Highly Activated Vinyl Hydrogen in a Significantly Twisted Styrene
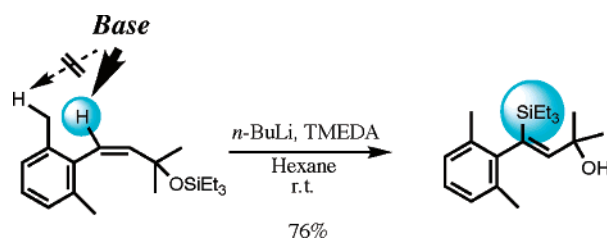
Hajime Mori,*,†,§ Takafumi Matsuo,† Yasunori Yoshioka,‡ and Shigeo Katsumura*,†

School of Science and Technology, Kwansei Gakuin University, 2−1 Gakuen, Sanda, Hyogo 669-1337, Japan, and Department of Chemistry, Mie University, 1577 Kurimamachiya-cho, Tsu-shi, Mie 514-8507, Japan

hmori@wakayama-kg.go.jp; katsumura@ksc.kwansei.ac.jp

The novel example of a vinylic hydrogen more reactive than a benzylic hydrogen was found by treatment of a twisted styrene derivative with a strong base followed by D_2O quenching. In this paper, the full details of the examples of the highly activated vinyl hydrogens in twisted styrene derivatives are described, with a discussion on the correlation between the reactivity of the vinyl hydrogens and the magnitude of the twist. The highly reactive vinyl hydrogens could be rationalized by considering the novel orbital interaction between the π^* orbital of the benzene ring and the σ orbital of the vinylic C−H bond in the twisted styrene derivatives.

Introduction

Vinylic σ bond activation based on $\sigma-\pi$ orbital interaction, which leads to a remarkable acceleration of the reactions, can be found in the chemistry of stabilized vinyl cations reported nearly 30 years ago.[1] Thus, it was reported that the solvolysis of vinyl halides, triflates, or tosylates in significantly twisted 1,3-dienes or styrenes around the central single bond was strongly accelerated based on the pronounced stabilization on the intermediary vinyl cations. Although this example can also

be regarded as the pioneering work to study the characteristic nature of these twisted 1,3-dienes or styrenes, for 30 years their unique character had not been paid any attention in other types of reactions such as an anionic reaction.

Recently, during the course of our synthetic study of the allene carotenoid peridinin, we have found the novel character of significantly twisted 1,3-dienes in the ene reaction of singlet oxygen.[2] Thus, the vinyl hydrogen in the significantly twisted *cis-β*-ionol derivatives was selectively abstracted by singlet oxygen over the allyl hydrogen to give the corresponding allene compound in good yield.[2,3] The detailed consideration concern-

* To whom correspondence should be addressed. (H.M.) Tel: +81-73-477-1271. Fax: +81-73-477-2880. (S.K.) Tel: +81-795-65-8314.

† Kwansei Gakuin University.

‡ Mie University.

§ Present address: Industrial Technology Center of Wakayama Prefecture, Ogura 60, Wakayama, 649-6261, Japan.

(1) (a) Grob, C. A.; Spaar, R. *Tetrahedron Lett.* **1969**, 1439. (b) Grob, C. A.; Spaar, R. *Helv. Chim. Acta* **1970**, *53*, 2119. (c) Grob, C. A.; Pfaendlar, H. R. *Helv. Chim. Acta* **1970**, *53*, 2130. (d) Lamparter, E.; Hanack, M. *Chem. Ber.* **1973**, *106*, 3216. (e) Yates, K.; Rerie, J. J. *J. Org. Chem.* **1974**, *39*, 1902. (f) Hanack, M. *Acc. Chem. Res.* **1976**, *9*, 364. (g) Rappoport, Z. *Acc. Chem. Res.* **1976**, *9*, 265. (h) Apeloig, Y.; Schleyer, P.; Pople, J. A. *J. Org. Chem.* **1977**, *42*, 3004. (i) Hanack, M.; Sposser, L. *J. Am. Chem. Soc.* **1978**, *100*, 7066.

(2) (a) Mori, H.; Ikoma, K.; Isoe, S.; Kitaura, K.; Katsumura, S. *Tetrahedron Lett.* **1996**, *37*, 7771. (b) Mori, H.; Ikoma, K.; Katsumura, S. *Chem. Commun.* **1997**, 2243. (c) Mori, H.; Ikoma, K.; Isoe, S.; Kitaura, K.; Katsumura, S. *J. Org. Chem.* **1998**, *63*, 8704. (d) Mori, H.; Matsuo, T.; Yamashita, K.; Katsumura, S. *Tetrahedron Lett.* **1999**, *40*, 6461.

(3) Although the first example of allene formation by the ene reaction of vinyl hydrogen in *trans-β*-ionol derivatives has been already reported, the yields of the allene were less than 10%. (a) Isoe, S.; Hyeon, B. S.; Ichikawa, H.; Katsumura, S.; Sakan, T. *Tetrahedron Lett.* **1968**, 5561. (b) Isoe, S.; Katsumura, S.; Hyeon, S. B.; Sakan, T. *Tetrahedron Lett.* **1971**, 1089. (c) Mousseron-Canet, M.; Dalle, J-P.; Mani, J-C. *Tetrahedron Lett.* **1968**, 6037. (d) Foote, C. S.; Brenner, M. *Tetrahedron Lett.* **1968**, 6041.

ing the results of both *cis-β*-ionol derivatives and acyclic twisted 1,3-dienes made it clear that their inherent reactivity toward singlet oxygen is nearly equal to or higher than that of the allyl hydrogen. The molecular mechanics and orbital calculations of the twisted substrates revealed that the activation of the vinyl hydrogen is due to the large orbital interaction between the σ^* orbital of the vinyl C−H bond and the π orbital of the double bond. This unique character during the cationic and concerted reactions has thus been demonstrated, and these results introduced us to the investigation of the anionic reaction media.

It is well-known that allyl and benzyl hydrogens are more reactive than vinyl hydrogens, and these sp³ hydrogens can be gradually abstracted with a strong base.[4] Their relatively higher reactivity is attributable to activation due to orbital interaction between the σ orbital of the allylic or benzylic C−H bond and the π orbital of the neighboring double bond and to delocalization of the generated anion into the neighboring double bond. If we could design a vinylic C−H bond, the σ orbital of which significantly interacts with the π orbital of the neighboring double bond, it might be activated equal to the allylic or benzylic C−H bond, and we might realize a chemoselective vinyl anion formation rather than the allyl or benzyl one as a result of their difference in pK_a values. Therefore, these hydrogens would be regarded as more reactive vinyl hydrogens than the allyl or benzyl hydrogens. Some noticeable examples about the above reactive vinyl hydrogen have been presented previously.[5−8] Thus, the acidity of 1,3-butadiene was investigated by Fourier-transform ion-cyclotron-resonance mass spectrometer and theoretical calculation.[5] It was revealed that 2-butadienyl anions are more stable than 1-butadienyl anions, and the former, which have two orthogonal π-systems, show additional stabilization due to charge delocalization. Furthermore, it was reported by Bierbaum et al. that the vinyl hydrogens of cyclooctatetraene, in which the double bonds are twisted in relation to each other, are also activated and the bond strength was much weaker than that of typical sp² C−H bond.[6]

The pioneering results concerning the facile vinyl proton abstraction by a strong base have been reported under specific circumstances, such as the hydrogen contained in a small ring system.[9] It was concluded that the increase of s character of a C−H bond in a strained ring system contributes to the ease of vinyl proton abstraction. Another example, in which the vinyl hydrogen is located at a seven-membersed ring, was also reported,[10] and the participation of the extra double bond for the kinetic acidity of the vinyl hydrogen was proposed. Although a few elegant examples have been demonstrated before,
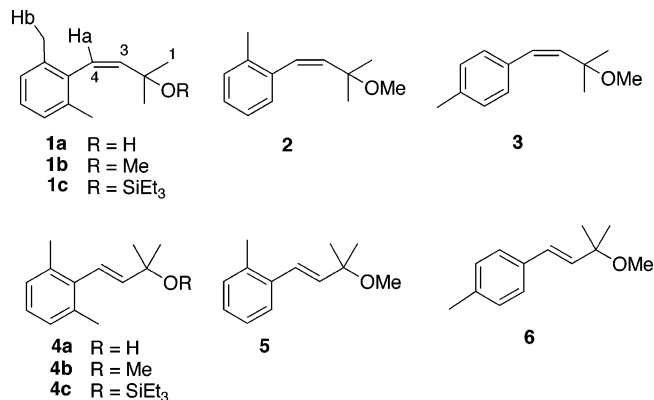
(4) For example: Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York, London, 1965; p 19.

