

Further demonstration of the higher reactivity of the vinyl hydrogen rather than the allyl hydrogen towards singlet oxygen

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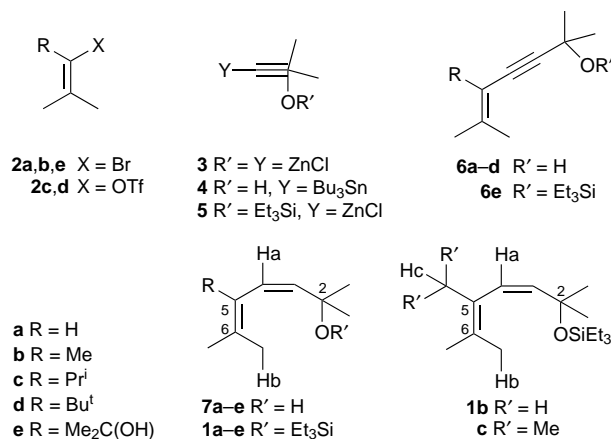
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In a new linear twisted 1,3-diene, an anomalously high reactivity of the vinyl hydrogen rather than the allyl hydrogen towards singlet oxygen is observed.

Previously, we reported the photosensitized oxygenation of significantly twisted *cis*- β -ionol derivatives, and found the vinyl hydrogen to be anomalously more reactive towards singlet oxygen than the allyl hydrogen in some significantly twisted compounds of *cis*- β -ionol derivatives. We proposed that this unusually high reactivity of the vinyl hydrogen in a significantly twisted 1,3-diene should be attributed to a large interaction between the σ^* orbital of the vinyl hydrogen and the π orbital of another double bond.¹ Since only a few examples of significantly twisted 1,3-dienes are found in the literature,² although conjugated dienes are some of the most common systems in organic reactions as represented by pericyclic reactions, further investigation on the design, synthesis and photosensitized oxygenation of significantly twisted 1,3-dienes has been required. Here we report the photosensitized oxygenation of a newly designed linear twisted 1,3-diene, and describe a further demonstration of the unusually high reactivity of the vinyl hydrogen towards singlet oxygen.

The substrates **1a–e** were chosen for the photosensitized oxygenation because the substituent R on the olefin can be changed from hydrogen to methyl, isopropyl and *tert*-butyl, and when R is a bulky substituent the 1,3-diene structure would be twisted. Syntheses of these *cis*-1,3-diene derivatives were accomplished by palladium catalysed coupling of the appropriate vinyl halides or enol trifluoromethanesulfonates (triflates) with zinc or stannyl acetylides followed by partial hydrogenation and then protection of the tertiary hydroxy group. Thus, compounds **6a,b** were prepared from commercially available vinyl bromides **2a,b** by reaction with zinc acetylide **3** in the presence of tetrakis(triphenylphosphine)palladium (THF, 60 °C; **6a**, 80%; **6b**, 45% yield), respectively.³ Compounds **6c,d** which have bulky substituents were synthesized by coupling of stannyl acetylide **4** with enol triflates **2c,d**,⁴ which were prepared from the corresponding ketones⁵ (LDA, *N*-phenyltrifluoromethanesulfonimide, THF), in the presence of the same palladium reagent (THF, room temp.; **6c**, 45%; **6d**, 52% yield).⁶ Another enyne compound **6e** was also synthesized by coupling of vinyl bromide **2e**, prepared from methyl 3,3-dimethylacrylate ($\text{Br}_2\text{-CH}_2\text{Cl}_2$, DBU-THF, MeMgI-THF ; 46% yield), with **5** under the same conditions as those of **2a,b** (**6e**, 84% yield). Partial reduction of the acetylene groups of **6a–e** to the corresponding *cis*-olefins by catalytic hydrogenation in hexane reflected the reactivity of their acetylene groups. Thus, **7a,b** were obtained with Lindlar catalyst in the presence of a catalytic amount of quinoline (**7a**, 47%; **7b**, 49% yield). In the absence of quinoline with Lindlar catalyst, **7c** was obtained (47% yield). Hydrogenation of **6d** with palladium on barium sulfate gave **7d** (60% yield) and of **6e** with palladium on charcoal gave **1e** (MeOH, 90% yield). The *cis*-alcohols obtained were transformed into the corresponding triethylsilyl ethers **1a–d** in excellent yield (Et_3SiCl , DMAP, Et_3N , DMF).[†] The maximum absorption values in the electronic spectra of compounds **1b–e** were less than 210 nm, whereas that of **1a** was 238 nm. These data clearly show that

1b–e are significantly twisted around the central single bond of the 1,3-diene. The most stable conformations of **1b–e** obtained by molecular mechanics calculations and molecular orbital calculations also support the significantly twisted structures.^{1§}

