of Alkenyl Ethers with Ketene Silyl Acetals**

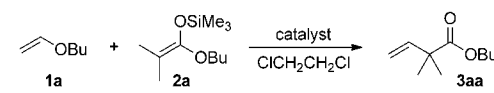
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The coupling reaction of alkenyl electrophiles with organometallics has been strenuously developed because it is a powerful tool for the construction of π -conjugated carbon frameworks, which are very valuable as functional materials.^[1] In general, alkenyl halides and pseudohalides are used as electrophilic coupling partners in the presence of a transition-metal catalyst. The use of these electrophiles, however, has some drawbacks in terms of high cost, storage instability, and the production of metal halide wastes. To overcome these drawbacks, significant effort has gone into replacing alkenyl halides with alkenyl alcohol derivatives such as alkenyl ethers,^[2] acetates,^[3] carbonates,^[4] carbamates,^[5] phosphates,^[6] and silyl enol ethers.^[7] Therefore, some success using alkyl- and arylmetals have been reported. However, to the best of our knowledge, the cross-coupling between alkenyl alcohol derivatives and metal enolates has never before been achieved^[8] in spite of the vital importance of α -alkenyl carbonyls.^[9]

Recently, we developed carbometalations of alkenes and alkynes using ketene silyl acetals and metal halides such as InBr_3 ,^[10] GaBr_3 ,^[11] and BiBr_3 ^[12] to conveniently produce the corresponding organometallics, wherein the independent *anti* addition of metal species and nucleophiles took place without the preliminarily generation of an organometallic intermediate. Herein, we wish to extend this carbometalation to a new type of catalytic coupling between alkenyl ethers and ketene silyl acetals.

At first, we focused on the carbometalation of butyl vinyl ether (**1a**) using dimethylketene butyl trimethylsilyl acetal (**2a**) and an equimolar amount of InBr_3 (Table 1, entry 1), in which the effective interaction between the double bond of **1a** and InBr_3 was expected because the electron density of **1a** is higher than that of the alkenes employed in our reported system.^[10b] Although a vigorous reaction took place, even at low temperature as expected, the coupling product **3aa** was obtained quantitatively instead of the expected alkyldium

Table 1: Effect of catalysts in coupling of alkenyl ether with ketene silyl acetal.^[a]

			
Entry	Catalyst (equiv)	T [°C]	Yield [%] ^[b]
1	InBr_3 (1)	−20	quant
2	InBr_3 (0.1)	80	86
3	GaBr_3 (0.1)	80	95
4	GaBr_3 (0.1)	RT	19
5	BiBr_3 (0.1)	80	6
6	—	80	0
7	$\text{BF}_3 \cdot \text{OEt}_2$ (0.1)	80	4
8	AlCl_3 (0.1)	80	0
9	TiCl_4 (0.1)	80	trace

[a] **1a** (1 mmol), **2a** (1.5 mmol), $\text{ClCH}_2\text{CH}_2\text{Cl}$ (2 mL), 2 h. [b] Determined by ^1H NMR spectroscopy.

derivative. This result indicated that **1a** acted as a vinylation reagent through the removal of the butoxy group. Gratifyingly, the coupling reaction was promoted at 80°C by a catalytic amount of InBr_3 (10 mol%) to give the product **3aa** in 86% yield (Table 1, entry 2). GaBr_3 was found to be more effective, thus affording **3aa** in 95% yield (Table 1, entry 3),^[11] and these conditions were determined to be optimal. In contrast, BiBr_3 showed quite a low catalytic effect (Table 1, entry 5) although it reportedly promoted the effective carbometalation of alkynes.^[12] No coupling, of course, took place without a catalyst (Table 1, entry 6), and representative Lewis acids such as $\text{BF}_3 \cdot \text{OEt}_2$, AlCl_3 , and TiCl_4 were not effective (Table 1, entries 7–9).

