

Electronic Control of Stereoselectivity in the Metal Hydride Reductions of 1,2,3,4-Tetrahydro-1,4-methanonaphthalen-9-ones¹⁾

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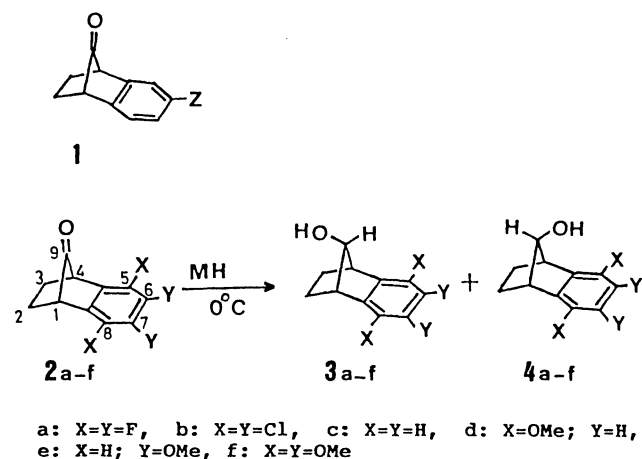
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Stereoselectivity in the metal hydride reduction of a series of substituted 1,2,3,4-tetrahydro-1,4-methanonaphthalen-9-ones was investigated in relation to their homoconjugation character. The observed stereoselectivity sequence was found to be parallel with the homoconjugation sequence: the portion of anti-attack increases as the benzene ring becomes electron-rich. The results are rationalized in terms of the transition state model proposed by Cieplak or of the contribution of the nonclassical carbocation in the transition state.

