

Room-Temperature Synthesis of Trisubstituted Allenylsilanes via Regioselective C–H Functionalization

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Supporting Information

ABSTRACT: A Rh(III)-catalyzed *o*-C–H bond functionalization-based allenylation reaction of allenylsilanes **2** with *N*-methoxybenzamides **1** affords poly-substituted allenylsilanes with a wide range of attractive functional groups in moderate to excellent yields under very mild conditions (20 °C, compatible with ambient air and moisture). Those products may be transformed to different products with attractive structural features. Careful mechanistic studies suggest the reaction proceeds via *o*-rhodation, regioselective insertion, and β -H elimination.

It is well established that Ar–Rh species may be formed readily via C–H bond cleavage.^{1,2} Such intermediates may react with alkenes to afford the Heck-type substituted olefins via β -H elimination at high temperatures (60–140 °C).³ However, upon reacting with allenes, there is an issue of regioselectivity⁴ in forming cyclization products⁵ via π -allyl metal intermediates **M1** or protonolysis products⁶ via alkenyl metal intermediates **M2** because a C–Rh bond favors protonolysis over β -H elimination.⁷ Such Rh-catalyzed reactions of allenes, forming Heck-type more-substituted allene products, have never been realized since β -H elimination forming allenes is usually believed to be thermally unfavorable due to a much higher energy level of this class of compounds as compared to **M2** (Scheme 1, b). We propose that the steric effect of the R¹/R² groups of geminal-disubstituted allenes may direct the R group in R–M to the 1-position of allenes, affording alkenyl metal intermediates **M2** (Scheme 1, lower). Moreover, the bulkier R¹/R² groups may further push the transition metal **M** in **M2** for a greater agostic interaction with the H^a atom at the 1-position, promoting facile β -H elimination to

afford allenylation products (Scheme 1, b). Herein, we report the first example of such a C–H functionalization-based room-temperature (rt) allenylation reaction of allenylsilanes with arenes affording the desired extra-substituted allenes (Scheme 1, b) by applying the versatile silyl functionality as the directing group, observing the β -H elimination of Rh–C–C–H at rt, or even at –20 °C.

First, although the regioselectivity of the carbometallation of allenes forming intermediate **M2** was confirmed by the reaction of arene **1a** with 1,1-dialkyl-substituted allene **2a** in the presence of 2 mol% of [Cp*RhCl₂]₂ and 30 mol% of CsOAc in MeOH/H₂O at –20 °C, as expected, protonolysis occurred exclusively, affording 82% of allylation product **4aa** (entry 1, Table 1).⁶ Interestingly, it was observed that 1,1-disubstituted allene **2b**, with a slightly bulkier phenyl substituent compared to **2a**, in the presence of 2 mol% of [Cp*RhCl₂]₂ and 30 mol% of CsOAc in MeOH/H₂O at –20 °C, afforded 62% of the normal insertion-protonolysis product **4ab**, together with a new allene compound **3ab**, albeit in 3% yield as judged by NMR analysis of the crude product (entry 2, Table 1), confirming the steric effect of the phenyl group as shown in Scheme 1. Furthermore, it is noted that this β -H elimination for allene synthesis may occur at –20 °C; such a reaction for alkene synthesis may generally require a high temperature.³ Moreover, when the *tert*-butyl-substituted substrate **2c** was applied, the more-substituted allenylation product

Scheme 1. Carbometallation of Allenes with R–M Species

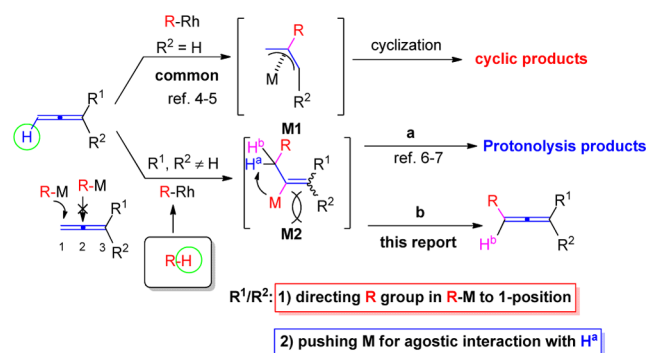


Table 1. The Substituent Effect

entry	R	M	temp, °C	NMR yield, %		
				3 (X = H)	1 (X = OMe)	4
1	Bu	Cs	–20	– (3aa)	– (1aa)	82 (4aa)
2	Ph	Cs	–20	3 (3ab)	– (1ab)	62 (4ab)
3	^t Bu	Cs	–20	70 (3ac)	8 (1ac)	4 (4ac)
4	TMS	Cs	–20	41 (3ad)	– (1ad)	– (4ad)
5	TMS	Na	–20	51 (3ad)	– (1ad)	– (4ad)
6	TMS	Na	–15	64 (3ad)	– (1ad)	– (4ad)
7	TMS	Na	–10	80 (3ad)	– (1ad)	– (4ad)
8	TMS	Na	20	91 (3ad)	– (1ad)	– (4ad)