(5) (a) Visser, S. P.; Koning, L. J.; Hart, W. J.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 267.

(6) (a) Kato, S.; Lee, H. S.; Gareyev, R.; Wenthold, P. G.; Lineberger, W. C.; Depuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1997**, *119*, 7863. (b) Kato, S.; Gareyev, R.; Depuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1998**, *120*, 5033.

(7) The typical reactive vinyl hydrogens at allylic positions can be found at an allene compound, and a strong base easily abstracted the vinyl protons. (a) Dongen, J. P. C. M.; Dijkman, H. W. D.; Bie, M. J. A. *Recl. Trav. Chim. Pays-Bas*, **1974**, *93*, 29. (b) Reich, H. J.; Holladay, J. E.; Walker T. G.; Thompson, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 9769.

(8) (a) Levin, G.; Jagur-Grodizinski, J.; Szwarc, M. *J. Org. Chem.* **1969**, *34*, 1702. (b) Levin, G.; Ward, T. A.; Szwarc, M. *J. Am Chem. Soc.* **1974**, *96*, 3590.
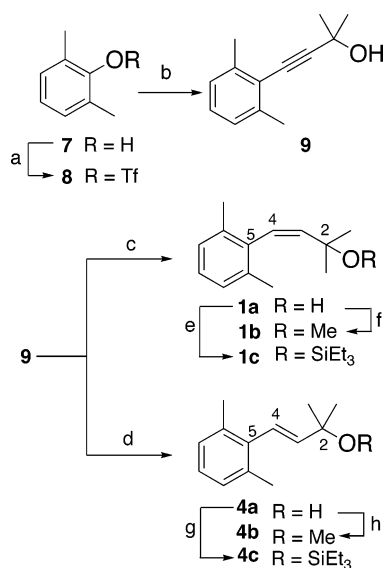
(9) (a) Morton, A. A.; Finnegan, R. A. *J. Polym. Sci.* **1959**, *38*, 19. (b) Broaddus, C. D.; Muck, D. L. *J. Am. Chem. Soc.* **1967**, *89*, 6533.

(10) Stähle, M.; Lehmann, R.; Kramar, J. Schlosser, M. *Chimia* **1985**, *39*, 229.

FIGURE 1. Designed styrene derivatives.

activated vinyl hydrogens rather than ally or benzyl hydrogens in a 1,3-diene system have not been fully investigated, especially with the discussion of the tendency of the twist.

In a preliminary communication, as a new entry for the unique character of the twisted 1,3-dienes or styrene derivatives, we have reported that the novel example of the vinyl hydrogens in the significantly twisted styrenes are more reactive than the benzyl hydrogens toward a base.[11]

In this paper, we describe the full details of the base treatment of various kinds of twisted styrenes, along with a discussion on the correlation between the magnitude of the twist and the reactivity of the vinyl hydrogens. The mechanistic consideration of the proton abstraction and the formation of the products, whose vinylic positions were substituted by deuterium or the triethylsilyl group, is also described.

Results and Discussion

Synthesis and Conformational Analysis of Twisted Styrene Derivatives. We designed new twisted styrene derivatives **1−6**, based on our previous studies concerning the investigation of the ene reaction of singlet oxygen (Figure 1).[3]

To efficiently synthesize the wide variety of styrene derivatives, our own Pd-catalyzed coupling method was adopted.[9] Although during the synthesis of the acyclic twisted 1,3-dienes the Pd catalyst worked well to give the corresponding coupling compounds, the catalyst did not work well for the cross-coupling between the aryl triflate **8**, which was prepared from commercially available 2,6-dimethylphenol **7**, and acetylene derivatives. The steric hindrance might be severe around the triflate moiety. The reaction was investigated under various conditions, and we finally found that the presence of tetrabutylammonium iodide was extremely effective for this reaction.[12] Thus, the reaction of the aryltriflate **8** with 2-methyl-3-butyn-2-ol in the presence of 3 equiv of tetrabutylammonium iodide, a catalytic amount of PdCl$_2$(PPh$_3$)$_2$, and CuI gave the coupling compound **9** in good yield (Scheme 1). Partial reduction of the acetylene moiety with Pd−C under a hydrogen atmosphere gave the *Z* isomer **1a**, and LAH reduction in THF[13] gave the *E* isomer **4a**. The methylation or silylation of the tertiary hydroxy group was conducted under the usual conditions to afford the corresponding

(11) Mori, H.; Matsuo, T.; Yoshioka, Y.; Katsumura, S. *Tetrahedron Lett.* **2001**, *42*, 3093.

(12) Powell, N. A.; Rychnovsky, S. D. *Tetrahedron Lett.* **1996**, *37*, 7901.

(13) Grant, B.; Djerassi, C. *J. Org. Chem.* **1974**, *39*, 968. Doering. W. E.; Benkhoff, J.; Carleton, P. S.; Pagnotta, M. *J. Am. Chem. Soc.* **1997**, *119*, 10947.

SCHEME 1 [a]

[a] Reagents and conditions: (a) Tf$_2$O, Et$_3$N (99%); (b) 2-methyl-3-butyn-2-ol, PdCl$_2$(PPh$_3$)$_2$, CuI, Bu$_4$NI, Et$_2$NH (47%); (c) Pd/C, H$_2$ (86%); (d) LAH/THF (72%); (e) TESCl, DMAP, Et$_3$N (90%); (f) NaH, Bu$_4$NI, MeI (98%); (g) TESCl, DMAP, Et$_3$N (42%); (h) NaH, Bu$_4$NI, MeI (75%).

FIGURE 2. Electronic spectra of various styrene derivatives.

methyl ether **1b** and **4b** and silyl ether **1c** and **4c**, respectively. The other derivatives **2**, **3**, **5**, and **6** (Figure 1) were also synthesized in good yields by the Pd-catalyzed cross-coupling strategy described above from the corresponding iodides, respectively.

Since we obtained the twisted styrene derivatives **1−6**, next was the investigation of the magnitude of the twist between the benzene ring and the double bond of these derivatives based on both the electronic spectra and molecular orbital calculations. The electronic spectra were taken in heptane. The maximum absorption values of all *Z* isomers **1a−1c** were less than 210 nm, and those of the *E* isomers **4a−c**, **5**, and **6** clearly appeared between 230 and 260 nm. The spectrum of **2** showed a broad absorption from 220−250 nm, and for compound **3** the maximum absorption of the K-band clearly appeared at 251 nm ($\epsilon = 13000$), as shown in Figure 2. Compared with the spectrum of styrene, the K-band of which clearly appears at 245 nm, we easily noted that the *Z* isomers **1a−1c** were definitely twisted around the C4−C5 single bond. The geometries of the methyl ethers **1b**, **2**, **3**, **4b**, **5**, and **6** were optimized at the Hartree−Fock/6-31G level using the Gaussian 94 program package, and the dihedral angles between the benzene ring and the double bond of the *Z* isomers **1b**, **2**, and **3** were 85°, 84°, and 53°, respectively, whereas those of the *E* isomers **4b**, **5**, and **6** were 65°, 39°, and 21°, respectively.[14]

Vinyl Proton Abstraction of *E* and *Z* Isomers of Twisted Styrene. Among the various kinds of strong bases that can abstract the proton of low acidic hydrocarbons, we chose the BuLi/*N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TMEDA) com-

plex[15] as a suitable base because of its simplicity of preparation and sufficient stability. Thus, the reaction was carried out for 1 h at room temperature using 5 equiv of *n*-BuLi and 2.5 equiv of TMEDA, and the resulting anion was quenched with D$_2$O. The obtained mixture was analyzed by ^{1}H NMR without any purification, and the yields were calculated on the basis of a comparison of the integral value of the ^{1}H NMR spectrum between the signal of the starting material and that of the deuterized compound. Treatment of the entirely twisted styrene **1b** with the base in hexane produced the *E* isomer **10**, whose vinylic hydrogen was deuterized in approximately 60% yield, along with the starting material (Scheme 2). The structure of the obtained product **10** was confirmed by a comparison with the independently synthesized compound, which was derived from **9** by LAH reduction followed by D$_2$O treatment and methyl ether formation.