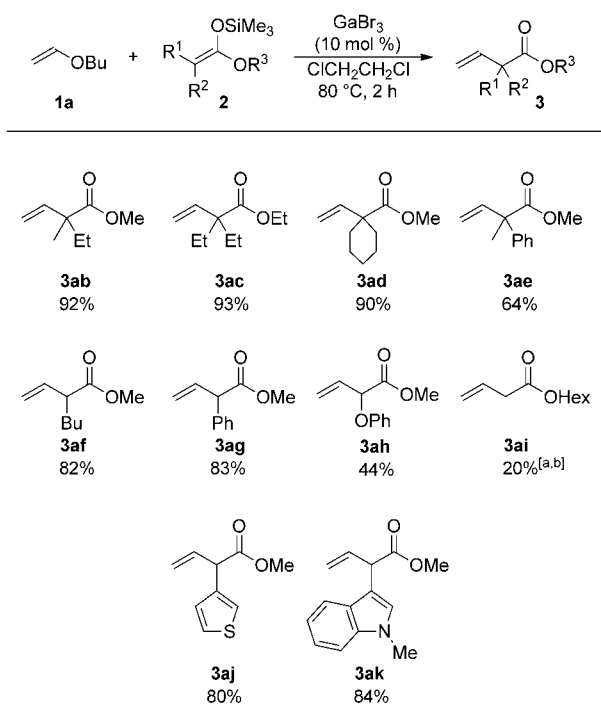
With the optimum reaction conditions in hand, the scope of with respect to the ketene silyl acetals **2** was investigated as shown in Scheme 1. Dialkylketene silyl acetals gave the corresponding α -vinyl esters in high yields (**3ab**, **3ac**, and **3ad**). The alkylarylketene silyl acetal also showed good reactivity, thus furnishing **3ae**. In the case of monosubstituted ketene silyl acetals, alkylketene and arylketene substrates gave the desired products **3af** and **3ag** in 90 and 83% yields, respectively. The phenoxy-substituted ketene silyl acetal furnished the α -phenoxy α -vinyl ester **3ah** in 44% yield, and the reaction using an unsubstituted ketene silyl acetal also took place, although the yield was only 20% (**3ai**). Heteroaryl-substituted ketene silyl acetals were found to be facile nucleophiles (**3aj** and **3ak**).

Furthermore, the applicable alkenyl ethers are shown in Table 2. The isopropyl vinyl ether (**1b**) gave the desired product in 50% yield, which was lower than that of **1a** as

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Scheme 1. Scope of reaction with respect to the ketene silyl acetal. Reaction conditions: **1a** (1 equiv), **2** (1.5 equiv), GaBr₃ (0.1 equiv), ClCH₂CH₂Cl, 80 °C, 2 h. Yields of isolated products are noted. [a] Determined by ¹H NMR spectroscopy. [b] **2** (3 equiv), GaBr₃ (0.2 equiv).

a result of bulk (Table 2, entry 1). The reaction of phenyl vinyl ether (**1c**) afforded a 98 % product yield (Table 2, entry 2). The 1-alkylated 1-methoxyethenes **1d** and **1e** were found to be facile substrates which gave the corresponding α -alkenylated esters in moderate yields (Table 2, entries 3 and 4). 1-Phenyl- and 1-naphthyl-1-methoxyethenes smoothly gave the desired products in 43 and 59 % yields, respectively (Table 2, entries 5 and 6). 1-Aryl-1-methoxyethenes possessing electron-withdrawing and electron-donating groups on phenyl rings were suitable coupling partners (Table 2, entries 7 and 8). Enyne ether **1j** effectively reacted with ketene silyl acetal **2i** to produce ester **3jl** in 73 % yield (Table 2, entry 9). The 2-substituted 1-alkoxyethenes also showed good reactivity. The reaction of (*E*)-1-nonyl-2-ethoxyethene (**1k**) with the ketene silyl acetal **2i** afforded methyl-2,2-dimethyltridec-3-enoate **3kl** in 91 % yield with an *E/Z* ratio of 54:46 (Table 2, entry 10). (*Z*)-1-Methyl-2-octoxyethene (**1l**) also gave a mixture of *E*- and *Z*-**3la** in a quantitative yield (Table 2, entry 11). Interestingly, the corresponding (*E*)- β,γ -unsaturated ester **3ma** was exclusively obtained from the reaction of (*Z*)-1-phenyl-2-phenoxyethene (**1m**; Table 2, entry 12). Unfortunately, more substituted alkenyl ethers such as 1,1-disubstituted and 1,2-disubstituted enol ethers, were not applicable.

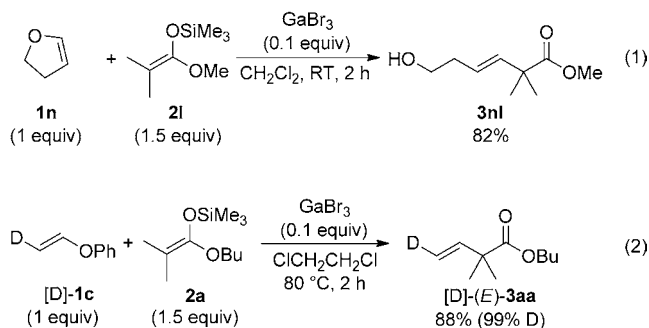
To reveal more of the stereochemistry, the reaction of dihydrofuran (**1n**) with **2i** was performed to produce the *E*-alkene **3nl** exclusively, through cleavage of the cyclic ether ring, with complete inversion of the stereochemistry [Eq. (1)]. In contrast, (*E*)-2-deuterated-1-phenoxyethene ([D]-**1c**) was treated with **2a** to furnish the (*E*)- β,γ -unsaturated ester selectively [Eq. (2)]. The stereochemical configuration of the

