

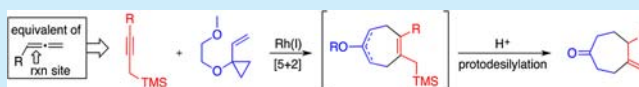
Propargyltrimethylsilanes as Allene Equivalents in Transition Metal-Catalyzed [5 + 2] Cycloadditions

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Supporting Information

ABSTRACT: Conventional allenes have not been effective π -reactive 2-carbon components in many intermolecular cycloadditions including metal-catalyzed [5 + 2] cycloadditions. We report herein that rhodium-catalyzed [5 + 2] cycloadditions of propargyltrimethylsilanes and vinylcyclopropanes provide, after in situ protodesilylation, a highly efficient route to formal allene cycloadducts. Propargyltrimethylsilanes function as safe, easily handled synthetic equivalents of gaseous allenes and hard-to-access monosubstituted allenes. In this one-flask procedure, they provide cycloadducts of what is formally addition to the more sterically encumbered allene double bond.



Since its introduction in 1995, the metal-catalyzed [5 + 2] cycloaddition of vinylcyclopropanes (VCPs) and π -systems, the homologous Diels–Alder reaction, has been shown to work intramolecularly with alkynes, alkenes, and allenes and successfully applied to step-economical syntheses of various seven-membered ring-containing natural products.^{1,2} In contrast, the intermolecular reaction has proven to be less general, working only with rhodium catalysts and being limited thus far to alkynes and some “activated” allenes incorporating a second coordinating group (e.g., alkyne or nitrile).³ Activated monosubstituted or 1,1-disubstituted allenes do not react while activated 1,3-disubstituted allenes react but with marginal regioselectivity (1:1–7:2). Some substituted allenes are also catalyst poisons. Importantly, the direct cycloaddition of VCPs with the larger family of unactivated allenes has not been reported. We realized, however, that for many allenes, including those highly useful for total syntheses⁴ and other synthetic applications,⁵ the use of an allene equivalent would be highly preferred, providing a potentially superior, more controllable, safer, and more chemoselective reaction (Scheme 1). For example, with respect to safety and handling,⁶ allene itself is a gas at room temperature. Its use thus requires a rather challenging and hazardous low temperature distillation of

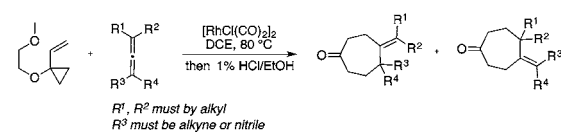
difficult to measure amounts into a sealable pressure tube and a similarly complicated work-up procedure. In contrast, commercially available propargyltrimethylsilane, a candidate equivalent of allene itself, has a boiling point of 91 °C, allowing for its easy handling, and upon cycloaddition and acidic protodesilylation⁷ would in principle give the same product as that derived from a [5 + 2] cycloaddition to allene itself. This equivalency represents a significant contribution to the rather limited body of known functional allene equivalents⁸ and a highly effective solution to the thus far unsolved problem of accessing allene [5 + 2] cycloadducts.

In principle, the propargyl silane cycloaddition and protodesilylation could be effected in one operation. Other propargyl silanes would similarly serve as allene equivalents providing access to [5 + 2] cycloadducts that thus far are not accessible directly from allenes. Moreover because the addition to an alkyne has unambiguous chemoselectivity, this strategy could be used to access cycloadducts that would not be selectively accessed, if at all (addition to more substituted π -bond), from allenes themselves. Herein, we report the first experimental study of the stepwise or one-flask [5 + 2] cycloaddition/protodesilylation of propargyltrimethylsilanes and VCPs providing a new, facile, and practical method for accessing what are formally allene [5 + 2] cycloadducts.

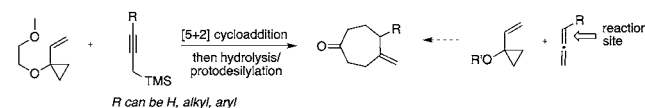
A catalyst screen was first conducted. Recently, we reported that cationic Rh(I) complexes featuring a cyclooctadiene (COD) or a dinaphtho[*a,e*]cyclooctatetraene (dnCOT) ligand, such as [Rh(C₁₀H₈)(COD)]SbF₆⁹ and [Rh(dnCOT)-(MeCN)₂]SbF₆¹⁰ are highly efficient catalysts for both inter- and intramolecular [5 + 2] cycloaddition reactions between VCPs and alkynes. To investigate the proposed cycloaddition between VCP **1** and propargyltrimethylsilane (**2a**), multiple catalysts were examined (see Supporting Information). When

Scheme 1. A General Route to Allene Cycloadducts

Previous Work:



This Work:



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VCP **1** and **2a** were treated with 1 mol % of $[\text{Rh}(\text{C}_{10}\text{H}_8)(\text{COD})]\text{SbF}_6$ in DCE or a mixture of DCE/TFE (0.15 M) at room temperature for 3 h, followed by a brief hydrolytic workup (1% HCl in EtOH), the desired cycloheptenone **3a** was isolated in 93% yield. Changing the solvent from DCE to a 9:1 mixture of DCE/TFE shortened the reaction time to 1 h and improved the yield to 98%. This represents the highest yield and shortest time of all screened Rh(I) catalysts. $[\text{Rh}(\text{dnCOT})(\text{MeCN})_2]\text{SbF}_6$ and its analogues containing substituted dnCOT ligands also gave **3a**, albeit in lower yields and with longer reaction times (12 h).