The base treatment of the *Z* silyl ether **1c** produced the unexpected product **11**, despite D$_2$O treatment of the reaction mixture. No deuterium compound was detected by the ^{1}H NMR spectra (Scheme 2). The detailed analysis of the spectral data (NMR, MS, IR) strongly suggested that the triethylsilyl group migrated to the vinylic position to produce **11**. Although the precise structure, in particular, the geometry of the double bond, could not be elucidated by the spectral data, the crystal structure of the corresponding chromium tricarbonyl complex **12** was fortunately determined by X-ray analysis to be the *Z* form, as shown in Figure 3. The geometry of the C7−C8 double bond of **11** was strongly suggested to be the *Z* form. The reaction pathway for the formation of the compounds **10** and **11** will be discussed in detail in the following paragraph.

Under the same treatment, the moderately twisted *E* isomer **4b** also gave compound **10** in 60% yield. The vinyl anion formation of the *E* isomer would be partly assisted by the

(14) Doering. W. E.; Benkhoff, J.; Carleton, P. S.; Pagnotta, M. *J. Am. Chem. Soc.* **1997**, *119*, 10947. A detailed investigation of the conjugation in substituted styrene was reported by Doering's group. The dihedral angles between the benzene ring and a double bond toward various types of styrene derivatives were shown in his report. In the *o*-dimethylphenyl styrene derivatives, they were nearly perpendicular to each other. A study on the solvolysis of a twisted styrene was reported by Yate and coworkers, and the *o*-dimethylphenyl styrene derivatives were adopted as a significantly twisted substrate.[2e]

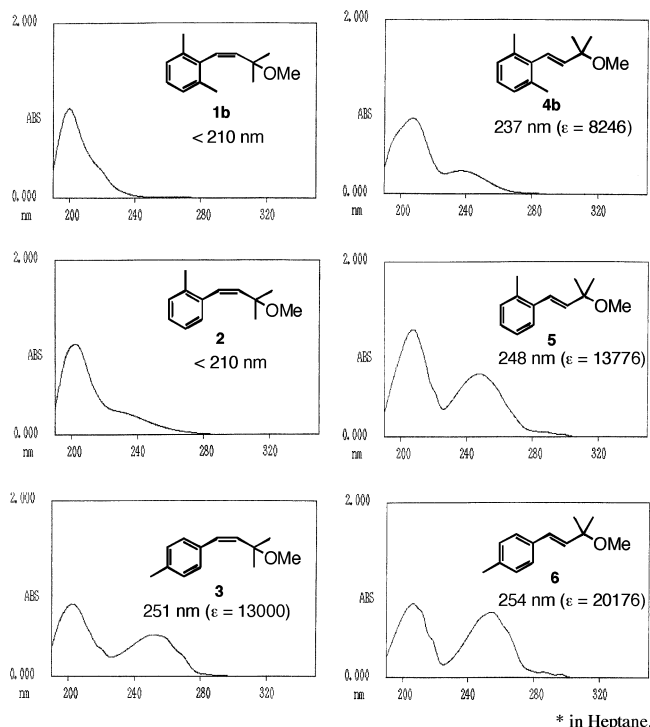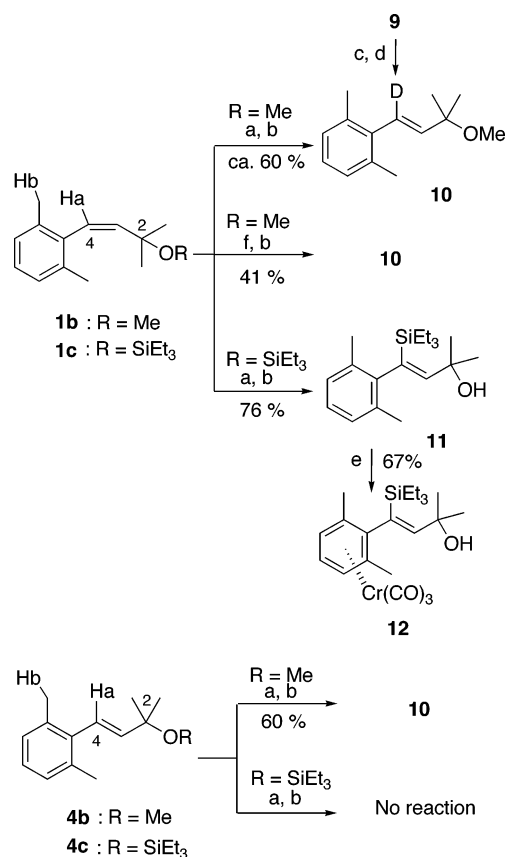(15) Klein, J.; Medlik-Balan, A. *J. Am. Chem. Soc.* **1977**, *99*, 1473.

SCHEME 2 [a]

[a] Reagents and conditions: (a) *n*-BuLi (5 equiv), TMEDA (2.5 equiv)/hexane, rt, 1 h; (b) D$_2$O; (c) LiAlH$_4$ then D$_2$O; (d) NaH, Bu$_4$NI, MeI; (e) Cr(CO)$_6$/(Bu)$_2$O−THF = 10:1; (f) *t*-BuOK (1.0 equiv), *n*-BuLi (1.0 equiv), TMEDA (1.0 equiv), hexane−THF = 3:1, −43 °C, 1 h.
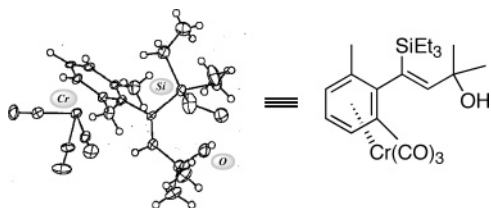

FIGURE 3. ORTEP drawing of compound **12**.

coordination between the base complex and the methoxy group. Unfortunately, no proton abstraction or silyl ether migration of the *E* silyl ether **4c** was observed, probably due to the severe steric hindrance around the vinyl hydogen Ha of **4c**. For all of the *E* and *Z* isomers, none of the compounds deuterated at the benzylic methyl position were observed after this base treatment (Scheme 2).

We then tried to treat the *Z* isomer **1b** with a stronger base, *t*-BuOK/BuLi/TMEDA,[16] which can abstract a vinyl proton at low temperature and can be easily prepared from the corresponding commercially available reagents. Treatment of the *Z* isomer **1b** with the base in hexane and THF (3:1) at −43 °C for 1 h followed by D$_2$O quenching gave the deuterized compound **10** (41%) and the protonated *E* isomer **4b** (14%). The

same reaction proceeded even at −95 °C to give **10** and **4b** in a relatively lower yield (40% yield in a ratio of one to one), and the *Z* isomer deuterized at the C4 vinylic position could not be detected at all. None of the compounds deuterized at the benzylic position were again detected by NMR (Scheme 2).

