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Oxidative Dimerization of Silylallenes via Activation of the Allenic C(sp^2)−H Bond Catalyzed by Copper(I) Chloride and *N*-Hydroxyphthalimide

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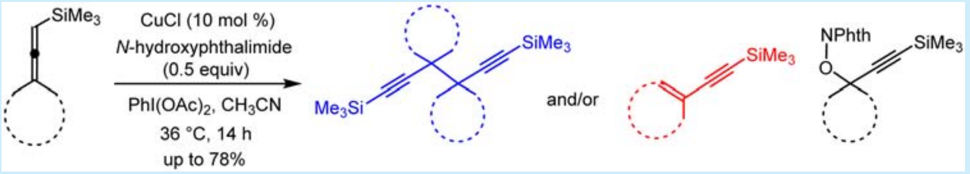
Supporting Information

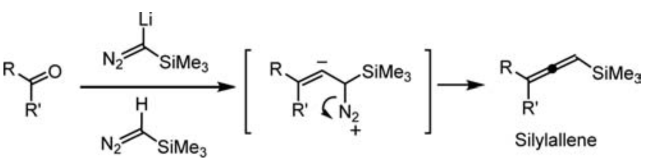


ABSTRACT: Novel oxidative dimerization of silylallenes is described. Treatment of silylallenes with a catalytic amount of copper(I) chloride, a substoichiometric amount of *N*-hydroxyphthalamide, and a stoichiometric amount of a terminal oxidant diacetoxyiodobenzene afforded head-to-head dimers as the main products. Silyallenes containing a small ring afforded only dimers, whereas as the ring size increased 1,3-enynes became more favorable products. For silylallenes containing an acyclic substituent, dimer formation is a norm with exceptions where *N*-hydroxyphthalimide reacts at the propargylic center to generate the corresponding aminoxy ethers.

Allenes play an important role for the development of new synthetic methods especially with transition-metal catalysts.[1] The vast array of reactions involving allenes is the consequence of the two cumulated alkenes connected by an *sp*-hydridized central carbon, which ultimately provides the increased reactivity of their π-bonds in allenes. In particular, allenes containing boronyl[2] or silyl substituents[3] are important building blocks readily reacting with carbonyl compounds to form homopropargylic alcohols.[4,5] Because of their versatility for further elaboration, homopropargylic alcohols are frequently employed in various complex molecule syntheses.[5j,6]

Recently, we developed a novel one-step protocol for the synthesis of trisubstituted silylallenes from ketones and (trimethylsilyl)diazomethane (Scheme 1).[7] The easy access to

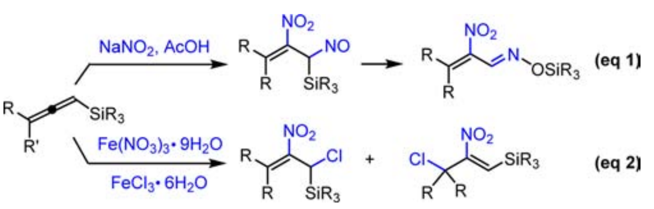
Scheme 1. One-Step Synthesis of Silylallenes from Ketones



these silylallenes prompted us to explore their unique reactivity. Although silylallenes have been employed in many synthetic transformations,[5] their utility has not been broadly defined especially for trisubstituted silylallenes.

The availability of these silylallens allowed us to examine their reactivity, which resulted in novel nitration to form functionalized nitroalkenes (Scheme 2).[8] In this transformation, the initial addition of a nitrogendioxyl radical ($^{\bullet}NO_2$) occurs on the *sp*-hydridized carbon to form an allylic radical intermediate,

Scheme 2. Nitration of Silylallenes To Form Functionalized Nitroalkenes



which is then trapped by the nitroxyl radical ($^{\bullet}NO$) or by the chloride nucleophile (S_N1 reaction) depending on the reaction conditions (Scheme 2, eqs 1 and 2).

Based on this facile addition of radical species with silylallenes, we envisioned that various other radicals might also react with these silylallenes under appropriate conditions to generate diversely functionalized alkene products.