Table 2: Reaction scope: alkenyl ethers.^[a]

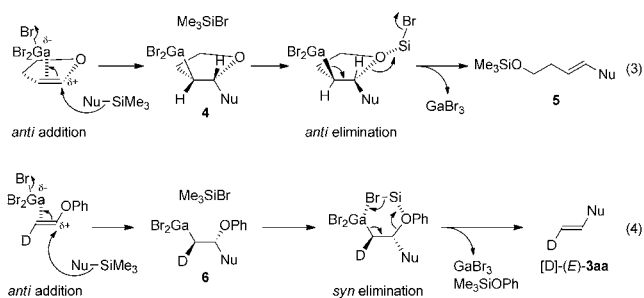
Entry	1	Product	Yield [%] ^[b]
1			50 ^[c]
2			98 ^[c]
3 ^[d]			77
4 ^[d]			69
5 ^[d,e]			43
6 ^[e]			59
7 ^[e]			61
8 ^[e]			43
9 ^[d]			73
10			91 (54:46)
11			quant. (63:37)
12 ^[f]			58

[a] **1** (1 equiv), **2** (1.5 equiv), GaBr₃ (0.1 equiv), ClCH₂CH₂Cl, 80 °C, 2 h. [b] Yields of isolated products are shown. [c] Determined by ¹H NMR spectroscopy. [d] 24 h. [e] **2** (3 equiv), GaBr₃ (0.2 equiv). [f] GaBr₃ (0.2 equiv), 70 °C.

starting alkene [D]-**1c** was completely retained in the course of the coupling reaction.



Possible mechanisms for these stereochemical phenomena are illustrated in Scheme 2 and are proposed on the basis



Scheme 2. Plausible mechanisms.

of our previously reported carboidation system.^[10b] The reaction using dihydrofuran (**1n**) occurs through the mechanism shown in Equation (3). GaBr₃ effectively interacts with the alkene moiety of **1n** to increase the positive charge on the carbon atom, α to the oxygen atom, because GaBr₃ moves to the electron-dense β-carbon atom. The nucleophilic attack of the ketene silyl acetal (Nu-SiMe₃) from the opposite side of GaBr₃ occurs regio- and stereoselectively,^[10b] and then the β-oxyalkylgallium intermediate **4** and Me₃SiBr are generated. Finally, the *anti* elimination of Br₂Ga and the alkoxide moieties occurs to give the *E*-alkene product **5**.^[13] The generated Me₃SiBr plausibly assists the *anti* elimination as illustrated because of the low leaving-group ability of an alkoxy group and the high oxophilicity of silicone. In the reaction of (*E*)-2-deuterated-1-phenoxyethene ([D]-**1c**) [Eq. (4)], the *anti* addition of GaBr₃ and ketene silyl acetal to [D]-**1c** also occurs to afford the β-phenoxyalkylgallium intermediate **6** and Me₃SiBr. The *syn* elimination of GaBr₂ and OPh groups takes place in succession via a six-membered transition state consisting of the alkylgallium **6** and Me₃SiBr to give the α-vinyl ester [D]-(*E*)-**3aa** and Me₃SiOPh and to regenerate GaBr₃.^[14,15] Although no direct experimental evidence exists, the assistance of Me₃SiBr on both *syn* and *anti* eliminations to compensate for the low oxophilicity of GaBr₃ is plausible. In addition, the sterics of the substituents of alkenyl ethers effectively determines the elimination mode that changes the *E/Z* ratio of the product olefins, as exemplified in entries 10–12 in Table 2.

In conclusion, we have accomplished the GaBr₃-catalyzed coupling reaction of alkenyl ether with ketene silyl acetals. The developed coupling reaction allows expedient access to β,γ-unsaturated esters. Various types of alkenyl ethers and ketene silyl acetals were applicable. Additional mechanistic studies are in progress.

Experimental Section

Butyl vinyl ether (**1a**, 1 equiv) was added to a solution of GaBr₃ (0.1 equiv, 0.05 M in dichloroethane) and ethylmethylketene methyl trimethylsilyl acetal (**2b**; 1.5 equiv). The mixture was stirred at 80 °C for 2 h and then was quenched by 1 M HCl. The mixture was extracted with diethyl ether. The collected organic layer was dried over MgSO₄. The solvent was evaporated and the residue was purified by column chromatography (hexane/ethyl acetate = 98:2, column length 11 cm) to give the product **3ab** (92%).

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