Plausible Reaction Pathway for the Formation of 10 and 11. The mechanistic pathway to the formation of **10** and **11** from the *Z* isomers **1b** and **1c** under the strong base treatment is proposed as shown in Scheme 3. Compounds **1b** and **1c** produced the corresponding *Z* vinyl anion **13**, which entirely isomerized to the *E* vinyl anion **15** as a result of stabilization based on the coordination between the generated vinyl lithium and the allylic oxygen function, then followed by quenching by D$_2$O (R = Me) or retro-[1,4]-Brook rearrangement (R = SiEt$_3$) (Path A). This hypothetical pathway is strongly supported by the study of Knorr and Panek,[17,18] in which the vinyl anion generated at the α-position of styrene derivatives easily isomerizes to give an equilibrium mixture of the corresponding *E* and *Z* isomers. The intramolecular rearrangement of the anion from the vinylic position to the thermodynamically more stable benzylic position of the tolylstilbene derivatives was also extensively investigated by Knorr and co-workers.[18] In our twisted styrene, the rearrangement pathway that arises from the kinetically generated benzyl anion **14** to the *E* vinyl anion **15** stabilized by the chelation effect through the *Z* vinyl anion **13** (Path B) was completely excluded, because no observation of the deuterized compound at the benzylic position of the twisted styrene **1b** was made even at −95 °C, although **1b** produced a mixture of **10** and **4b** (1:1) in 40% yield at −95 °C. In addition, the benzylic anion, if generated, is not situated close enough to rearrange to the vinyl position in the significantly twisted styrene derivatives. These described results clearly demonstrated that the vinyl proton Ha in **1b** or **1c** is selectively abstracted by the base in preference to the benzyl proton Hb.
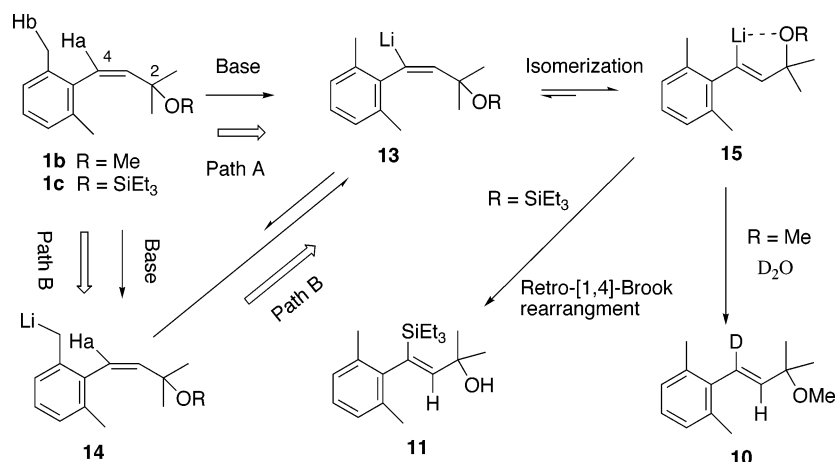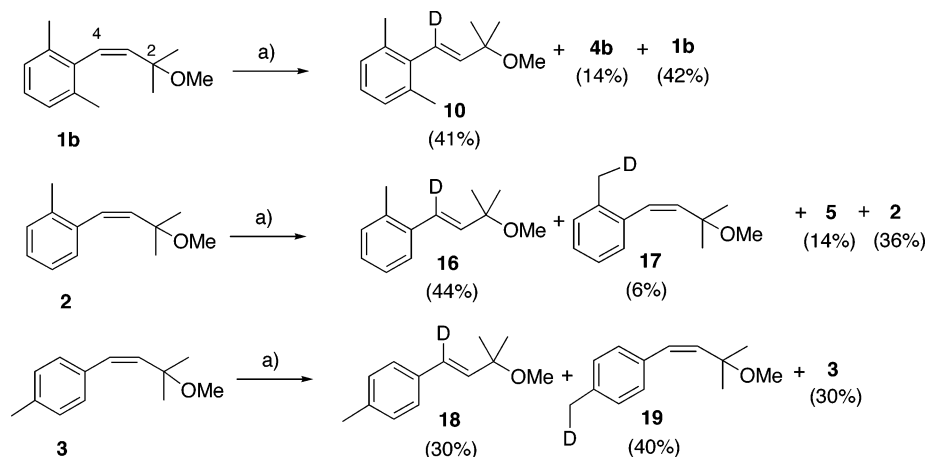
Correlation between the Twist Magnitude and the Reactivity of the Vinyl Hydrogens. We then attempted to treat other kinds of twisted styrene derivatives **2**, **3**, **5**, and **6** (Figure 1) with the base at −43 °C. The results of **1b**, **2**, and **3** are summarized in Scheme 4. As previously described, the base treatment of the entirely twisted *Z* isomer **1b** gave compounds **10** (41%) and **4b** (14%) along with the starting compound (42%). In the case of the moderately twisted *Z* isomers **2** and **3**, although vinyl proton abstraction was clearly observed, benzylic proton abstraction was also observed. Thus, in the *o*-methylphenyl styrene derivative **2**, compound **16** deuterized at the vinylic position was obtained as the major product (44%) along with compound **17** deuterized at the benzylic position (6%), compound **5** (14%), and the starting material (36%). With the *p*-methylphenyl styrene derivative **3**, the major reaction was benzyl proton abstraction, **19** (40%); the vinyl proton abstraction was also observed, **18** (30%). Thus the tendency of the proton abstraction varied from the vinyl proton to the benzyl proton in the three types of twisted styrene derivatives **1b**, **2**, and **3**.

As previously described, the electronic spectra (Figure 2) and the molecular orbital calculations of the *Z* isomers of styrene

(16) (a) Schlosser, M.; Strunk, S. *Tetrahedron Lett*. **1984**, *25*, 741. (b) Schlosser M. *Pure Appl. Chem*. **1988**, *60*, 1627. (c) Brandsma, L.; Verkruijsse, H. D.; Schade, D.; Schleyer, P. R. *J. Chem. Soc., Chem. Commun*. **1986**, *260*.

(17) (a) Panek, E. J.; Neff, B. L.; Chu, H.; Panek, M. G. *J. Am. Chem. Soc*. **1975**, *97*, 3996. (b) Zwaifel, G.; Rajagopalan, S. *J. Am. Chem. Soc*. **1985**, *107*, 700.

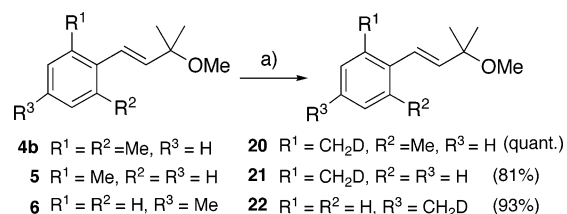(18) (a) Knorr, R.; Lattke, E. *Tetrahedron Lett*. **1977**, *45*, 3969. (b) Knorr, R.; Lattka, E.; Rapple, E. *Chem. Ber*. **1981**, *114*, 1581. (c) Knorr, R.; Lattke, E.; Ruf, F.; Reissig, H.-U. *Chem. Ber*. **1981**, *114*, 1592. (d) Lattke, E.; Knorr, R. *Chem. Ber*. **1981**, *114*, 1600. (e) Knorr, R.; Lattke, E. *Chem. Ber*. **1981**, *114*, 2116. (f) Knorr, R.; Roman, T. *Angew. Chem*. **1984**, *96*, 349.

SCHEME 3

1b R = Me
1c R = SiEt$_3$

Base
Path A

Isomerization

13

15

Path B
Base

Path B

R = SiEt$_3$

R = Me
D$_2$O

14

Retro-[1,4]-Brook
rearrangment

11

10

SCHEME 4 [a]

1b

a)

10
(41%)

+ **4b** + **1b**
   (14%)   (42%)

2

a)

16
(44%)

17
(6%)

+ **5** + **2**
  (14%) (36%)

3

a)

18
(30%)

19
(40%)

+ **3**
(30%)

[a] Reagents and conditions: (a) *t*-BuOK (1.0 equiv), *n*-BuLi (1.0 equiv), TMEDA (1.0 equiv), hexane−THF = 3:1, −43 °C, 1 h, then D$_2$O.

derivatives **1b**, **2**, and **3** indicated that the tendency of the twist of these derivatives **1b**, **2**, and **3** arranges in this order. It is easily noticed that the proportion between vinyl proton abstraction and benzyl proton abstraction shifted to the latter with diminution of the twist. The results obtained here clearly showed a correlation between the reactivity of the vinyl hydrogen at the C4 position and the magnitude of the twist at the central single bond. From the view point of the steric effect, the surroundings of the vinyl hydrogen are crowded by an *o*-methyl group at the benzene ring. Although the steric hindrance toward the attack of the strong base would be severest in the *o*-dimethylstyrene derivatives **1b**, the vinyl proton of **1b** was mainly abstracted. This result is understandable by considering the sufficient activation due to the novel orbital interaction between the σ* orbital of the vinyl hydrogen and the π orbital of the benzene ring resulting from the twist. The moderate vinyl proton abstraction was observed in the other styrene derivatives **2** and **3**, despite the low magnitude of the twist. The loose steric hindrance around the vinyl hydrogen would contribute to the facile access of the strong base to the vinyl hydrogen. On the contrary, the treatment of the *E* isomers **4b**, **5**, and **6** with 2.5 equiv of the same base at −43 °C chemoselectively produced the compound deuterized at the benzylic position to give **20**−**22** in excellent yield (Scheme 5). In these cases, the surroundings of the vinyl hydrogen are more crowded than those of *Z* isomers and it would be difficult for the bulky base complex to access

SCHEME 5 [a]

R^1
R^3 R^2
OMe

a)

R^1
R^3 R^2
OMe

4b R^1 = R^2 =Me, R^3 = H   **20** R^1 = CH$_2$D, R^2 =Me, R^3 = H (quant.)
5 R^1 = Me, R^2 = R^3 = H   **21** R^1 = CH$_2$D, R^2 = R^3 = H   (81%)
6 R^1 = R^2 = H, R^3 = Me   **22** R^1 = R^2 = H, R^3 = CH$_2$D   (93%)

[a] Reagents and conditions: (a) *t*-BuOK (2.5 equiv), *n*-BuLi (2.5 equiv), TMEDA (2.5 equiv), hexane−THF = 3:1, −43 °C, 1 h, then D$_2$O.

the vinyl hydrogen. Furthermore, the coordination of the base complex with the methoxy group would not be effective to abstract the vinyl hydrogen, in addition to the low activation of the vinyl hydrogen due to the small orbital interaction. None of the possibilities concerning the intramolecular rearrangement of the anion from the benzylic position to the vinylic position are again proposed. The obtained results strongly suggested that the abstraction of the vinyl proton was kinetically more favorable than that of the benzylic proton, and the produced vinyl anion was easily isomerized into the thermodynamically favorable *E* isomer. Thus, we found a novel example of a vinyl hydrogen more reactive than a benzyl hydrogen.

