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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.

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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 $\sigma^* \cdot \pi$ 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 CH₂Cl₂ 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 5⁵ 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



Scheme 2



Table 1

entry		R1	R ²	Solv.	R ¹	5 : 6 ^a (yield) ^b		R ¹	7:8ª	(yield) ^b
1	(1a)	н	TES	CH2CI2	н	19 : 1	(63%)	н	7.6 : 1	(28%)
2	(1a)	н	TES	MeOH	н	7.6 : 1	(58%)	н	3.3 : 1	(23%)
3	(1b)	TBS	TES	CH ₂ Cl ₂	н	2.7 : 1	(49%)	н	1.9 : 1	(27%)
4	(1c)	Ac	TES	CH ₂ Cl ₂	Ac	2.7 : 1	(50%)	Ac	2.0 : 1	(27%)
5	(1d)	Piv ^c	TES	CH2CI2	Piv ^c	2.8 : 1	(55%)	Piv ^c	1.2 : 1	(26%)
6	(1e)	н	н	CH2Cl2	н	47:1	(27%)	н	19:1	(59%)
7	(1f)	TBS	н	CH ₂ Cl ₂	TBS	> 99 : 1	(26%)	TBS	> 99 : 1	(73%)
8	(1g)	Ac	н	CH ₂ Cl 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.² 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 (entry1). 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 that 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.¹ 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 elcohols were much higher than those of triethylsilylether 1a. However, in the case of silyl ether 1f, surprisingly only one 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.







The structures of the obtained major isomers of both the allene and the allyl alcohol were determined by Xray 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 2,3syn-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 intrahydrogen molecular bond was admitted between the C2 or **C**6 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 1,3allylic 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 1.2allylic 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 CI 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. Acknowledgement: This work was supported by Grant-in-Aid for Scientific Research on Priority Areas(No. 283, "Innovative Synthetic Reactions") from Monbusho. References and Notes

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- 5. Data for 5; ¹H NMR(400 MHz, CDCl₃) 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.
- In ¹H 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.