Reaction of Silylallenes with Triplet Molecular Oxygen

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Reaction of Silylallenes with Triplet Molecular Oxygen

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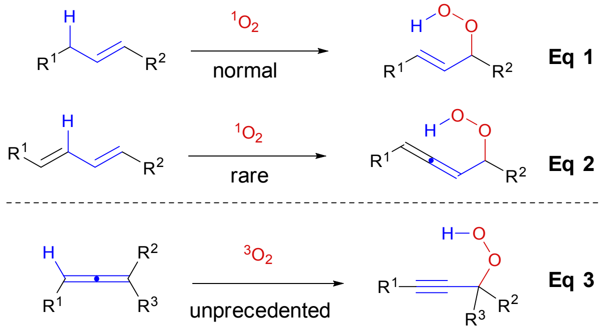
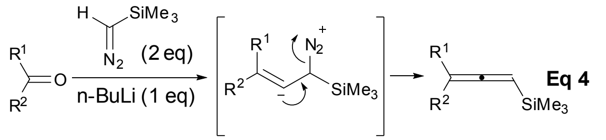
A facile formal ene reaction of trisubstituted silylallenes with triplet molecular oxygen involving the cleavage of a H–C(sp^2) bond has been discribed. For this formal ene reaction, the silyl substituent was found to be critical to induce the peroxide formation. The DFT calculations clearly shows the dramatic weaking of the allenic C(sp^2)–H bond by the α-silyl group.

Ene reaction is an allylic H–C bond is activated by the π-bond of an enophile, replacing the H–C bond with a C–C or C–X (X = O, N) bond with a concomitant double bond transposition.[1] Singlet oxygen[2] is a good enophile, which typically undergoes ene reactions with an allylic H–C(sp^3) bond (Eq 1). Rare examples of singlet oxygen-based Alder-ene reaction involving a C(sp^2)–H bond generating an allene product are also reported (Eq 2).[3,4] However, to the best of our knowledge, the corresponding ene reaction involving an allenic H–C(sp^2) bond generating an alkyne with a concomitant installation of propargylic peroxide has not been described in the literature (Eq 3).[5,6] Herein we report a formal ene reaction of silylallenes with triplet molecular oxygen, efficiently delivering propargylic peroxides.



Recently, we described one-step synthesis of silylallenes[7] **1** (Eq 4) and their reactivity[8] under various conditions involving oxidants and/or enophiles to induce nitration,[8a] copper-catalysed oxidative dimerization,[8b] and iron-catalysed oxidative transformations.[8c] During the synthesis of silylallenes **1**, sometimes the isolation of pure allene product was hampered by a contaminated byproduct. Soon after, it turned out that this byproduct is peroxide **2**,[9] which is assumed to be an autooxidation[10] product of the initially formed allene with molecular oxygen. Mechanistically, this formal ene reaction with triplet oxygen is quite intriguing, and thus we decided to examine the generality of this reaction with various allenes derived from a range of acyclic and cyclic ketones with different substituent patterns and ring sizes.[11]



First, we examined the autooxidation of allenes **1a–h** derived from the acyclic ketones (Table 1). Several salient features for these reactions involve that propargylic peroxides **2a–h** were isolated in excellent yields with complete conversion. The reaction in neat condition was much faster than in solution, but there was no difference between reactions under oxygen and air.[12] Even with minor structural difference in certain substrates, a significant rate difference ranging from 6 hours to two days was noticed. For example, complete conversion of cyclopropyl- and methyl-substituted allene **1b** was observed within 6 h as opposed to 48 h for allene **1a** containing phenylethyl- and methyl- substituents (Table 1, entries 1 and 2). On the other hand, the electronically different phenyl- and methyl-substituted allene **1c** was converted to the propargyl peroxide within 12 h (Table 1, entry 3). Also, allenes **1d** and **1e** differ by only oxygen vs. methylene at a remote site from the allene moiety showed significant difference in their overall reaction times. For example, allene **1d** took 24 h while allene **1e** took 48 h for completion (Table 1,