Trapping the Vinyl Anion with Aldehydes. Next, to examine the potential of the generated vinyl anions, we tried to

SCHEME 6[a]

R = Ph   **23** : 53% + 7% + 17%
R = n-Pr **24** : 45% + 16% + 18%
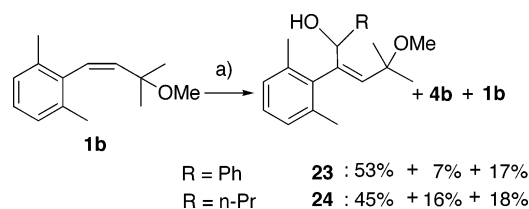
[a] Reagents and conditions: (a) *t*-BuOK, *n*-BuLi, TMEDA, hexane−THF = 3:1, −43 °C, 1 h, then LiBr (9 equiv), RCHO.
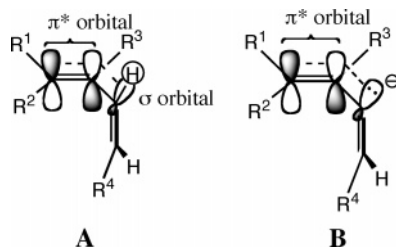

FIGURE 4. Orbital interaction of a twisted styrene derivative.

trap the vinyl anion using some aldehydes as an electrophile (Scheme 6). The vinyl anion, which was produced from **1b** under the same conditions, was treated with 2 equiv of benzaldehyde and *n*-propyl aldehyde in the presence of LiBr (9 equiv) to yield the secondary alcohols **23** and **24** in 53% and 45% yields, respectively, along with the corresponding *E* isomer **4b** in 7% and 16% yields in addition to 17−18% of the starting material, respectively. In these cases, the absence of LiBr did not produce the addition products. Thus, no adducts at the benzylic position were again admitted. Attempts to trap with other electrophiles, such as MeI and TMSCl, did not show any clear results.

Orbital Interaction in a Twisted Styrene. The obtained results described above clearly showed the remarkable activation of the vinyl proton in twisted styrenes, and these phenomena could be rationalized by considering orbital interaction due to the twist around the single bond of the styrene derivatives. Thus, in a significantly twisted styrene, the σ orbital of the vinyl C−H bond effectively interacts with the π* orbital of another double bond as shown in Figure 4 (A). In addition, the stabilizing effect by the development of the vinyl anion to the neighboring π* orbital (B) should be also considered. Since it is well-known that the acidity of the hydrogen attaching at an sp^2 carbon is higher than that attaching at a sp^3 carbon,[19] the combination of this well-known phenomenon with the present novel σ−π orbital interaction made it possible to realize the presence of a more acidic vinyl hydrogen rather than an allyl hydrogen. In other words, the vinyl hydrogen of the significantly twisted 1,3-diene derivatives is the allyl hydrogen attaching at the sp^2 carbon.

The present results of the significantly twisted styrenes are a new entry for the unique character of the twisted 1,3-unsaturated compounds and novel examples of the highly activated vinyl hydrogen.

Experimental Section

2,6-Dimethylphenyltrifluoromethanesulfonate (8). To a solution of 2,6-dimethylphenol (6.0 g, 49 mmol) in chloroform (100

---

(19) We also checked the coupling constant of C4−H4 in order to examine the *s* character of the most "twisted" 1,3-diene **1a** and found that it was the normal value of an sp^2 carbon ($J_{C−H}$ = 157.5 Hz).

mL) were added triethylamine (10.5 mL, 75 mmol) and trifluoromethanesulfonic anhydride (10 mL, 58 mmol) at −78 °C, and the reaction mixture was gradually warmed to room temperature. After being stirred at the same temperature for 25.5 h, the reaction mixture was poured into saturated aqueous NaHCO$_3$ solution, and the resulting mixture was extracted with dichloromethane. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silca gel (3% triethylamine in hexane) gave **8** (12.4 g, 99%): IR (neat, cm^{-1}) 2928, 1462, 1408, 1380, 1210, 1144; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.16−7.11 (3H, m), 2.39 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 146.9, 131.5, 129.9, 128.0, 120.2, 117.0, 17.1.; EI HRMS *m/e* calcd for C$_9$H$_9$F$_3$O$_3$S (M$^+$) 254.0225, found 254.0223.

2-Methyl-4-(2,6-dimethylphenyl)-3-butyn-2-ol (9). To a solution of **8** (3.0 g, 11.8 mmol), diethylamine (25 mL, 242 mmol), and tetra-*n*-butylammonium iodide (13.0 g, 35.4 mmol) in DMF (22 mL) were added dichlorobis(triphenylphosphine) palladium (331 mg, 0.472 mmol) and copper iodide (270 mg, 1.42 mmol). The reaction mixture was stirred for 5 min at room temperature, and 2-methyl-3-butyn-2-ol (2.3 mL, 24 mmol) was added at the same temperature. After being stirred at 70 °C for 3 h, the mixture was diluted with saturated NH$_4$Cl solution and extracted with ether. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (3% ethyl acetate in hexane) gave **9** (1.05 g, 47%): mp 64−69 °C; IR (KBr disk, cm^{-1}) 3328, 2980, 1576, 1468, 1376, 1246, 1160; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.10−7.01 (3H, m), 2.41 (6H, s), 1.66 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.2, 127.7, 126.6, 122.3, 102.5, 79.7, 65.9, 31.7, 21.0; EI HRMS *m/e* calcd for C$_{13}$H$_{16}$O (M$^+$) 188.1201, found 188.1202.

(3Z)-2-Methyl-4-(2,6-dimethylphenyl)-3-buten-2-ol (1a). To a solution of **9** (1.05 g, 5.58 mmol) in hexane (40 mL) was added Pd−C (260 mg), and the mixture was stirred at room temperature for 1 h under hydrogen atmosphere. The reaction mixture was filtered, and the filtrate was concentrated in vacuo to give crude products. Column chromatography on silica gel (10% ethyl acetate in hexane) gave **1a** (913 mg, 86%): mp 40−41.5 °C; IR (KBr disk, cm^{-1}) 3292, 2972, 1464; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.07−7.00 (3H, m),), 6.22 (1H, d, *J* = 12.4 Hz), 5.77 (1H, d, *J* = 12.4 Hz), 2.23 (6H, s), 1.23 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.7, 136.5, 135.6, 127.1, 126.9, 124.4, 72.6, 29.8, 20.9.

(3Z)-2-Methoxy-2-methyl-4-(2,6-dimethylphenyl)-3-butene (1b). To a solution of **1a** (500 mg, 2.6 mmol) in THF (15 mL) were added sodium hydride (150 mg, 3.7 mmol) and tetra-*n*-butylammonium iodide (1.45 g, 3.9 mmol). The reaction mixture was stirred at room temperature for 3 h, and methyl iodide (0.3 mL, 4.8 mmol) was added. After being stirred at room temperature for 14 h, the mixture was diluted with saturated aqueous NH$_4$Cl solution and extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (5% ethyl acetate in hexane) gave **1b** (524 mg, 98%): IR (neat, cm^{-1}) 2980, 1468, 1376, 1166, 1078; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.06−6.98 (3H, m), 6.41 (1H, d, *J* = 12.8 Hz), 5.72 (1H, d, *J* = 12.8 Hz), 3.22 (3H, s), 2.26 (6H, s), 1.03 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.8, 137.3, 135.2, 128.5, 126.9, 126.5, 76.2, 50.6, 25.4, 20.7; EI HRMS *m/e* calcd for C$_{14}$H$_{20}$O (M$^+$) 204.1514, found 204.1513.

