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LETTERS

Novel Diastereoselective Allene Formation by an Ene Reaction of Significantly Twisted 1,3-Dienes with Singlet Oxygen

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Abstract

The highly diastereoselective allene formation by photosensitized oxygenation of the significantly twisted novel 1,3-dienes which possess an sp^3 chiral center due to a secondary hydroxy group and a tertiary alkoxy group at allylic positions is described. © 1999 Elsevier Science Ltd. All rights reserved.

Key words: Diastereoselective, Allene formation, Twisted diene, Singlet oxygen.

Abstraction of an allylic hydrogen with singlet oxygen to produce an allyl hydroperoxide is a common ene reaction and has been known as the Schenck reaction. In 1993, it was reported that the ene reaction of secondary allyl alcohols with singlet oxygen proceeded in a highly diastereoselective manner, and it was pointed out that singlet oxygen would have some affinity for a hydroxy group.[1] Recently, we reported that the ene reaction of significantly twisted 1,3-dienes with singlet oxygen produced allenes in over 60% yield, resulting from the selective abstraction of vinyl hydrogens rather than allyl hydrogens.[2] This abnormal phenomenon is understandable by considering both effects of the large σ^*-π orbital interaction of the vinyl C-H bond with another double bond and the so called " nonbonding large group effect", which was proposed by Orfanopolas to understand the regioselectivity of the singlet oxygen ene reaction.[3] To advance our novel ene reaction, we investigated the diastereoselectivity of the photosensitized oxygenation of significantly twisted 1,3-dienes which possess an sp^3 chiral center due to a secondary hydroxy group or an alkoxy group at an allylic position. We now report the highly diastereoselective allene formation resulting from the ene reaction of a vinyl hydrogen. This is a novel example that the chirality at a sp^3 carbon is projected to the axial chirality of an allene by way of an atropisomerism of the twisted 1,3-diene.

Various twisted 1,3-dienes **1a-g** were synthesized by our own method, which involved sp^2-sp coupling catalyzed by Pd(0) followed by the partial reduction of the triple bond.[2a,b] Thus, vinyl bromide **2** prepared from mesityl oxide by bromination, dehydrobromination, followed by LAH reduction (90 % yield for 3 steps), was coupled with zinc acetylide **3** with the aid of Pd(0) catalysis to yield the ene-yne compound **4**,[4] which was followed by partial hydrogenation of its ethynyl group to produce **1a** in good yield. Diol **1e** was obtained by deprotection of the siloxy group in **1a**. Protection of the secondary hydroxyl group gave **1b-d**, and deprotection of the tertiary alkoxy moiety gave **1f-g** (Scheme 1). The photosensitized oxygenations of dienes **1** were carried out in CH_2Cl_2 by irradiation using a halogen lamp under oxygen atmosphere in the presence of a catalytic amount of tetraphenylporphin and two equivalents of triethylphosphite at 0 °C, and in the case of triethylsilyl ether **1a-d**, followed by TBAF treatment. The results of the photosesitized oxygenation are summarized in Scheme 2 and Table 1. The reactions of triethyl

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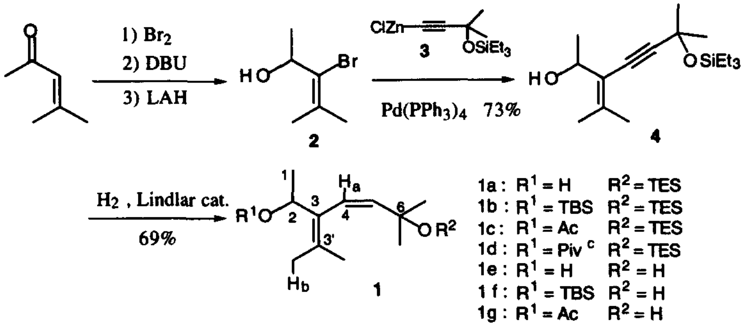
silyl ether **1a-d** preferentially produced allenes **5**[5] and **6** resulting from the abstraction of the vinyl hydrogen Ha rather than allyl alcohols **7** and **8** which were produced by the abstraction of the allyl hydrogen Hb, respectively (entries 1-5), whereas tertiary hydroxy compounds **1f-g** (entries 6-8) gave allyl alcohols **7** and **8** as major products. This selective production of the

Scheme 1



1a : R^1 = H R^2 = TES
1b : R^1 = TBS R^2 = TES
1c : R^1 = Ac R^2 = TES
1d : R^1 = Piv[c] R^2 = TES
1e : R^1 = H R^2 = H
1f : R^1 = TBS R^2 = H
1g : R^1 = Ac R^2 = H