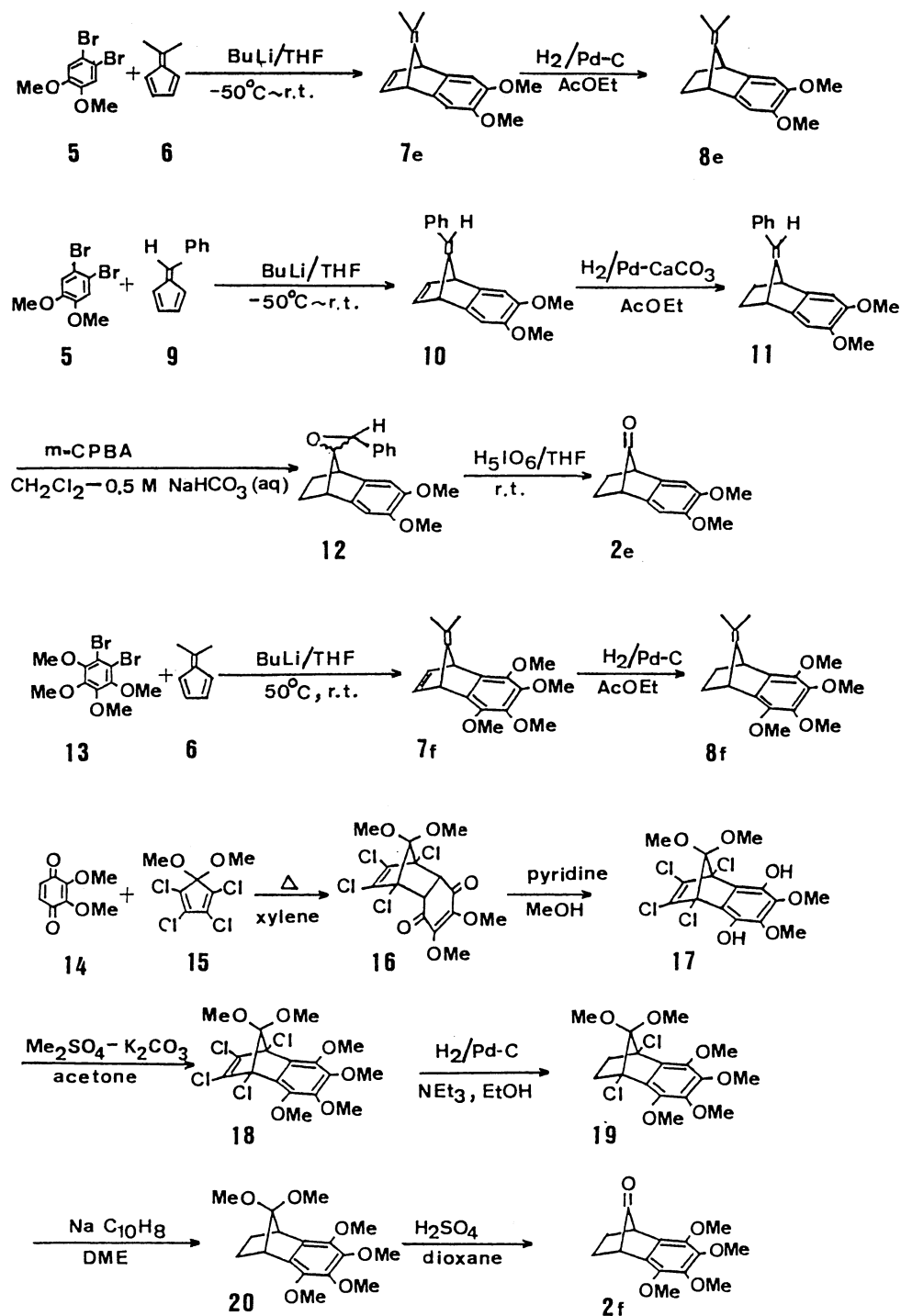
Since Dauben, Fonken, and Noyce presented a rationalization of “product development control” for the predominant axial attack of nucleophiles on cyclohexanones in 1956,²⁾ a number of ingenious rationalizations as well as many experimental investigations on the nucleophilic addition to cyclic ketones have appeared.³⁾ 7-Norbornenone has also attracted attention in its relationship to the homoconjugation character between the carbonyl group and the endocyclic double bond. Brown and Muzzio originally expected that the anti/syn-stereoselectivity towards 7-norbornenone might reflect the homoconjugation property. Such interaction would lead to the preferential anti-attack. However, the opposite selectivity was observed.⁴⁾ Experimental data so far available show that the nucleophiles stereoselectively attack the carbonyl group from the syn-side of the double bond. For example, the reactions with sodium borohydride,⁴⁾ Grignard reagents,^{5,6)} alkyllithium reagents,⁷⁾ diazomethane,⁸⁾ and with sulfonium⁹⁾ or sulfoxonium⁶⁾ ylides gave the products of syn-attack in a stereoselective or stereospecific manner. Exceptions can be seen in the reaction with vinyl lithium¹⁰⁾ and phenyllithium.¹¹⁾ Mechanistic problems as to whether the observed stereoselectivity is due to steric or electronic effects are controversial. Attack from the anti-side of the double bond seems to be slightly more hindered owing to the steric repulsion between the exo-protons of ethano-bridge and the incoming nucleophiles. An empirical calculation evaluating congestion or torsion-corrected congestion, however, suggests that attack from the side of the double bond is slightly more hindered, leading to a consideration that the stereoselectivity may be due to a chelating effect of the double bond rather than a steric or torsional effect.¹²⁾ A similar electronic interpretation was also proposed by Bly and Bly.⁶⁾ An insight into this selectivity can be drawn by the experiments reported by Tanida who investigated the metal hydride reductions of monosubstituted benzonorbornenones **1** as a reference for the solvolysis experiments of the corresponding anti-brosylates. A maximum variation for the selectivity of anti/syn-alcohol was obtained in the disiamylborane reduction (52/48 for Z=Cl, 45/55 for Z=H, 36/64 for Z=OMe). However, the author argued the selectivity in terms of

the subtle change of steric environment because the change of stereoselectivity was too small in comparison with the large variation of solvolysis rates.¹³⁾ For demonstration of the electronic effect, much widely variable selectivity is desirable. We wish to report the metal hydride reductions of a series of substituted 1,2,3,4-tetrahydro-1,4-methanonaphthalen-9-ones (9-benzonorbornenones),¹⁴⁾ **2a–f**. Because of simplicity, the name “9-benzonorbornenone” is used in the text hereafter.