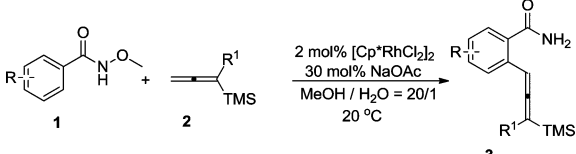
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3ac was formed in 70% yield as the major product together with only 4% of insertion-protonolysis product **4ac**, detected in the reaction by NMR analysis of the crude product (entry 3, Table 1). For the major product **3ac**, there is no methoxy group in the final product, indicating that it may act as an intramolecular oxidant.² Based on such results, we considered that this *tert*-butyl may be replaced with a synthetically more attractive trialkylsilyl group: in the presence of 2 mol% of $[\text{Cp}^*\text{RhCl}_2]_2$ and 30 mol% of CsOAc in MeOH/H₂O at -20°C , the reaction of allenylsilane **2d** with 1.0 equiv of **1a** exclusively afforded “more-substituted” allenylation product **3ad** in 42% yield, and no insertion-protonolysis product **4ad** was detected. When CsOAc was replaced with NaOAc, the yield of **3ad** was improved to 51% (entry 4, Table 1). The yield was further improved by elevating the temperature (entries 5–8, Table 1), and finally we found that, when the reaction was conducted at 20°C , **3ad** was formed in 91% yield (entry 8, Table 1), so this was defined as the standard conditions for further investigation.

With this set of optimized reaction conditions, the scope of C–H allenylation of allenes via C–H functionalization of arenes is demonstrated with a variety of differently substituted *N*-methoxybenzamides (**1a–1g**) and allenes (**2d–2j**). Gratifyingly, good to excellent yields for the allenylation of arenes were generally obtained for most of the substrates at rt (Table 2). The reaction provided the allenylation products **3** regardless of the substrates **1** with either electron-donating substituents, such as 4-OMe (**1b**) and 4-Bu^t (**1c**), or synthetically attractive electron-withdrawing groups, such as 4-Br (**1d**), 4-Cl (**1e**), 4-COOMe (**1f**), and 3-CF₃ (**1g**); when *N*-methoxy-3-trifluoromethylbenzamide **1g** was applied, the reaction occurred highly selectively at the *o*-C–H with less steric hindrance, affording the corresponding allenylation product **3gd** in 91% yield (entry 7, Table 2);

Table 2. Rh(III)-Catalyzed Heck Allenylation Reactions of *N*-Methoxybenzamides **1** with Silyl Allenes^a



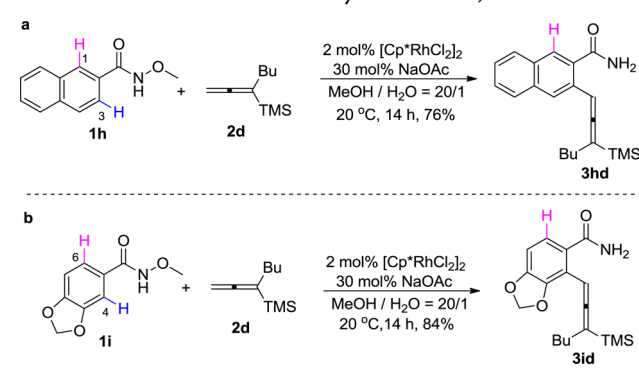
entry	R	R ¹	time, h	yield of 3 , %
1	H (1a)	Bu (2d)	11	91 (3ad)
2	4-OMe (1b)	Bu (2d)	11	86 (3bd)
3	4-Bu (1c)	Bu (2d)	12	85 (3cd)
4	4-Br (1d)	Bu (2d)	11	85 (3dd)
5 ^b	4-Cl (1e)	Bu (2d)	16	80 (3ed)
6	4-CO ₂ Me (1f)	Bu (2d)	14	86 (3fd)
7 ^c	3-CF ₃ (1g)	Bu (2d)	36	91 (3gd)
8	H (1a)	ⁿ C ₅ H ₁₁ (2e)	14	84 (3ae)
9	H (1a)	Bn (2f)	72	86 (3af)
10	H (1a)	ⁱ Pr (2g)	16	84 (3ag)
11 ^d	H (1a)	Ph (2h)	59	59 (3ah)
12	H (1a)	CH ₂ CO ₂ Et (2i)	36	63 (3ai)
13	H (1a)	(CH ₂) ₂ OTBS (2j)	16	82 (3aj)
14 ^b	H (1a)	Bu (2d)	13	85 (3ad)