Having determined the optimum catalyst and conditions, we next studied the Rh(I)-catalyzed [5 + 2] cycloaddition of various propargyltrimethylsilane derivatives (Table 1). VCP **1**

Table 1. Rhodium-Catalyzed [5 + 2] Cycloaddition of VCP **1 and Propargyltrimethylsilanes **2a–h****

entry	SM	R	[Rh] (mol%)	time (hr)	yield (%)
1 ^a	2a	H	1	1	98
2	2b	Me	1	3	97
3	2c	<i>n</i> -hex	3	3	81
4 ^b	2d	<i>i</i> -Pr	5	2	74
5 ^c	2e	Ph	5	3	85
6 ^b	2f		5	3	99
7 ^c	2g		5	2	84
8 ^{b,d}	2h		5	1	82

^aDCE/TFE (9:1, 0.15 M). ^bDCE/TFE (3:1, 0.15 M) was used as a solvent. ^cTFE (0.15 M) was used as a solvent. ^dHeated at 40 °C.

was reacted with 1.1 equiv of each substrate (**2a–h**) in the presence of catalytic $[\text{Rh}(\text{C}_{10}\text{H}_8)(\text{COD})]\text{SbF}_6$ in DCE (0.15 M) at room temperature to provide, after brief hydrolytic workup with 1% HCl in EtOH, a range of 5-substituted-4-silylmethylcyclohept-4-enones (**3a–h**) in good to excellent yields. The results indicate that the cycloaddition reaction is widely tolerant of a variety of propargyltrimethylsilane substitutions including hydrogen, *n*- and *i*-alkyl, aryl, and heteroatom groups.

We next examined the protodesilylation of 4-silylmethylcyclohept-4-enones **3a–h** with Brønsted acids to investigate whether the [5 + 2] cycloaddition and protodesilylation could be conducted in a stepwise manner. Treatment of **3a** with 5 equiv of *p*-TsOH·H₂O in Et₂O at room temperature gave the desired *exo*-methylene product **4a**¹¹ in excellent yield. While cycloheptenones featuring methyl and hexyl groups (**3b,c**) were converted to the desired product in high yields, long reaction times (>24 h) and heating (in the case of **3c**) were needed. The

phenyl derivative (**3e**) did not undergo protodesilylation at all over the course of 2 days, likely a result of its conjugated (styrenyl) system.¹² To address this problem, we screened several acids and found that treating our 4-silylmethylcyclohept-4-enones with 5 M HCl/EtOAc¹³ in DCM was highly effective for the protodesilylation of all substrates (Table 2). These

Table 2. Protodesilylation of 4-Silylmethylcyclohept-4-enones (3a–h**) Using Brønsted Acid**

entry	SM	R	time	product	yield (%)
1	3a	H	<5 min	4a	98
2	3b	Me	15 min	4b	90
3	3c	<i>n</i> -hex	15 min	4c	90
4	3d	<i>i</i> -Pr	30 min	4d	89
5	3e	Ph	2 hr	4e	94
6	3f		1.5 hr	4f	89
7	3g		2 hr	4g	96
8	3h		3 hr	4h	96

conditions enabled us not only to shorten the reaction time (15 min or less for entries 1–3) but also to furnish 5-aryl-4-methylenecycloheptanones **4e–g** from the conjugated cycloheptenones **3e–g** in high yields at room temperature.

With the success of this two-step process, we next set out to determine whether a serial, one-flask [5 + 2] cycloaddition/protodesilylation could be developed that would produce 4-methylenecycloheptanone derivatives in a single operation from VCP **1** and select propargyltrimethylsilanes (Table 3). After the cycloaddition was complete, the reaction was quenched with 1 M HCl/EtOAc to produce the (5-substituted-)4-methylenecycloheptanone derivatives **4a,c,e–h** in yields comparable or even superior to the overall yield of the two-flask procedure. The 1 M HCl/EtOAc solution chosen to execute the single-flask protodesilylation was superior to 5 M HCl/EtOAc, *p*-TsOH·H₂O, and concentrated aq. HCl in terms of yield and minimization of side product formation.

In conclusion, we have developed efficient stepwise as well as serial intermolecular [5 + 2] cycloaddition/protodesilylation reactions of propargyltrimethylsilanes and VCPs for the formation of 4-methylenecycloheptanones and a wide range of 5-substituted-4-methylenecycloheptanone derivatives, allene cycloadducts, in high yields. Significantly, the propargyltrimethylsilanes not only work as synthetic equivalents of gaseous or otherwise difficult to handle allenes but also enable access to a product that is derived from chemoselective cycloaddition to the more hindered allene double bond. This strategy provides simple, safe, and efficient access to previously

Table 3. One-Flask [5 + 2] Cycloaddition/Protodesilylation Processes

entry	SM	R	time	product	yield (%)
1 ^a	2a	H	15 min	4a	92
2 ^b	2c	n-hex	1 hr	4c	69
3 ^c	2e	Ph	3 hr	4e	94
4 ^c	2f		4 hr	4f	89
5 ^c	2g		3 hr	4g	96
6 ^c	2h		4 hr	4h	96

^a1 mol % Rh, DCE/TFE (9:1, 0.15 M), rt. ^b3 mol % Rh, DCE (0.15 M), rt. ^c5 mol % Rh, DCE/TFE (3:1, 0.15 M), rt.

inaccessible allene [5 + 2] cycloadducts and has utility for other cycloadditions.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and 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.

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- (12) Using TFE as solvent, <57% yield of **4e** was obtained after 17 h.

- (13) 5 M HCl in EtOAc was made by reacting 5 mol AcCl with 5 mol EtOH in a total volume of 1 L EtOAc.