Results and Discussion

Synthesis. Compounds **2a**, **2b**, **2c**, and **2d** were synthesized according to the literature procedures.^{15,16)} Dimethoxy derivatives **2e**, **8e** and tetramethoxy derivatives **2f** and **8f** are new compounds. At first, we attempted the syntheses of **2e** and **2f** from the corresponding isopropylidene derivatives **8e** and **8f**, which were prepared by cycloaddition of 6,6-dimethylfulvene (**6**) with the appropriate benzyne, followed by reduction of the endocyclic double bond, in total yields of 38 and 44%, respectively (Scheme 1). Ozonolysis or oxidative cleavage ($\text{KMnO}_4\text{--NaIO}_4$, $\text{OsO}_4\text{--NaIO}_4$) of the isopropylidene derivatives gave **2e** and **2f** in very poor yields because of facile oxidation of the benzene rings. More rewarding routes to **2e** and **2f** are also outlined in Scheme 1. Cycloaddition of 6-phenylfulvene (**9**) with 4,5-dimethoxybenzyne gave the adduct **10** in 24% yield. Reduction of the endocyclic double bond and



Scheme 1.

successive epoxidation followed by oxidative cleavage with H_5IO_6 in THF produced the desired **2e** in 28% yield from **10**. Compound **2f** was synthesized by a modification of the reported method.¹⁶⁾ Cycloaddition of 2,3-dimethoxy-*p*-benzoquinone (**14**) with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (**15**) gave **16** in 97% yield. Enolization followed by *O*-methylation afforded dimethyl acetal **18** in 78% yield. Direct transformation of **18** to **20** with metal reduction ($\text{Li}/t\text{-BuOH}$ -THF) failed and a mixture of the di-

methoxy and trimethoxy derivatives was obtained instead. This conversion was achieved by two step reduction with use of $\text{H}_2/\text{Pd-C-Et}_3\text{N-EtOH}$ and sodium naphthalenide/DME. Acidic hydrolysis of **20** gave **2f** in 85% yield.

Stereochemistry of Anti- (3a–f) and Syn-Alcohols (4b–f). ^1H NMR data of the produced anti- (**3a–f**) and syn-alcohols (**4b–f**) are listed in Table 1. Stereochemistry of the anti- and syn-alcohols were determined by use of a NMR shift reagent, $\text{Eu}(\text{fod})_3$. The

Table 1. Chemical Shifts (δ)^{a)} and Relative Shift Values^{b)} Induced by Eu(fod)₃ for Protons of **3a**–**f** and **4b**–**f**

	OH	H _{1,4}	H _{2,3} -endo	H _{2,3} -exo	H ₉	Methoxy protons	Aromatic protons
X=Y=F 3a	2.02	3.42 (1.00)	1.22 (0.76)	2.19 (1.23)	3.82 (2.02)		
X=Y=Cl 3b	2.02	3.46 (1.00)	1.23 (0.66)	2.24 (1.20)	3.92 (2.16)		
X=Y=H 3c	1.87	3.11 (1.00)	1.18 (0.65)	2.10 (1.20)	3.80 (2.09)		7.06 (0.21) ^{c)}
X=OMe, Y=H 3d	2.02	3.11 (1.00)	1.17 (0.62)	2.10 (1.18)	ca. 3.7 (2.0)	3.72 (0.11)	6.54 (0.96)
X=H, Y=OMe 3e	2.12	3.07 (1.00)	1.14 (0.65)	2.08 (0.76)	3.81 (1.44)	3.82 (1.44)	6.77 (1.71)
X=Y=OMe 3f	1.98	3.34 (1.00)	1.03 (0.66)	2.16 (0.83)	3.82 (1.38)	3.83, 3.86 (0.55, 1.24)	
X=Y=Cl 4b	1.76	3.52 (1.00)	1.18 (0.35)	2.08 (0.36)	4.20 (1.71)		
X=Y=H 4c	1.58	3.16 (1.00)	1.11 (0.35)	1.96 (0.39)	4.10 (1.82)		6.99–7.30 (0.34) ^{c)}
X=OMe, Y=H 4d	1.63	3.40 (1.00)	1.12 (0.37)	1.92 (0.42)	4.06 (1.81)	3.73 (0.20)	6.61 (0.26)
X=H, Y=OMe 4e	1.72	3.11 (1.00)	1.08 (0.36)	1.94 (0.39)	4.11 (1.87)	3.86 (0.25)	6.89 (0.55)
X=Y=OMe 4f	1.58	3.42 (1.00)	1.18 (0.33)	2.00 (0.35)	4.11 (1.57)	3.85, 3.90 (0.36, 0.54)	