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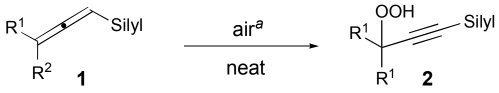
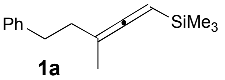
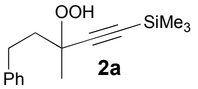
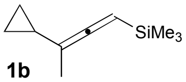
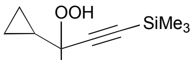
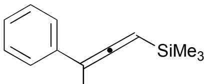
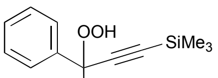
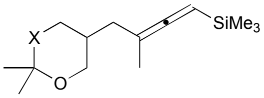
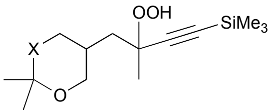
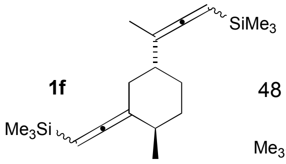
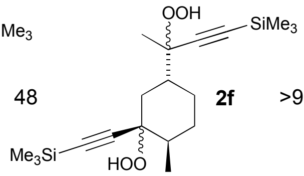
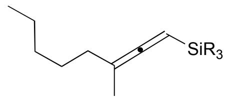
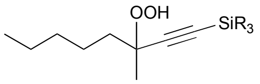
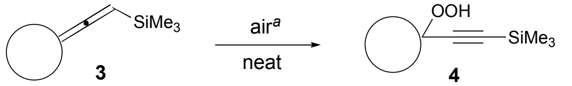
Table 1. Peroxide formation from silylallenes and oxygen

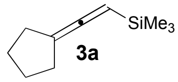
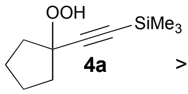
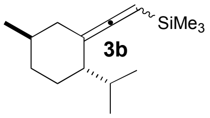
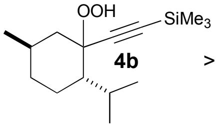
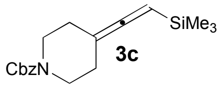
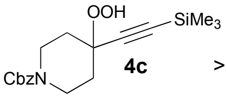
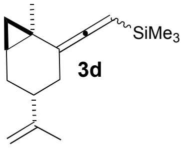
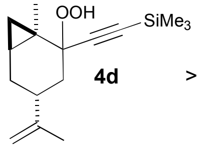
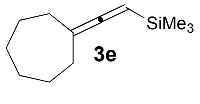
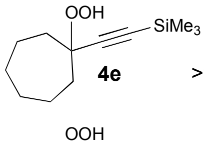
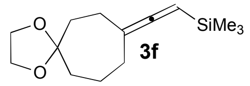
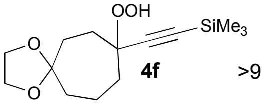
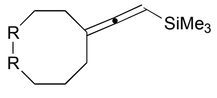
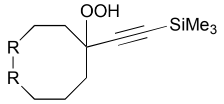
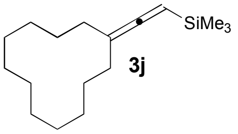
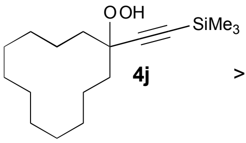


entry	allene	time (h)^b	peroxide	yield (%)^c
1	 **1a**	48	 **2a**	>95
2	 **1b**	6	 **2b**	>95
3	 **1c**	12	 **2c**	>95
4	 **1d** X = O	24	 **2d**	>95
5	**1e** X = CH_2	48	**2e**	>95
6	 **1f**	48	 **2f**	>95
7	 **1g** R = Et	48	 **2g**	>95
8	**1h** R = *i*Pr	48	**2h**	>95

[a] Reactions occurred in neat conditions under air. [b] Reaction times are reported based on the complete disappearance of the starting material. [c] ^1H and ^{13}C NMRs showed quantitative formation of peroxides with complete conversion, thus purification was unnecessary.

Table 2. Peroxide formation from cycloalkyl-based silylallenes and triplet oxygen