(3Z)-2-Methyl-4-(2,6-dimethylphenyl)-2-triethylsiloxy-3-butene (1c). To a solution of **1a** (2.23 g, 12 mmol), 4-(dimethylamino)pyridine (400 mg, 3.3 mmol), and triethylamine (5.6 mL, 40 mmol) in DMF (80 mL) was added triethylsilyl chloride (5.8 mL, 35 mmol) at 0 °C, and the reaction mixture was gradually warmed to room temperature. After being stirred at the same temperature for 5 h, the reaction mixture was diluted with cold water and then extracted with ethyl acetate. The organic layers were combined, neutralized by saturated aqueous NaHCO$_3$ solution,

washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (3% triethylamine in hexane) gave a colorless oil. In order to remove hexaethyldisiloxane, the oil was heated in vacuo (1−2 mmHg) at 80 °C for 3 days to give pure silyl ether **1c** (3.24 g, 90%). : IR (neat, cm^{-1}) 2956, 1464, 1144, 1040; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.03−6.96 (3H, m), 6.10 (1H, d, J = 12.8 Hz), 5.73 (1H, d, J = 12.8 Hz), 2.24 (6H, s), 1.15 (6H, s), 0.88 (9H, t, J = 8.0 Hz), 0.45 (6H, q, J = 8.0 Hz); ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.2, 138.1, 135.2, 126.7, 126.0, 124.0, 74.2, 30.0, 20.9, 7.0, 6.4; EI HRMS m/e calcd for C$_{19}$H$_{32}$O$_1$Si$_1$ (M$^+$) 304.2222, found 304.2224.

(3Z)-2-Methoxy-2-μethyl-4-(2-methylphenyl)-3-butene (2). Following the procedure of preparation of **1a**, 2-iodotoluene (2.00 g, 9.17 mmol), 2-mehtyl-3-butyn-2-ol (1.8 mL, 18.4 mmol), diethylamine (28.0 mL, 271 mmol), tetra-n-butylammonium iodide (10.2 g, 27.5 mmol), dichlorobis(triphenylphosphine)palladium (258 mg, 0.367 mmol), and copper iodide (210 mg, 1.10 mol) in DMF (25 mL) for 2.5 h gave, after the usual workup and column chromatography (11% ethyl acetate in hexane), the corresponding coupling compound (1.59 g, 99%).

2-Methyl-4-(2-methylphenyl)-3-butyn-2-ol: mp 32−33 °C; IR (KBr disk, cm^{-1}) 3227, 2984, 2930, 2866, 2224, 1952, 1919, 1883, 1838, 1804, 1599, 1485, 1454, 1377, 1362, 1200, 1157, 754; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39−7.37 (1H, m), 7.23−7.10 (3H, m), 2.41 (3H, s), 2.10 (1H, s), 1.64 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.1, 131.8, 129.4, 128.3, 125.5, 122.4, 97.9, 81.0, 65.7, 31.6, 20.6.

The coupling compound (925 mg, 5.31 mmol) and Pd−C (231 mg) under hydrogen atmosphere in hexane (50 mL) for 30 min gave, after the usual workup and column chromatography (9% ethyl acetate in hexane), the corresponding Z olefin (422 mg, 45%).

(3Z)-2-Methyl-4-(2-methylphenyl)-3-buten-2-ol: IR (neat, cm^{-1}) 3385, 2973, 2930, 2874, 1917, 1811, 1642, 1601, 1485, 1460, 1375, 1362, 1221, 1144, 754; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.20−7.12 (4H, m), 6.38 (1H, d, J = 12.4 Hz), 5.80 (1H, d, J = 12.4 Hz), 2.27 (3H, s), 1.56 (1H, s), 1.29 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.2, 137.1, 136.03, 129.8, 128.7, 127.3, 126.5, 125.4, 72.3, 30.9, 20.2.

The Z olefin (422 mg, 2.39 mmol), sodium hydride (ca. 60% in oil, 144 mg, 3.59 mmol), tetra-n-butylammonium iodide (1.33 g, 3.59 mmol), and methyl iodide (0.3 mL, 4.79 mmol) gave, after the usual workup and column chromatography (from 1% to 4% ethyl acetate in hexane), the titled compound **2** (417 mg, 91%): IR (neat, cm^{-1}) 2976, 2934, 2822, 1601, 1485, 1460, 1373, 1362, 1171, 1076, 741; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.19−7.10 (4H, m), 6.52 (1H, d, J = 12.7 Hz), 5.68 (1H, d, J = 12.7 Hz), 3.15 (3H, s), 2.26 (3H, s), 1.15 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.4, 137.2, 135.5, 129.7, 129.3, 129.1, 127.0, 125.1, 76.0, 50.4, 26.9, 20.1.

(3Z)-2-Methoxy-2-methyl-4-(4-methylphenyl)-3-butene (3). Following the procedure for the preparation of **1a**, 4-iodotoluene (1.00 g, 4.59 mmol), 2-methyl-3-butyn-2-ol (0.89 mL, 9.17 mmol), diethylamine (14.0 mL, 135 mmol), tetra-n-butylammonium iodide (5.08 g, 13.8 mmol), dichlorobis(triphenylphosphine)palladium (129 mg, 0.184 mmol), and copper iodide (105 mg, 0.55 mol) in DMF (25 mL) for 2.5 h gave, after the usual workup and column chromatography (17% ethyl acetate in hexane), the corresponding coupling compound (1.59 g, 99%).

2-Methyl-4-(4-methylphenyl)-3-butyn-2-ol: mp 47 °C; IR (KBr disk, cm^{-1}) 3316, 2986, 2926, 2866, 2232, 1912, 1657, 1510, 1439, 1375, 1362, 1215, 1165, 1140, 818; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (2H, m), 7.10 (2H, m), 2.33 (3H, s), 2.15 (1H, s), 1.61 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.3, 131.5, 129.0, 119.6, 93.0, 82.2, 65.6, 31.5, 21.4.

The coupling compound (800 mg, 4.59 mmol), quinoline (125 μL, 0.00106 mmol), and Pd−C (200 mg) under hydrogen atmosphere in hexane (50 mL) for 30 min gave, after the usual workup

and column chromatography (9% ethyl acetate in hexane), the corresponding Z olefin (582 mg, 72%).

(3Z)-2-methyl-4-(4-methylphenyl)-3-buten-2-ol: IR (neat, cm^{-1}) 3410, 2975, 2928, 1613, 1510, 1462, 1632, 1144, 820; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (2H, d, J = 7.8 Hz), 7.12 (2H, d, J = 7.8 Hz), 6.42 (1H, d, J = 12.7 Hz), 5.71 (1H, d, J = 12.7 Hz), 2.33 (3H, s), 1.68 (1H, s), 1.36 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.9, 136.7, 134.4, 128.9, 128.7, 127.8, 72.0, 31.1, 21.1.

The Z olefin (582 mg, 3.3 mmol), sodium hydride (ca. 60% in oil, 190 mg, 4.95 mmol), tetra-n-butylammonium iodide (1.83 g, 4.95 mmol), and methyl iodide (0.41 mL, 6.6 mmol) in THF (20 mL) gave, after the usual workup and column chromatography (from 1% to 4% ethyl acetate in hexane), the titled compound **3** (571 mg, 91%): IR (neat, cm^{-1}) 2976, 2934, 2824, 1628, 1613, 1510, 1464, 1375, 1360, 1171, 1076, 833; UV (heptane) λ_{max} 251.0 nm (ϵ = 12989); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37 (2H, d, J = 8.05 Hz), 7.11 (2H, d, J = 7.81 Hz), 6.48 (1H, d, J = 12.9 Hz), 5.49 (1H, d, J = 12.9 Hz), 3.11 (3H, s), 2.34 (3H, s), 1.31 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.6, 135.3, 134.2, 131.0, 129.5, 128.5, 75.5, 50.2, 27.3, 21.2.; EI HRMS m/e calcd for C$_{13}$H$_{18}$O (M$^+$) 190.1358, found 190.1353.