a) Measured in CDCl₃ (ca. 25–30 mg/0.3 ml). b) In parenthesis; averaged values determined by successive addition of 5 mg of Eu(fod)₃ up to ca. 25 mg. c) An averaged value of the two kind of protons.

relative shift values (1.00 for H_{1,4}-protons in both alcohols) induced by Eu(fod)₃ for H_{2,3}- and other protons are also summarized in Table 1. It is clear that H_{2,3}-exo protons in anti-alcohols (**3b**–**f**) have larger relative shifts (0.76–1.20) than those (0.35–0.42) of syn-alcohols (**4b**–**f**). The same trend is observed for H_{2,3}-endo protons. These results clearly elucidate the stereochemistry of the alcohols as assigned in the text. Although the partial coordination of Eu(fod)₃ onto methoxyl groups is also recognizable from the table, this coordination would not much affect the shift of H_{2,3}-protons for the relatively long distance between these protons and the coordinated metal center. The assignment is also supported by the fact that H₉-methine protons of anti-alcohols appear in higher field (δ ca. 3.7–3.92) than those of syn-alcohols (δ 4.06–4.20) because of the anisotropy effect of the benzene rings. Similarly, hydroxyl protons of anti-alcohols have lower chemical shifts (δ 1.87–2.12) than those (δ 1.58–1.76) of syn-alcohols in usual concentration (ca. 25–30 mg/0.3 ml CDCl₃). It is interesting to note that the shift of aromatic protons of **3e** and **4e** is larger than those of **3d** and **4d** upon the contact with Eu(fod)₃. This may suggest that the two adjacent methoxyl groups might form a better ligand for Eu(fod)₃ than the two methoxyl groups at *p*-position. It may be also interesting to refer to GC retention time (column; OV-17) of these alcohols: syn-alcohols have shorter retention time than anti-alcohols in all cases. This may be a reflection of the expected hydrogen bond between the hydroxyl group and the benzene π -

bond. This relation might be used as a convenient method of stereochemical assignment for the related compounds.

Homoconjugation Interaction of the Carbonyl Group and the Benzene Ring. Although the expectation that anti/syn-stereoselectivity may reflect the homoconjugation interaction in 7-norbornenone was rather disappointing,⁴⁾ it is worthy to reconsider the possibility that the same expectation may be realized in a series of substituted 9-benzonorbornenones. Before entering the section of stereoselective metal hydride reduction, the donating ability of the substituted benzene rings is discussed here in relation to the homoconjugation property. As to 7-norbornenone, extensive studies by means of ¹³C NMR,¹⁷⁾ PES,¹⁸⁾ and CD (for unsymmetrically deuterated or substituted derivatives)¹⁹⁾ spectra have shown the homoconjugation interaction between the endocyclic double bond and the carbonyl group. The similar homoconjugation interaction is expectable if the endocyclic double bond is replaced by the benzene ring. Electron-donating substituents on the benzene ring of 9-benzonorbornenones (**2a**–**f**) would decrease the double bond character of the carbonyl group. Therefore, the homoconjugation in **2a**–**f** may be revealed in IR stretching frequency of the carbonyl groups. Initially, we thought that electron-donating property would increase in the sequence of **2a**→**2b**→**2c**→**2d**→**2e**→**2f**. However, the observed frequency for **2f** falls in the range between **2b** and **2c**: [IR(CCl₄, $\nu_{C=O}$); 1793 for **2a**: 1786 (CHCl₃) for **2b**: 1782 for **2c**: 1781 for **2d**: 1778 for