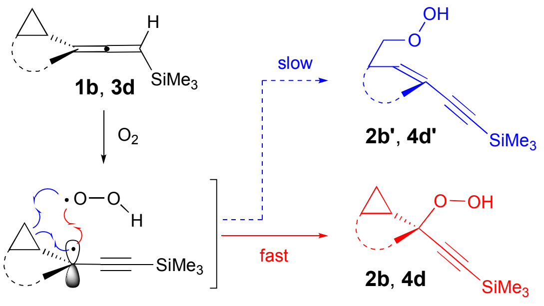
entry	allene	time (h)^b	peroxide	yield (%)^c
1	 **3a**	48	 **4a**	>95
2	 **3b**	48	 **4b**	>95
3	 **3c**	48	 **4c**	>95
4	 **3d**	48	 **4d**	>95
5	 **3e**	46	 **4e**	>95
6	 **3f**	46	 **4f**	>95
7	 **3g**, R−R = $H_2C{-}CH_2$	3	 **4g**^{d}	>95
8	**3h**, R−R = HC=CH	96	**4h**	>95
9	**3i**, R−R = $\underset{\mathrm{O}}{\mathrm{HC{-}CH}}$	72	**4i**	>95
10	 **3j**	48	 **4j**	>95

[a] Reactions occurred in neat conditions under air. [b] Reaction times are reported based on the complete disappearance of the starting material. [c] ^1H and ^{13}C NMRs showed quantitative formation of peroxides with complete conversion, thus purification was unnecessary. [d] The reaction time was confirmed by monitoring the reaction with ^1H NMR.

entries 4 and 5).[13] Allene moieties in **1f** showed similar reactivity, generating bis- peroxide **2f** (entry 6).[13] By the time when **1f** consumed completely, **2f** became predominant product although mono-peroxy intermediate was temporarily observed. Different silyl group other than trimethylsilyl ($SiMe_3$) in allenes **1g** containing $SiEt_3$ and **1h** containing Si^iPr_3 did not affect their reaction profiles, and thus propargyl peroxide products **2g** and **2h** were obtained in greater than 95% yields (Table 1, entries 7 and 8). In all cases, the propargyl peroxide are stable and the corresponding propargyl alcohols were not observed.

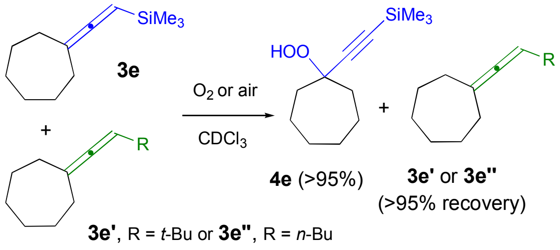
Next, we examined the autooxidation of cyclic ketones-derived silylallenes **3a–j** (Table 2). The general reactivity trend of these allenes is similar to that of **1a–h** except that the reaction times have a broader span, ranging from 3 h to 4days.[14] For example, cyclooctanylidene allene **3g** completely consumed within 3 h (entry 7)[15] while most allenes took 48 h. Allenes **3a–3d** with carbo- and heterocyclic five- and sixmembered rings provided peroxides **4a**–**4d** with similar reaction rates (Table 2, entries 1–4).[16] Seven-membered ring-containing allenes **3e** and **3f** also gave peroxide **4e** and **4f** (entries 5 and 6). Eight membered ring-containing allenes **3g**–**3i** showed somewhat contradicting behaviours. While **3g** was converted to peroxide **4g** within 3 h (Table 2, entry 7) the double bond-containing allene **3h** took 96 h for its complete conversion to **4h** (Table 2, entry 8), and the epoxide-containing allenes **3i** took 72 h to generate peroxide **4i** (Table 2, entry 9). Similarly, twelve membered ring-containing allene **3j** afforded peroxide **4j** within 48 h as other allenes (Table 2, entry 10).

In terms of reaction mechanism of this formal ene reaction, it is worth to note that the cyclopropyl moiety in **1b** and **3d** remained intact during the formation of peroxide **2b** and **4d**, and their cyclopropane ring-opened product **2b'** and **4d'** were not obtained (Scheme 1).[17] This implies that although the current peroxidation occurs through a stepwise mechanism involving a discrete radical intermediates the rate of the recombination of the carbon- and oxygen-centred radical species is faster than opening of the cyclopropane ring. In addition, identical reaction profiles were observed when **3d** was exposed to oxygen in dark or under sunlamp. However, when it was exposed to oxygen in the presence of a radical scavenger such as 4-methyl-2,6-ditertbutylphen-1-ol, **4d** was not observed even after 3 days. These experimental results suggest that triplet oxygen is involved in the reaction via its diradical nature[18] instead of singlet oxygen, but the rate of the reaction of the resultant propargylic radical with oxygen-centred radical should be faster than opening of the cyclopropane ring.