^aReaction was conducted with **1** (1.0 mmol), **2** (1.0 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (0.02 mmol), NaOAc (0.3 mmol), MeOH (6 mL), and H₂O (0.3 mL), and monitored by TLC. ^bReaction was conducted on 10 mmol scale. ^cReaction occurred at the C–H bond with less steric hindrance. ^d3.0 equiv of **1a** and 4 mol% of $[\text{Cp}^*\text{RhCl}_2]_2$.

carbon–halogen bonds (**1d,1e**) and ester group (**1f**) were tolerated, affording the corresponding C–H allenylation products **3dd–3fd** in good yields (entries 4–6, Table 2). The R¹ substituent of silyl allenes **2** could be alkyl (**2d–2g**) or phenyl (**2h**); the *c*-Pr group with a highly strained ring was also tolerated (**2g**). Intriguingly, when terminal allenes **2i,2j** with different functionalities were treated with arene **1a**, the corresponding allenylation products **3ai,3aj** were afforded in moderate yields, and all these functionalities, such as the ester group of **2i** (entry 12, Table 2) and the silyl ether group of **2j** (entry 13, Table 2), remained untouched. Gratifyingly, large-scale reactions of **1a,1e** with **2d** also afforded **3ad,3ed** in 85% and 80% yield, respectively (entries 14 and 5, Table 2).

When *N*-methoxy-2-naphthamide **1h** was used in the reaction, the 3-position C–H bond with less steric hindrance was selectively functionalized to afford the corresponding product **3hd** in 76% yield (Scheme 2, a), with no reaction at the 1-position C–H bond of the naphthyl skeleton. Interestingly, treatment of *N*-methoxybenzo[*d*][1,3]dioxole-5-carboxamide **1i** with **2d** provided the 4-position allenylation product **3id** in 84% yield; the reaction occurred at the C–H bond with more steric hindrance, with no 6-position C–H allenylation product (Scheme 2, b), which may be explained by a coordination effect between the oxygen atom at the 3-position and the transition metal.⁸

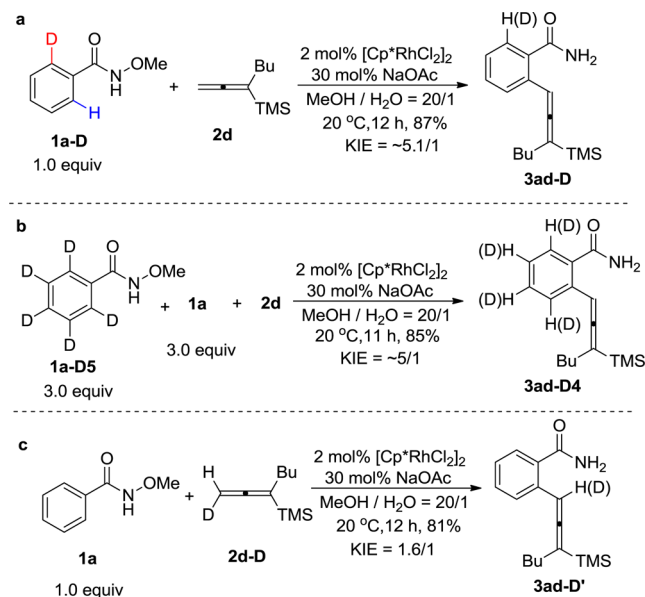
Scheme 2. Selective Heck Allenylation of **1h,1i** with **2d**



To further probe the reaction mechanism, firstly, the intra- and intermolecular kinetic isotope effects (KIEs, $k_{\text{H}}/k_{\text{D}}$) of C–H bond cleavage were determined to be ~5.1:1, respectively, by reacting **1a-D** and **1a-DS** with **2d** (Scheme 3, a,b). The KIE of the β -H elimination process had been determined to be 1.6:1 by using **2d-D** as the substrate.