2e: 1785 cm^{-1} for **2f**]. This may suggest that tetramethoxybenzo moiety may not be an effective electron donor, contrary to our initial expectation. To elucidate this point, other reliable methods to evaluate the electron-donating ability of the substituted benzene rings favorably using the related molecules were sought. 9-Isopropylidenebenzonorbornenes are known to be homoconjugated compounds.^{16,20,22} In these compounds, it has been established that the degree of homoconjugation can be evaluated by ^{13}C NMR parameter, $\Delta\delta$ ($\text{C}_9\text{--C}_{10}$)^{20,22} and also by the anti/syn-stereoselectivity in the reaction with singlet oxygen and other electrophiles.²² For these reasons, 9-isopropylidene analogues **8e** and **8f** were prepared and their ^{13}C NMR and the reactions with singlet oxygen were examined. Table 2 shows the results together with the reported data.^{16,22} Both $\Delta\delta$ ($\text{C}_9\text{--C}_{10}$) and the anti/syn-attack selectivity indicate the poor electron-donating ability of tetramethoxybenzene ring: the ^{13}C NMR parameters and the stereoselectivities for **8a–f** are roughly lined in the order of **8a** $\approx$ **8b** $\rightarrow$ **8f** $\rightarrow$ **8c** $\rightarrow$ **8d** $\rightarrow$ **8e**. This is the same sequence with that the IR experiments showed for **2a–f**. From these results, we conclude that the donating ability of the substi-

tuted benzene rings increases in the order of **2(8)a** $\approx$ **2(8)b** $\rightarrow$ **2(8)f** $\rightarrow$ **2(8)c** $\rightarrow$ **2(8)d** $\rightarrow$ **2(8)e**. The poor electron-donating property in **2(8)f** is probably due to nonplanar conformation of tetramethoxybenzo moiety arising from the steric congestion of four adjacent methoxyl groups.

Stereoselective Metal Hydride Reductions of 9-Benzonorbornenones. The reductions of substituted 9-benzonorbornenones (**2a–f**) with various metal hydrides gave the corresponding anti- (**3a–f**) and syn-alcohols (**4b–f**) in high yields (71–99%). The produced alcohols can be separated by the preparative TLC or gas chromatography. Table 3 summarizes the results of the reductions with various typical reagents along with the reaction conditions. In spite of considerably different sizes and reactivities of the reagents, the portion of anti-attack (syn-alcohol) increases in the order of **2a** $\rightarrow$ **2b** $\rightarrow$ **2f** $\rightarrow$ **2c** $\rightarrow$ **2d** $\rightarrow$ **2e** with slight deviation. Especially, the reduction with diisobutylaluminum hydride (DIBALH), and bis(1,2-dimethylpropyl)borane (common name "disiamylborane" is used hereafter) follows this sequence. A small change in the sequence is observed for other reagents. In addition, the following features are notable from Table 3. (1) **2a**

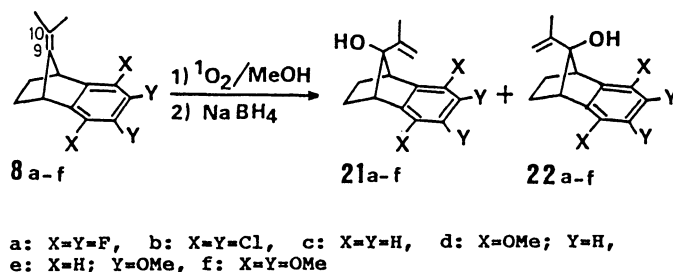


Table 2. ^{13}C NMR Parameters^{a)} and Anti/Syn-Stereoselectivity in the Singlet Oxygen Reaction of **8a–f**