Scheme 2

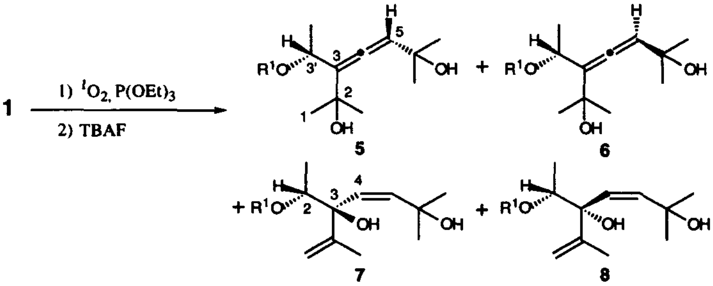


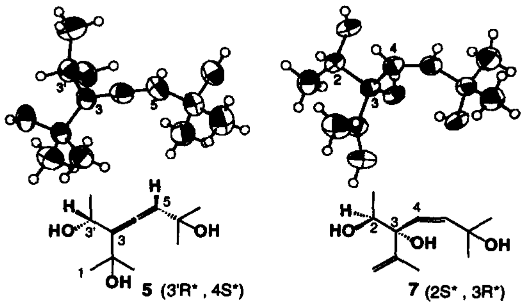
Table 1

entry		R^1	R^2	Solv.	R^1	5 : 6[a]	(yield)[b]	R^1	7 : 8[a]	(yield)[b]
1	(**1a**)	H	TES	CH_2Cl_2	H	19 : 1	(63%)	H	7.6 : 1	(28%)
2	(**1a**)	H	TES	MeOH	H	7.6 : 1	(58%)	H	3.3 : 1	(23%)
3	(**1b**)	TBS	TES	CH_2Cl_2	H	2.7 : 1	(49%)	H	1.9 : 1	(27%)
4	(**1c**)	Ac	TES	CH_2Cl_2	Ac	2.7 : 1	(50%)	Ac	2.0 : 1	(27%)
5	(**1d**)	Piv[c]	TES	CH_2Cl_2	Piv[c]	2.8 : 1	(55%)	Piv[c]	1.2 : 1	(26%)
6	(**1e**)	H	H	CH_2Cl_2	H	47 : 1	(27%)	H	19 : 1	(59%)
7	(**1f**)	TBS	H	CH_2Cl_2	TBS	> 99 : 1	(26%)	TBS	> 99 : 1	(73%)
8	(**1g**)	Ac	H	CH_2Cl_2	Ac	14 : 1	(34%)	Ac	14 : 1	(59%)

a) The ratios of each diastereomer were calculated based on the integral values of ^1H NMR spectra obtained.
b) Isolated yields c) Piv represents a pivaloyl group.

allenes **5** and **6** or the allyl alcohols **7** and **8** is understandable by considering the most stable conformation of the diene **1** as discussed previously.[2c] Meanwhile, the diastereoselectivity between **5** and **6** or **7** and **8** in the reaction of **1a** was, as expected, excellent, 19 : 1 and 7.6 : 1, respectively (entry 1). On the other hand, the diastereoselectivities in the cases of TBS ether **1b**, acetate **1c**, and pivalate **1d** were apparently poorer than that of the free hydroxy compound **1a** (entries 3-5). In addition, in methanol the photosensitized oxygenation of **1a** showed lower selectivity than that in dichloromethane (entry 2). These results obtained clearly demonstrated that the remarkable hydroxy group directing effect was also observed in our twisted 1,3-diene system as well as the simple allyl secondary hydroxy compounds.[1a] Moreover, in the case of diol **1e** which produced allyl alcohols **7** and **8** as major products,[2] the diastereoselectivities of both the allenes and the allyl alcohols were much higher than those of triethylsilylether **1a**. However, in the case of silyl ether **1f**, surprisingly only one diastereomer in both the allene and the allyl alcohol was obtained, respectively, and the diastereoselectivity of the ene reaction of acetate **1g** was also excellent, although the secondary hydroxy group at the chiral center C1 in **1f-g** was thus protected.