(3E)-2-Methyl-4-(2,6-dimethylphenyl)-3-buten-2-ol (4a). To a suspension of lithium aluminum hydride (420 mg, 11 mmol) in THF (30 mL) was added a THF (10 mL) solution of **9** (2.0 g, 10.6 mmol) at 0 °C. After the reaction mixture was stirred under reflux for 3.75 h, excess lithium aluminum hydride was carefully decomposed by addition of water under ice-cooling. The mixture was filtered, and the filtrate was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (from 9 to 17% ethyl acetate in hexane) gave the title compound (1.45 g, 72%): mp 57−58 °C; IR (KBr disk, cm^{-1}) 3352, 2972, 1468, 1362, 1146; UV (heptane) λ_{max} 237.4 nm (ϵ = 7910); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.03 (3H, brs), 6.52 (1H, d, J = 16.4 Hz), 5.83 (1H, d, J = 16.4 Hz), 2.28 (6H, s), 1.44 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.7, 136.7, 135.8, 127.6, 126.4, 123.7, 71.2, 29.90, 20.8.

(3E)-1-Methoxy-2-methyl-4-(2,6-dimethylphenyl)-3-butene (4b). To a solution of (3E)-2-mehtyl-4-(2,6-dimethylphenyl)-3-buten-2-ol **4a** (700 mg, 3.7 mmol) in THF (21 mL) was added sodium hydride (210 mg, 5.3 mmol) and tetra-n-butylammonium iodide (2.03 g, 5.5 mmol). The reaction mixture was stirred at room temperature for 3 h, and methyl iodide (0.42 mmol, 6.7 mmol) was added. After being stirred at room temperature for 1 h, the mixture was diluted with saturated aqueous NH$_4$Cl solution and extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (5% ethyl acetate in hexane) gave **4b** (569 mg, 75%): IR (neat, cm^{-1}) 2976, 1470, 1170, 1076; UV (heptane) λ_{max} 237.6 nm (ϵ = 8380); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.05 (3H, m), 6.45 (1H, d, J = 16.8 Hz), 5.67 (1H, d, J = 16.8 Hz), 3.27 (3H, s), 2.30 (6H, s), 1.40 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 140.2, 136.9, 135.8, 127.7, 126.9, 126.5, 75.4, 50.7, 26.0, 20.9; EI HRMS m/e calcd for C$_{14}$H$_{20}$O (M$^+$) 204.1514, found 204.1513.

(3E)-2-Methyl-4-(2,6-dimethylphenyl)-2-triethylsiloxy-3-butene (4c). To a solution of **4a** (405 mg, 1.9 mmol), 4-(dimethylamino)pyridine (70 mg, 0.57 mmol), and triethylamine (0.96 mL, 6.9 mmol) in DMF (10 mL) was added triethylsilyl chloride (0.96 mL, 5.7 mmol) at 0 °C, and the reaction mixture was gradually warmed to room temperature. After being stirred at the same temperature for 6 h, the reaction mixture was diluted with cold water and extracted with ether. The organic layers were combined, neutralized by saturated aqueous NaHCO$_3$ solution, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel (3% triethylamine in hexane) gave **4c** (250 mg, 42%): IR (neat, cm^{-1}) 2960, 1466, 1236, 1044; UV λ_{max}. (heptane); 237.4 nm (ϵ = 8950); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.03 (3H, brs), 6.50 (1H, d, J =

16.3 Hz), 5.77 (1H, d, J = 16.3 Hz), 2.29 (6H, s), 1.42 (6H, s), 0.97 (9H, t, J = 8.3 Hz), 0.62 (6H, q, J = 8.1 Hz); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.6, 137.2, 136.0, 127.6, 128.2, 123.1, 73.4, 30.7, 20.9, 7.1, 6.8; EI HRMS m/e calcd for C$_{19}$H$_{32}$O$_1$Si$_1$ (M$^+$) 304.2222, found 304.2207.

(3E)-2-Methoxy-2-methyl-4-(2-methylphenyl)-3-butene (5). Following the procedure of preparation of **4a**, 2-methyl-4-(2-methylphenyl)-3-butyn-2-ol (200 mg, 1.15 mmol) and lithium aluminum hydride (44 mg, 1.15 mol) in THF (4.4 mL) gave, after the usual workup and column chromatography (17% ethyl acetate in hexane), the corresponding E olefin(188 mg, 93%).

(3E)-2-Methyl-4-(2-methylphenyl)-3-buten-2-ol: IR (neat, cm^{-1}) 3366, 2973, 2928, 1806, 1603, 1487, 1460, 1375, 1148, 968, 750; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44−7.40 (1H, m), 7.18−7.13 (3H, m), 6.80 (1H, d, J = 16.1 Hz), 6.23 (1H, d, J = 15.9 Hz), 2.35 (3H, s), 1.61 (1H, s), 1.43 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 139.0, 136.0, 135.5, 130.2, 127.3, 126.1, 125.6, 124.1, 71.2, 30.0, 19.8.

The E olefin (1.35 g, 7.68 mmol), sodium hydride (ca.60% in oil, 441 mg, 11.5 mmol), tetra-n-butylammonium iodide (4.25 g, 11.5 mmol), and methyl iodide (0.96 mL, 15.4 mmol) in THF (46 mL) gave, after the usual workup and column chromatography (from 1% to 4% ethyl acetate in hexane), the title compound **5** (1.41 g, 96%): IR (neat, cm^{-1}) 2976, 2934, 2824, 1912, 1806, 1603, 1487, 1460, 1377, 1362, 1169, 1076, 974, 748; UV λ_{max} (heptane) 247.8 nm (ϵ = 13776), 207.0 nm (ϵ = 23472); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46−7.42 (1H, m), 7.19−7.11 (3H, m), 6.71 (1H, d, J = 16.1 Hz), 6.06 (1H, d, J = 16.1 Hz), 3.23 (3H, s), 2.36 (3H, s), 1.39 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 136.6, 136.1, 135.4, 130.2, 127.4, 127.0, 126.0, 125.6, 75.2, 50.5, 26.0, 19.8; EI HRMS m/e calcd for C$_{13}$H$_{18}$O (M$^+$) 190.1358, found 190.1366.

(3Z)-2-Methoxy-2-methyl-4-(4-methylphenyl)-3-butene (6). Following the procedure of preparation of **4a**, 2-Methyl-4-(4-methylphenyl)-3-butyn-2-ol (100 mg, 0.57mmol) and lithium aluminum hydride (22 mg, 0.57 mol) in THF(2.2 mL) gave, after the usual workup and column chromatography (9% ethyl acetate in hexane), the corresponding E olefin(86 mg, 85%).

(3E)-2-Methyl-4-(4-methylphenyl)-3-buten-2-ol: mp 69 °C; IR (KBr disk, cm^{-1}) 3287, 2980, 2928, 1906, 1611, 1514, 1445, 1377, 1362, 1206, 1148, 978, 804; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.27 (2H, dt, J = 8.1, 2.0 Hz), 7.12 (2H, d, J = 8.1 Hz), 6.55 (1H, d, J = 16.1 Hz), 6.30 (1H, d, J = 16.1 Hz), 2.33 (3H, s), 1.59 (1H, s), 1.41 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.2, 136.5, 134.1, 129.2, 126.3, 126.2, 71.0, 29.9, 21.1.

The E olefin (553 mg, 3.14 mmol), sodium hydride (ca.60% in oil, 180 mg, 4.71 mmol), tetra-n-butylammonium iodide (1.74 g, 4.71 mmol), and methyl iodide (0.39 mL, 6.27 mmol) in THF (19 mL) gave, after the usual workup and column chromatography (from 1% to 4% ethyl acetate in hexane), the title compound **6** (537 mg, 96%): IR (neat, cm^{-1}) 2976, 2934, 2824, 1628, 1613, 1510, 1464, 1375, 1360, 1171, 1076, 833; UV (heptane) λ_{max} 251.0 nm (ϵ = 12989); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (2H, d, J = 8.1 Hz), 7.13 (2H, d, J = 7.8 Hz), 6.46 (1H, d, J = 16.4 Hz), 6.14 (1H, d, J = 16.4 Hz), 3.20 (3H, s), 2.34 (3H, s), 1.37 (6H, s); ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.3, 134.1, 129.2 129.0, 126.2, 75.1, 50.5, 25.9, 21.1; EI HRMS m/e calcd for C$_{13}$H$_{18}$O (M$^+$) 190.1358, found 190.1380.