To test this hypothesis, we subjected silylallene **1a** to the conditions that are known to generate an oxygen-centered radical,[9] expecting that the bis-oxygenated product should be formed (Scheme 3). Unexpectedly, however, dimer **2a** was isolated as the sole product. Clearly, this dimerization event implies that the putative oxygen-centered radical derived from *N*-hydroxyphthalimide did not add to the central carbon of the allene. Instead it abstracted the allenic C(sp^2)−H hydrogen[10] to generated a propargylic radical, which then dimerized.[11]

On the basis of this initial observation, we further investigated the oxidative the dimerization behaviors of silylallenes containing

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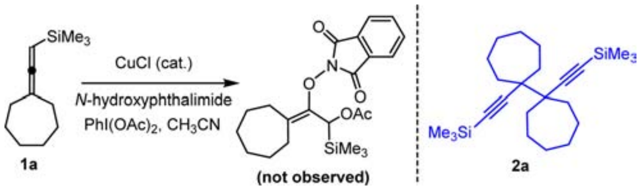
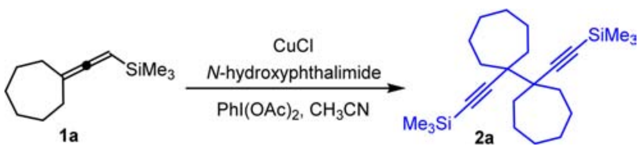
Scheme 3. Initial Observation of Silylallene Dimerization



different structural features, and herein we report their general trend and selectivity.

We commenced our investigation by optimizing the reaction conditions in terms of the catalyst loading, stoichiometry of reagents and oxidant, reaction time, and temperature (Table 1).

Table 1. Optimization of Reaction Conditions for Dimerization of Silylallenes



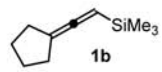
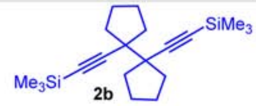
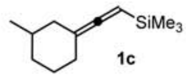
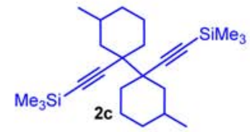
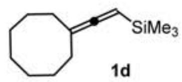
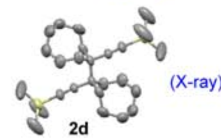
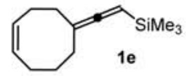
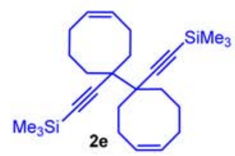
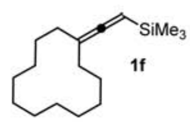
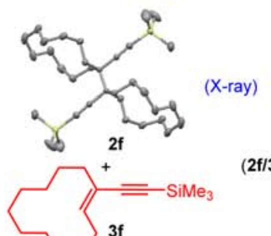
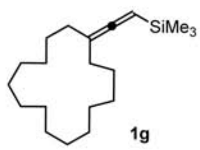
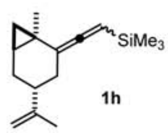
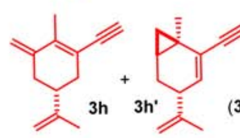
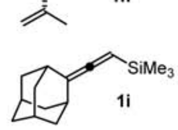
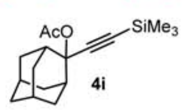
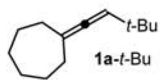
entry	catalyst (10 mol %)	*N*-Hpth (equiv)	$PhI(OAc)_2$ (equiv)	temp (°C)	time (h)	yield[a] (%)
1	CuCl	1	1	70	12	76
2	CuCl	1	1	36	14	78
3	CuCl	1	0	36	14	N/R
4	CuCl	0	1	36	14	N/R
5	CuCl	0.5	1	36	14	78
6	CuCl	0.3	1	36	14	40
7	CuOAc	0.5	1	36	12	unknown
8	$Cu(OAC)_2$	0.5	1	36	12	unknown

[a]Isolated yields.

Using cycloheptanylidyl allene **1a** as a test substrate with a catalytic amount of CuCl (10 mol %) and stoichiometric amounts of *N*-hydroxyphthalimide (*N*-Hpth) and $PhI(OAc)_2$ in CH_3CN at 70 °C gave the dimer product of 1,5-diyne **2a** in 76% yield (Table 1, entry 1). By lowering the reaction temperature from 70 to 36 °C, the yield of the reaction was slightly increased to 78% (Table 1, entry 2). Next, we explored the effect of the amounts of *N*-Hpth and $PhI(OAc)_2$; without oxidant and/or *N*-Hpth, no reaction occurred (Table 1, entries 3 and 4). Lowering the amount of *N*-Hpth down to 50 mol % did not affect the yield of the reaction (Table 1, entry 5). However, further lowering *N*-Hpth to 30 mol % significantly lower the yield of **2a** (Table 1, entry 6). Changing the catalyst from CuCl to CuOAc or $Cu(OAc)_2$ provided unknown products (Table 1, entries 7 and 8).