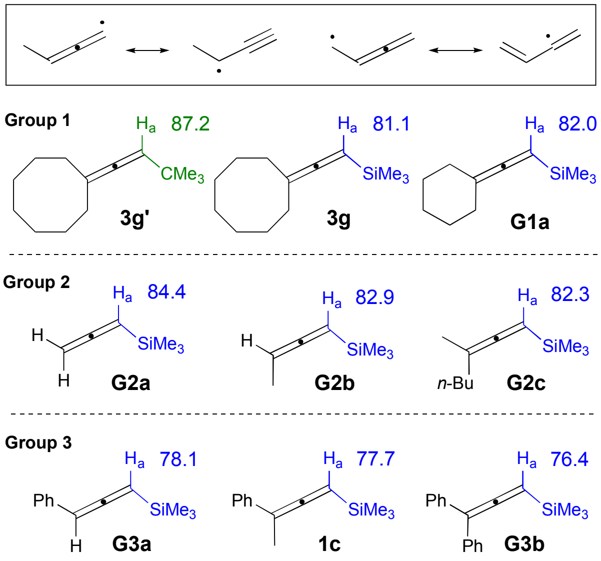
Scheme 1. A proposed mechanism for the reaction of silylallenes with triplet oxygen

At this juncture, we surmised that the silyl group in these allenes plays a critical role for activating the allenic $C(sp^2)$–H bond toward triplet oxygen because the related autooxidation of typical allenes with triplet molecular oxygen has no precedents in the literature. This notion was further supported by the lack of reactivity of *t*-butyl or *n*-Bu group-containing allenes **3e'** or **3e''** under oxygen atmosphere after 7 days, as opposed to the complete conversion of structurally similar trimethylsilyl group-containing allene **3e**, forming peroxide **4e** within 48 h, indicating dramatic activation of the α-$C(sp^2)$–H bond by the silyl group (Scheme 2).[19]



Scheme 2. Reactivity difference between silyl- and alkyl-substituted allenes

To rationalize the unusual reactivity of silylallenes toward molecular oxygen, we carried out DFT calculations on the bond-dissociation energy (BDE) of the allenic $C(sp^2)$–H bonds of structurally different allenes (Scheme 3). We surmised that the BDE of allenic $C(sp^2)$–H bond should be similar to that of typical allylic $C(sp^3)$–H bonds. This assumption is based on the consideration of the resonance contribution of the propargylic radical character. If the major contributing factor is indeed the stable propargylic radical, the substituents that can stabilize the radical would ultimately weaken the allenic $C(sp^2)$–H bond. The calculated BDE of allenes in Group 1–3 clearly support this hypothesis. The BDE of silylallenes containing a cycloalkyidene moiety (Group 1) and parent or alkyl-substituted silylallenes (Group 2) are similar, which is significantly lower that of non-silylated allene such as **3g'**. The BDE of phenyl-substituted silylallenes (Group 3) is roughly 6 kcal/mol lower than that of the corresponding alkyl-substituted allenes. The difference in BDE of different allenes correlates with their observed reactivity molecular oxygen.



Scheme 3. Calculated bond-dissociation energies (BDE) of structurally different allenes

In conclusion, we have discovered a new mode of formal ene reaction of silylallenes with triplet molecular oxygen involving the cleavage of a $C(sp^2)$–H bond. The reaction profile of this autooxidation process is significantly affected by the nature of substrate structure including the size of the ring as well as the degree of unsaturation and substituents around the ring. The reaction of a cyclopropyl-containing silylallenes provided products with intact cyclo-propane moiety, which is quite unexpected considering putative radical intermediate generated by triplet molecular oxygen. The facile reaction of silylallenes with molecular oxygen can be justified by DFT calculations of the BDE of allenic C(sp^2)–H bond of silylallenes, which is significantly low compared to the corresponding alkyl-substituted allenes.

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13 A mixture of two diastereomers of **2e** and a mixture of four diastereomers of **2f** was observed.

14 Under pure oxygen atmosphere, the reaction reached completion within much shorter time frame than under air.

15 For **3g**, the reaction was monitored with ^{1}H NMR twice to confirm the unusually short reaction time. The ^{1}H NMRs are added to Supporting Information.

16 A single diastereomer was observed for both peroxides **4b** and **4d**.

17 DFT calculations were performed to gain insight into the reaction mechanism. However, the calculated energies of transition states for both the concerted and stepwise mechanisms do not fall under reasonable ranges.

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