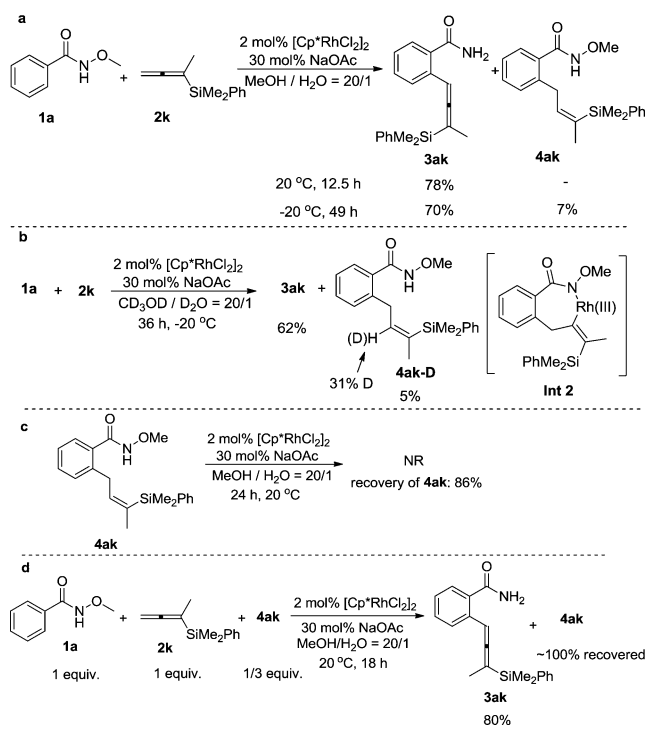
Furthermore, to capture the Rh intermediate before β -elimination, 3-(dimethylphenyl)silyl-1,2-butadiene **2k** was prepared as the probe substrate: besides 70% of allenylation product **3ak**, the reaction at -20°C afforded 7% of insertion-protonolysis product **4ak**; in comparison, the reaction at 20°C afforded the corresponding allenylation product **3ak** in 78% yield, exclusively (Scheme 4, a). These facts indicate that the reaction should proceed through the Rh(III) intermediate **Int 2**, which undergoes a β -H elimination to afford **3ak** exclusively at rt or partial protonolysis, producing **4ak**, at -20°C (Scheme 4, b). This conclusion was further confirmed by running the reaction in CD₃OD/D₂O, yielding the product **4ak-D** in 5% yield with 31% of deuterium incorporation at the olefinic position. Moreover, when the protonolysis product **4ak** was subjected to the standard conditions, no allenylation product was observed, and 86% of **4ak** was recovered, even after stirring for 24 h. Even when the

Scheme 3. Kinetic Isotopic Experiments



reaction of **1a** and **2k** was conducted in the presence of **4ak** at 20 °C for 18 h, **4ak** was recovered in ~100% NMR yield, with **3ak** still being formed in 80% yield. These facts exclude the possibility that **3ak** originated from the dehydrogenative elimination of **4ak** (Scheme 4, c).

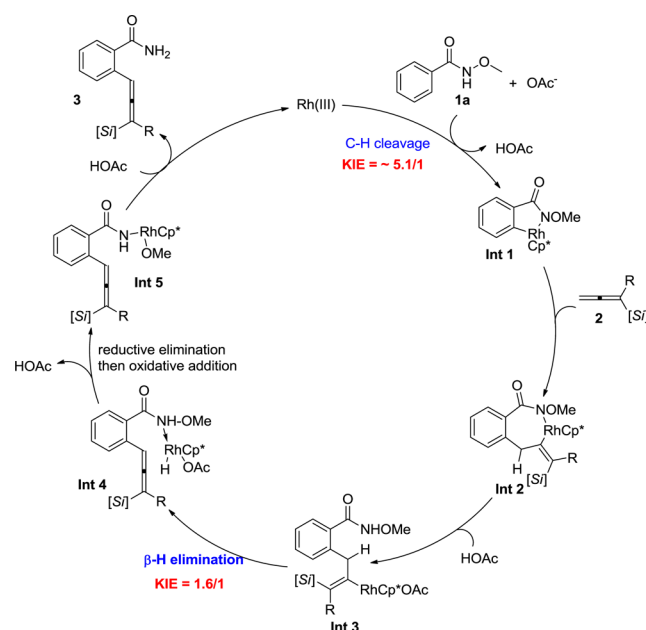
Scheme 4. Mechanistic Studies



Based on this evidence, a plausible mechanism for this reaction is proposed as shown in Scheme 5. The first step of the transformation should be C–H bond rhodation of **1a** in the presence of NaOAc, providing cyclic intermediate **Int 1**,^{2–6} followed by insertion of allene to afford the sp² C–Rh intermediate **Int 2**,⁴ exclusively, as controlled by the steric effect of both the R and [Si] groups. Protonolysis with the in situ-