With the optimized conditions for the dimerization of silyl allenes in hand, we next examined the substrates differing in their ring sizes ranging from five to eight, 12, and 15 as well as the substitution pattern around the allene skeleton (Table 2). Small ring-based allenes **1b** and **1c** afforded dimers **2b** and **2c** in 62 and 58% yield (Table 2, entries 1 and 2), and allene **1d** containing a cyclooctylidene moiety provided a dimeric product **2d** in 72% yield (Table 2, entry 3). The reaction of allene **1e** containing an extra double bond on the eight-membered ring also yielded dimer **2e** in 68% yield without any other side product derived from the involvement of the double bond (Table 2, entry 4).[9] Unexpectedly, however, increasing the ring size beyond eight diverted the product distribution. The reaction of allene **1f** with a

Table 2. Dimerization of Silylallenes Derived from Cyclic Ketones

entry	silylallene	product	yield (%)[a]
1	 **1b**	 **2b**	62
2	 **1c**	 **2c**	58
3	 **1d**	 **2d** (X-ray)	72
4	 **1e**	 **2e**	68
5	 **1f**	 **2f** (X-ray) + **3f**	70 (**2f**/**3f** = 2:1)[b]
6	 **1g**	 **3g**	75
7	 **1h**	 **3h** + **3h'**	55 (**3h**/**3h'** = 1:2)[c]
8	 **1i**	 **4i**	45
9	 **1a-*t*-Bu**	decomposed	---

[a]Isolated yields. [b]The ratio was determined by [1]H NMR. [c]Protodesilylation of trimethylsilane was observed.

12-membered ring afforded a 2:1 mixture of dimer **2f** and 1,3-enyne **3f** in 70% combined yield (Table 2, entry 5), and that of **1g** containing a 15-membered ring generated 1,3-enyne **3g** in 75% yield as a sole product (Table 2, entry 6). Carvone-derived cyclopropane-containing silylallene **1h** resulted in a 55% combined yield of cyclopropane-opened[12] **3h** and 1,3-enyne

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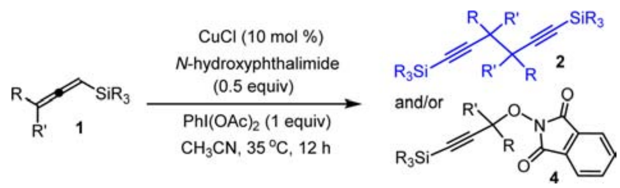
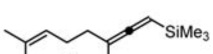
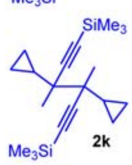
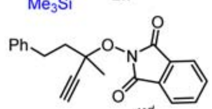
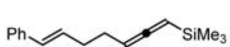
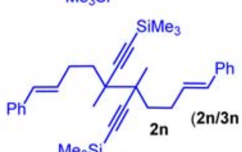
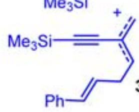
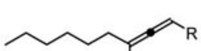
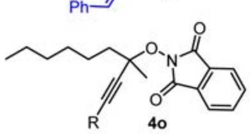
3h′ in a 2:1 ratio (Table 2, entry 7). On the other hand, adamantanone-derived silylallene **1i** generated an acetoxy group trapped product **4i** in 45% yield (Table 2, entry 8). The reaction of **1a-*t*-Bu** where the $SiMe_3$ of **1a** is replaced with a *tert*-butyl group led to only decomposition under identical conditions (Table 2, entry 9). The stark difference in reactivity between silylallene **1a** and the corresponding *tert*-butyl counterpart **1a-*t*-Bu** suggests that the silyl group plays a crucial role in weakening the allenic C−H bond.[13]

Having seen the general trend of reactivity of cyaloalkane-based silylallenes in dimerization, we next examined the reactivity of acyclic alkane-based silylallenes toward dimerization (Table 3). Silylallene **1j** bearing a prenyl group afforded dimer **2j** in 72% yield (Table 3, entry 1),[14] yet a cyclopropyl group-containing silylallene **1k** resulted in severe decomposition with only a trace amount of dimer **2k** (Table 3, entry 2). Surprisingly, silylallene **1l** did not generate an expected dimer product; instead, phthalimidoxy-trapped product **4l** was generated in 34% yield. By employing a stoichiometric amount of *N*-Hpth, the yield of **4l** increased to 61% (Table 3, entry 3). The results obtained from allenes **1j**, **1k** ,and **1l** imply that even a remote unsaturated functional groups such as a prenyl or a phenyl group may significantly affects the dimerization of these silylallenes. This notion is further strengthened by the reaction of allenes **1m−p**. Although the reaction of silylallene **1m** containing a terminal double delivered only dimer product **2m** in good yields (Table 3, entry 4),[14] the corresponding silylallene **1n** containing a styryl group afforded a mixture of dimer **2n**[14] and 1,3-enyne **3n** in 69% combined yield (Table 3, entry 5). Interestingly, allenes **1o** and **1p** containing different silyl groups such as $SiEt_3$ and $SiMe_2$-*t*-Bu, respectively, delivered only the propargylic aminoxy ethers **4o** and **4p** in moderate yields (Table 3, entries 6 and 7). On the other hand, disubstituted silylallene **1q** did not produce any identifiable product but rather decomposition under identical reaction conditions (Table 3, entry 8).