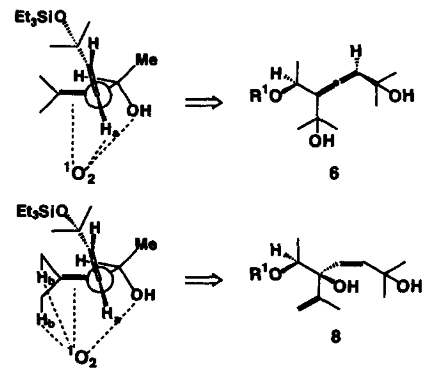
Fig.1



5 (3'R*, 4S*)

7 (2S*, 3R*)

Fig.2



6

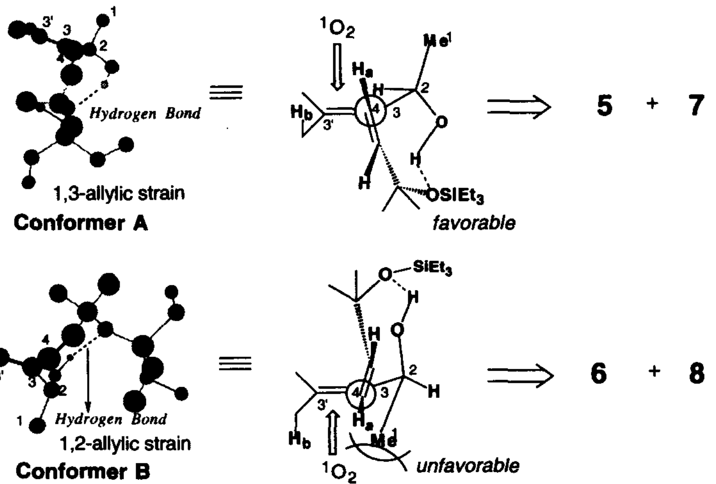
8

The structures of the obtained major isomers of both the allene and the allyl alcohol were determined by X-ray analysis as 3',5-*syn*-**5** and 2,3-*anti*-**7**, respectively, as shown in Fig.1. If the previously proposed mechanism for diastereoselective photosensitized oxygenation of allyl alcohols was applied to the present compounds, the alcohol **1a** should produce 3',5-*anti*-**6** and 2,3-*syn*-**8** as major diastereomers as shown in Fig.2. Thus, X-ray analysis revealed that the face selectivity of the singlet oxygen ene reaction toward **1** was proved to be contrary to the case of the reported normal olefins. The stable conformation of the twisted 1,3-diene **1a**, which was obtained by MM2 calculation,[6] indicated that an intramolecular hydrogen bond[7] was admitted between the C2 or C6 hydroxy group and the C6 or C2 oxygen atom, respectively, and it can exist in two atropisomers, conformers A and B, as shown in Fig.3.[8] In the conformer A, the rotation around the C2 chiral center is restricted due to 1,3-allylic strain between the C2 substituent and the C4' methyl group. In the other conformer B, the rotation around the C2 chiral center is restricted by 1,2-allylic strain between the C2 substituent and the C4 twisted vinyl group. When we focus on the allene formation step, the attack of singlet oxygen to conformer A gives the allene **5** having the 3',5-*syn* configuration, while that to conformer B gives the allene **6** having the 3',5-*anti* configuration as shown in Fig.3. Considering the nonbonding interaction between singlet oxygen and the C1 methyl group in the transition state of this reaction, the C1 methyl group in conformer A is located outside of the C3-C3' olefin plane, while in conformer B it is present inside of that plane. The reaction would proceed through the conformer

A rather than the conformer B because of the severe nonbonding interaction between singlet oxygen and the C1 methyl group in the conformer B. A similar discussion as described above can also be applicable to the selective formation of the allyl alcohol **7**.

In conclusion, we have found the highly diastereoselective allene formation by photosensitized oxygenation of the significantly twisted 1,3-dienes which possess an sp^3 chiral center due to a secondary hydroxy group and a tertiary alkoxy group at allylic positions. The observed novel chiral projection from an sp^3 carbon into an allene is understandable by consideration of the following two factors : one is the conformational analysis based on the intramolecular hydrogen bonding in the substrate, which stabilizes the two atropisomers A and B, and the other is the nonbonding interaction between singlet oxygen and the substituent.

Fig. 3



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5. Data for 5; ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.44(1H, d, J=1.7 Hz), 5.18(1H, s), 4.91(1H, s), 4.85(1H, d, J=3.9 Hz), 4.59(1H, dqd, J=3.7, 6.4, 1.7 Hz), 1.38-1.34(12H, m), 1.26(3H, d, J=6.4 Hz).
6. The geometries were optimized with MM2 forcefield using Macro Model verson 5.5 and 6.0.
7. In ^{1}H NMR, the hydroxy groups in **1a**, **e** and **f** were observed at 3.2-4.2 ppm, while those of the **2** and **4** were 1.6-2.0 ppm. These differences would support the intramolecular hydrogen bonding in **1a,e** and **f**.
8. The stable conformations of **1a,e** and **f** were very similar, therefore, the pictorial conformation is represented by that of **1a**.