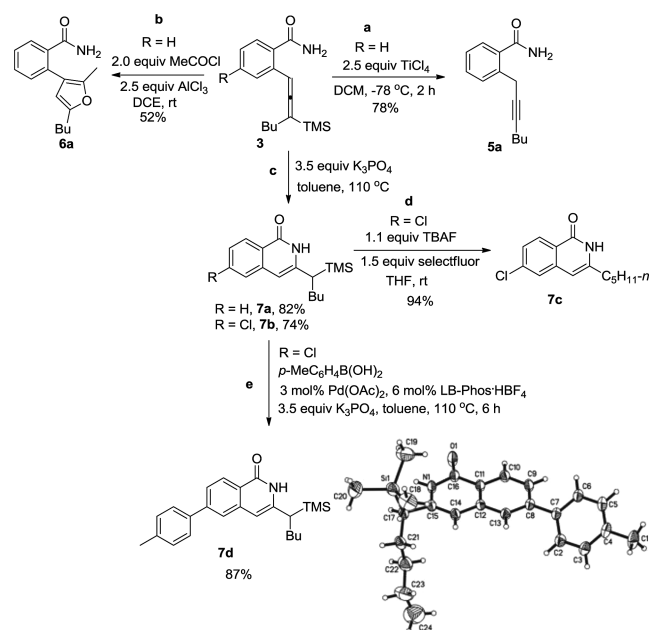
generated HOAc affords the intermediate **Int 3**. This is followed by a very fast β-H elimination, yielding the intermediate **Int 4**, with which the Rh(I) species coordinates with the amide functionality. Reductive elimination forming HOAc, oxidative addition of Rh(I) with C(O)–OMe bond, and protonolysis with HOAc would remove the methoxy group from the amide functionality and regenerate the catalytically active Rh(III) species. Thus, the N-methoxy group leaves the product as an efficient intramolecular oxidant² to finish the catalytic cycle.

Scheme 5. Possible Mechanism



Finally, the synthetic potentials of the prepared 2-(silylallenyl)benzamides were examined (Scheme 6): (a) Alkyne **5a** could be afforded in 78% yield by treating the product **3ad** with 2.5 equiv of TiCl₄ in dichloromethane at –78 °C for 2 h.⁹

Scheme 6. Application of the Products



(b) Product **3ad** could serve as alkynylation reagent to react with acetyl chloride in the presence of AlCl_3 . Subsequent cyclization reaction would afford substituted furan product **6a** in moderate yield.⁹ (c) The isoquinolinone products **7a** and **7b** could be obtained by K_3PO_4 -promoted cyclization reaction of **3** in toluene at 110 °C. (d) The product **7b** could be further converted to **7c** by desilylation reaction in the presence of TBAF and Selectfluor reagent in excellent yields.⁹ (e) Diarylation product **7d**, whose structure was confirmed by single-crystal X-ray diffraction study,¹⁰ could be formed in a decent yield by Suzuki coupling reaction of **7b** with aryl boronic acid in the presence of $\text{Pd}(\text{OAc})_2$ and LB-Phos .¹¹

In conclusion, we have developed the first example of a direct allenylation reaction of allenes with *N*-methoxybenzamides via C–H bond cleavage, allene insertion, and β -H elimination affording useful 2-(3-silylallenyl)benzamides. These reactions proceed at 20 °C and are compatible with ambient air and moisture. Moreover, a wide range of both arenes and allenylsilanes with many synthetically attractive functionalities are applicable for this reaction. The products obtained could be used for the highly stereoselective synthesis of substituted alkynes, furans, and isoquinolinones. Considering the easy availability of the starting silylallenes¹² and *N*-methoxybenzamides and the broad applications of the products, this protocol will be of high interest in organic chemistry and related disciplines. Further studies in this area are being carried out in our laboratory.

■ ASSOCIATED CONTENT

■ Supporting Information

Experimental procedures and spectroscopic characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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(10) **7d**: $\text{C}_{24}\text{H}_{31}\text{NOSi}$, MW = 377.59, triclinic, space group $\text{P}\bar{1}$, final *R* indices [$> 2\sigma(I)$], $R_1 = 0.0934$, $wR_2 = 0.2574$; *R* indices (all data), $R_1 = 0.1562$, $wR_2 = 0.3161$; $a = 9.1348(16)$ Å, $b = 10.404(2)$ Å, $c = 13.375(3)$ Å, $\alpha = 103.609(17)^\circ$, $\beta = 94.386(16)^\circ$, $\gamma = 108.491(17)^\circ$, $V = 1155.8(4)$ Å³, $T = 293(2)$ K, $Z = 2$, reflections collected/unique 7410/4212 ($R_{\text{int}} = 0.0505$); number of observations [$> 2\sigma(I)$] 2214; parameters, 249. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, CCDC 948623.

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