On the basis of this general trend and selectivity, we proposed a tentative mechanism for the dimerization (Scheme 4). As the first step in the catalytic cycle, Cu(I) is oxidized to Cu(II) by $PhI(OAc)_2$, which then reacts with *N*-Hpth to generate *N*-Hpth-Cu(I) adduct **A**. Upon homolysis of **A**, *N*-phthalimidoxy radical[9,15] **B** is generated together with Cu(I), which is oxidized back to Cu(II) to reenter the catalytic cycle. In the next step, *N*-phthalimidoxy radical **B** reacts with a substrate silylallene by abstracting the allenic $C(sp^2)$−H hydrogen to generate a propargylic carbon-centered radical **C** and *N*-Hpth, which completes the full catalytic cycle. The main downstream events of radical C are its dimerization to form product **2** or further oxidation to the corresponding carbocation **D**, which then

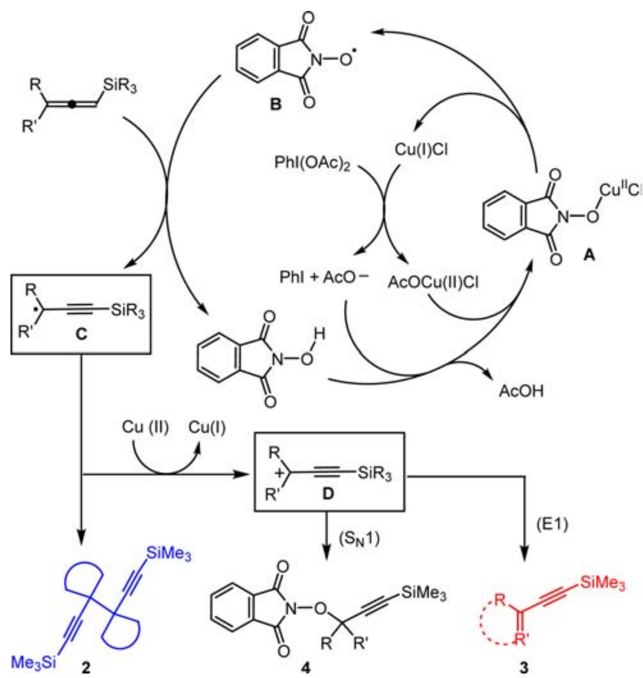
Table 3. Dimerization/Oxidation of Silylallenes Derived from Acyclic Ketones



entry	silylallene	product	yield (%)^a
1	 **1j**	 **2j**	72
2	 **1k**	 **2k**	trace^b
3	 **1l**	 **4l**^{d}	34 (61)^{c,d}
4	 **1m**	 **2m**^{d}	66
5	 **1n**	 **2n**  **3n** (**2n**/**3n** = 1.3:1)	69
6	 **1o**, R = $SiEt_3$	 **4o**	38 (67)^c
7	**1p**, R = $SiMe_2{}^tBu$	**4p**	31 (58)^c
8	 **1q**	decomposed	---

^{a}Isolated yields. ^{b}Trace amounts of dimeric product was observed by HRMS. ^{c}Yields in the parentheses are from reactions with 1 equiv of *N*-hydroxypthalimide. ^{d}Protodesilylation was observed.

Scheme 4. Proposed Reaction Mechanism



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undergoes an elimination and/or substitution to generate products **3** and/or **4**, respectively.

In summary, we have discovered a novel oxidative dimerization reaction of silylallenes using a catalytic system of copper(I) chloride and *N*-hydroxyphthalamide (*N*-Hpth) along with a stoichiometric amount of a terminal oxidant diacetoxyiodobenzene. Noticeable dependency on substrate structure for the formation of dimers, 1,3-enynes, and *N*-Hpth adducts was recognized; silylallenes containing a small ring substructure afforded only head-to-head dimers, whereas large ring-containing silylallenes provide 1,3-enynes as an accompanying minor or exclusive product depending on the size of the macrocycle. On the other hand, silylallenes containing an acyclic substituent generated dimers except in a few cases where *N*-Hpth reacted at the propargylic center predominantly to form the corresponding aminoxy ethers. From these different products, we proposed a plausible mechanism for the reaction, which involved the abstraction of the allenic C(sp^2)−H hydrogen by *N*-phthalimidoxy radical to generate a propargylic carbon-centered radical as the key intermediate.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, spectral reproductions for all new compounds, and cif for **2d** and **2f**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02433.

Experimental procedures, characterization data, and spectral reproductions for all new compounds (PDF)
X-ray crystallographic data for **2d** (CIF)
X-ray crystallographic data for **2f** (CIF)

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Notes

The authors declare no competing financial interest.

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