General Procedure for the Treatment with n-BuLi/TMEDA. To a solution of 5 equiv of n-butyllithium (1.6 M solution in hexane) was added 2.5 equiv of TMEDA at 0 °C, and then a hexane solution (1.0 mL) of **1a−c**, **4a−c** (0.2−0.5 mmol) was added drop by drop. After the reaction mixture was stirred for 1 h at room temperature, the reaction was quenched with D$_2$O (0.5 mL). The mixture was stirred at room temperature for 15 min, poured into saturated aqueous NH$_4$Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. The NMR measurement of the crude products was carried out without any purification.

2-Methyl-4-(2,6-dimethylphenyl)-4-triethylsilyl-3-buten-2-ol (11). To a solution of n-butyllithium (1.6 M solution in hexane, 1.0 mL, 1.6 mmol) was added tetramethylethylenediamine (TMEDA) (0.12 mL, 0.80 mmol) at 0 °C. A hexane (1 mL) solution of **1c** (100 mg, 0.33 mmol) was added drop by drop at 0 °C, and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by H$_2$O (0.5 mL), and the mixture was stirred at room temperature for 15 min, poured into saturated aqueous NH$_4$-Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography on silica gel gave **11** (76 mg, 76%): IR (neat, cm^{-1}) 3596, 3460, 2960, 1464, 1368, 1238, 1210; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.97 (3H, brs), 5.85 (1H, s), 2.15 (6H, s), 1.37 (6H, s), 0.88 (9H, t, J = 7.2 Hz), 0.68 (6H, q, J = 8.0 Hz); ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.7, 146.6, 137.4, 134.6, 127.1, 125.0, 72.6, 30.7, 21.3, 8.4, 7.1; EI HRMS m/e calcd for C$_{19}$H$_{32}$O$_1$Si$_1$ (M − H)$^-$ 303.2136, found 303.2139.

Tricarbonyl-{2,6-dimethyl-1-(2-hydroxy-2-methyl-4-triethyl-silyl-3-but-4-enyl)}benzene Chromium (12). To a solution of **11** (300 mg, 0.98 mmol) in dibutyl ether (12 mL) and THF (1.2 mL) was added chromium hexacarbonyl (306 mg, 1.39 mmol). After being stirred at 140 °C for 16 h, the reaction mixture was filtered and concentrated in vacuo to give crude products. Recrystalization of crude solid (471 mg) from hexane gave yellow crystal **12** (288 mg, 67%). The product contained very small amounts of impurities derived from the substrate **11**: mp 149.5−151.5 °C; IR (KBr disk, cm^{-1}) 3500, 2960, 1960, 1872, 1464, 1382; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.39 (1H, s), 5.52 (1H, t, J = 6.3 Hz), 4.90 (2H, d, J = 6.3 Hz), 2.15 (small impurity), 2.07 (6H, s), 1.44 (6H, s), 1.26 (small impurity), 1.38 (small impurity), 0.91 (9H, t, J = 7.8 Hz), 0.67 (6H, q, J = 7.8 Hz) 0.51−0.54 (small impurity); ^{13}C NMR (100 MHz, CDCl$_3$) δ 234.4, 159.8, 130.8, 127.1, 126.4, 110.9, 96.6, 88.2, 72.4, 30.7 (small impurity) 30.6, 29.7 (small impurity), 20.5, 8.4, 8.3 (small impurity) 7.5, 7.2−6.4 (small impurity). The chemical structure of **12** was also identified by X-ray crystallographic analysis of a small amount of the purified crystal.

General Procedure for the Treatment with t-BuOK/n-BuLi/TMEDA. To a suspension of 1 equiv of t-BuOK in hexane (1 mL) was added 1 equiv of n-butyllithium (1.6 M solution in hexane) at 0 °C. After the reaction mixture was stirred at 0 °C for 5 min, 1 equiv of TMEDA was added at −43 °C. The mixture was stirred at −43 °C for 5 min, and a solution of the substrate (**1a−c**, 0.2−0.5 mmol) in hexane (0.5 mL) and THF (0.5 mL) was added at −43 or −95 °C. After the reaction mixture was stirred at the same temperature for 1 h, the reaction was quenched with D$_2$O (0.5 mL). The mixture was stirred for 10 min at the same temperature and for 5 min at 0 °C, poured into saturated aqueous NH$_4$Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. The NMR measurement of the crude products was carried out without any purification.

Reaction with an Aldehyde. (2Z)-4-Methoxy-4-methyl-2-(2,6-dimethylphenyl)-1-phenyl-2-penten-1-ol (23). To a suspension of t-BuOK (82 mg, 0.73 mmol) in hexane (1 mL) was added n-butyllithium (1.6 M solution in hexane, 0.46 mL, 0.73 mmol) at 0 °C. After the reaction mixture was stirred at 0 °C for 5 min, TMEDA (0.11 mL, 0.73 mmol) was added at −43 °C. The mixture was stirred at −43 °C for 5 min, and a solution of **1b** (100 mg, 0.49 mmol) in hexane (0.5 mL) and THF (0.5 mL) was added at −43 °C. After the reaction mixture was stirred at the same temperature for 1 h, lithium bromide (383 mg, 4.41 mmol) and then benzaldehyde (0.1 mL, 0.98 mmol) were added. The reaction mixture was stirred for 40 min at −43 °C and for 35 min at room temperature, poured into saturated aqueous NH$_4$Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo to give crude products. Column chromatography (6% ethyl acetate in hexane) on silica gel gave the title compound **23** (80

mg, 53%). The product contained small amounts of impurities derived from the reagents and substrates: mp 61−63 °C; IR (KBr disk, cm^{-1}) 3422, 2975, 2936, 2834, 1742, 1578, 1454, 1383, 1366, 1196, 1065, 760, 727, 706; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 (small impurity), 7.15−6.85 (8H, m), 5.84 (1H, d, *J* = 6.3 Hz), 5.58 (1H, brd, *J* = 5.9 Hz), 5.23 (1H, d, *J* = 1.2 Hz), 3.51 (3H, s), 3.20−3.40 (small impurity), (2.14 (3H, s), 1.79 (3H, s)), 1.54 (3H, s)), 1.50 (3H, s)), 0.80−1.40 (small impurity); ^{13}C NMR (100 MHz, CDCl$_3$) δ 142.6, 142.5, 141.5, 136.7, 136.0, 135.4, 127.6, 127.3, 127.3, 127.1, 127.0, 126.6, 76.4, 75.8, 50.5, 27.1, 26.6, 20.0, 19.9; EI HRMS *m/e* calcd for C$_{20}$H$_{22}$O (M − CH$_4$O$^+$) 278.1671, found 278.1685.

(5Z)-7-Methoxy-7-methyl-5-(2,6-dimethylphenyl)-5-octen-4-ol (24). According to the procedure described above, butyraldehyde (0.09 mL, 0.98 mmol) gave the title compound **24** (61 mg, 45%) after the usual workup and column chromatography. The product contained small amounts of impurities derived from the reagents: IR (neat, cm^{-1}) 3380, 2961, 2936, 2872, 1927, 1740, 1578, 1464, 1379, 1362, 1100, 770; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.08−7.00 (3H, m), 5.15 (1H, d, *J* = 1.2 Hz), 5.00 (1H, brd, *J* = 7.1 Hz), 4.39 (1H, brdd, *J* = 7.6, 7.3 Hz), 4.00−4.10 (small impurity), 3.41 (3H, s), 3.10−3.30 (small impurity), 2.31 (3H, s), 2.26 (3H, s), 1.68−1.54 (signals contain small impurity; 1H, m), 1.46 (3H, s), 1.43 (3H, s), 1.39 (signals contain small impurity; 1H, m), 1.35−

1.24 (signals contain small impurity; 2H, m), 0.9−1.0 (small impurity), 0.84 (3H, t, *J* = 7.08 Hz); ^{13}C NMR (100 MHz, CDCl$_3$) δ 144.4, 142.6, 135.9, 135.7, 134.9, 127.5, 127.3, 126.4, 76.4, 72.4, 50.5, 38.0, 29.7 (small impurity), 27.1, 26.5, 21.0, 20.3, 19.8, 14.0; EI HRMS *m/e* calcd for C$_{17}$H$_{24}$O (M − CH$_4$O$^+$) 244.1827, found 244.1832. The structure of compound **24** was also identified by 2D-NMR (COSY and C−H COSY) spectrum.

Supporting Information Available: ^{1}H and ^{13}C spectra for compounds **1−6**, **8−12**, **23** and **24**, X-ray crystallographic data for compound **12** in CIF format, and Cartesian coordinates of optimized structures for compounds **1b**, **2**, **3**, **4b**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061092Z