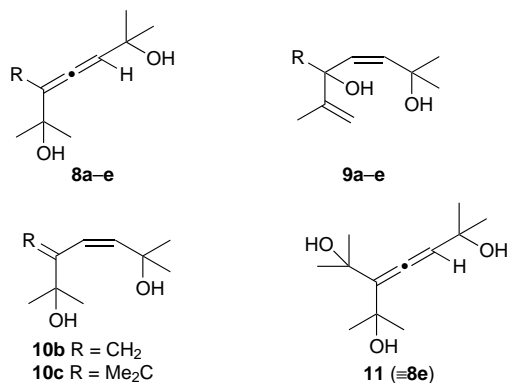


The photosensitized oxygenation of **1a–e** was carried out in CH_2Cl_2 (1.0–2.0 mmol scale) by irradiation using a halogen lamp under an oxygen atmosphere in the presence of a catalytic amount of tetraphenylporphine and 1 equiv. of triphenylphosphine at 0 °C. The products were isolated by column chromatography and all of them were characterized by ^1H , ^{13}C NMR and IR spectroscopy, and by elemental analysis or high resolution mass spectra for some compounds. The ene reaction of Ha and Hb gave allene **8** and isopropenyl compound **9**, respectively. In the case of **1b,c**, the ene reaction of Hc gave compounds **10b,c**, which might produce allene **11** by further oxygenation. The results of the photosensitized oxygenation are shown in Table 1. For compounds **1d,e**, allenes **8d,e** (mp 76–77 °C) were produced in 75 and 74% yield along with isopropenyl compounds **9d,e** in 8 and 9% yield, respectively. In these cases, the abstracted vinyl hydrogen Ha and allyl hydrogen Hb are located at the opposite sides of the C5–C6 double bond, and the vinyl hydrogens Ha were much more reactive than the allyl hydrogens Hb toward singlet oxygen.^{7¶}

Table 1 Ene reaction of acyclic twisted 1,3-dienes with singlet oxygen

Substrate	Yield (%)			
	8^a	9^a	10^{a,b}	11^{a,b}
1a	29 ^b	45 ^b	—	—
1b	32 ^b	12 ^b	42	—
1c	38 ^b	27 ^b	8	17
1d	75 ^b	8 ^b	—	—
1e	74 ^c	9 ^c	—	—

^a Isolated yield. ^b The yields are over three steps; silylation of the corresponding alcohol followed by photosensitized oxygenation and then desilylation. ^c The yields are over two steps; photosensitized oxygenation and desilylation.



These results are compatible with those of the cyclic system reported previously. On the other hand, compound **1a** produced allene **8a** in 29% and isopropenyl compound **9a** in 45% yield, respectively. Photosensitized oxygenation of **1b** gave allene **8b** and allyl alcohol **10b** in 32 and 42% yield, respectively, along with isopropenyl compound **9b** in 12% yield. Since both the abstracted vinyl hydrogen Ha and the allyl hydrogen Hc in **1b** are located at the same side of the C5–C6 double bond, and the ene reactions of the Ha and the Hc with singlet oxygen gave the allene **8b** and the allyl alcohol **10b**, respectively, the relative yields of **8b** and **10b** obviously reflect the relative reactivity of the vinyl hydrogen and the allyl hydrogen. It is worth noting that the vinyl hydrogen shows comparable reactivity to the allyl hydrogen. Next, in the photooxygenation of **1c**, allene **8c**, isopropenyl compound **9c**, diene **10c** and trihydroxyallene **11**, which is identical to **8e**, were obtained in 38, 27, 8 and 17% yield, respectively. In this case, compound **11** must be produced from **10c**, giving a 25% yield of allyl hydrogen Hc abstracted products. It is noteworthy that the vinyl hydrogen Ha of **1c** was more reactive than the isopropyl hydrogen Hc, and that the sterically hindered hydrogen Hc in **1c** reacted with singlet oxygen to a similar extent as the allyl hydrogen Hb.

Unfortunately, we did not observe a clear relationship between the bulkiness of the C5 substituent and the twisting of

the two double bonds, and hence between the extent of twisting and the yield of the oxygenated products. However, the evidence suggests that twisting and/or the C5 substituent have an effect on the reactivity of 1,3-dienes, since the relative proportions of C6 and C5 hydroxy products in the significantly twisted **1b–e** were the opposite to that of the conjugated **1a**, thus the proportions of C6 and C5 hydroxy products in **1b–e** were 63–75 vs. 27–8, while for **1a** the proportion was 29 vs. 45.

The results obtained here seem to support our proposal on the activation of the vinyl hydrogen based on $\sigma^*-\pi$ orbital interaction between the vinyl C–H bond and another double bond in significantly twisted 1,3-dienes.¹

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Footnotes and References

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† The triethyl group on the silyl ethers is essential. See ref. 1.

§ The calculations were performed using software packages INSIGHT II 2.1.0 program, Biosym. Technol. Inc. San Diego, USA, with CFF91 forcefield and SPARTAN version 3.1 and 4.0 Wavefunction, Inc., Irvine, CA with STO-3G basis set.

¶ The regioselectivity of an ene reaction with singlet oxygen is discussed in ref. 7.

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