	8a ^{b,c)}	8b ^{b,c)}	8c ^{b,c)}	8d ^{b,c)}	8e	8f
$\delta(\text{C}_9)$	145.26	145.74	148.61	148.03	148.34	146.80
$\delta(\text{C}_{10})$	113.94	114.62	110.88	109.42	109.74	111.09
$\Delta\delta(\text{C}_9\text{--C}_{10})$	31.3	31.1	37.7	38.6	38.6	35.7
$^1\text{O}_2$; anti(21): syn(22)	44:56	41:59	76:24	83:17	91:9	72:28

a) Measured in CDCl_3 . b) L. A. Paquette, L. W. Hertel, R. Gleiter, M. C. Böhm, M. A. Beno, and G. G. Christoph, *J. Am. Chem. Soc.*, **103**, 7106 (1981). c) K. Okada and T. Mukai, *J. Am. Chem. Soc.*, **100**, 6509 (1978); L. A. Paquette, L. W. Hertel, R. Gleiter, and M. Böhm, *ibid.*, **100**, 6512 (1978).

Table 3. Product Ratios (**3a–f**: **4a–f**) in the Metal Hydride Reductions of **2a–f**^{a)}

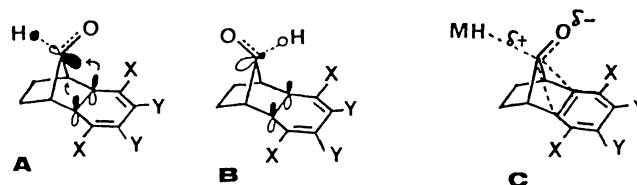
Reagent	Solvent	2a	2b	2c	2d	2e	2f
LAH	THF	100:0	92:8	62:38	45:55	51:49	59:41
LAH	Ether	100:0	95:5	81:19	79:21	64:36	78:22
DIBALH	Ether	100:0	86:14	43:57	37:63	26:74	60:40
LTBA ^{b)}	Ether	100:0	100:0	93:7	93:7	95:5	96:4
NaBH_4	EtOH	100:0	95:5	81:19	79:21	81:19	89:11
$(\text{BH}_3)_2$	THF	100:0	93:7	75:25	70:30	54:46	70:30
$\text{Sia}_2\text{BH}^{\text{c)}$	Diglyme	100:0	— ^{d)}	57:43	46:54	22:78	61:39

a) All reactions were performed at 0°C . b) Lithium tri-*t*-butoxyaluminum hydride. c) Bis(1,2-dimethylpropyl)borane (Disiamylborane). d) 70–95% recovery.

and **2b** show high syn-selectivity toward all the reagents giving anti-alcohols. (2) High selectivity of syn-attack is observed in the reduction with tri-*t*-butoxyaluminum hydride for all the substrates. (3) The anti/syn-selectivity is widely varied in the reduction with lithium aluminum hydride in THF, diisobutylaluminum hydride, and disiamylborane; in these cases, the main product is switched from anti- to syn-alcohol when the benzene ring becomes electron-donating. Obviously, steric effect of the substituents on the benzene ring or the H_{2,3}-exo protons do not provide a rationalization for the observed stereoselectivity sequence. On the other hand, this sequence is the one that was discussed in homoconjugation interaction, strongly indicating the importance of electronic effects.

Several electronic factors have been previously reported on the stereoselectivity in the nucleophilic addition to cyclic ketones. Especially with regard to cyclohexanones, the origin of the selectivity is highly controversial: product development control, torsional strain,²³⁾ orbital interaction,²⁴⁾ antiperiplanar interaction with axial hydrogen,²⁵⁾ steric effect of axial hydrogen at C₄,²⁶⁾ and electrostatic potential field²⁷⁾ have been proposed. Recently, Hudec and Giddings reported a new view of "twist-angle," which is determined by the relative signs of coefficients of p_{x,y,z}-orbitals of carbonyl carbon in LUMO of ketones, to rationalize the stereoselectivity in the nucleophilic addition to cyclic ketones including 7-norbornenone.²⁸⁾ For 7-norbornenone, they predicted that the endocyclic double bond facilitates the syn-attack and rationalized the result of syn-attack in sodium borohydride reduction. However, our experiments clearly show that anti-attack increases when the electron-donating substituents are situated on the benzene ring. Therefore, the model proposed by Hudec and Giddings cannot explain our results. A related but more successful transition state model has been recently reported by Cieplak.²⁹⁾ He assumed that the incipient C-Nu bond is weak and essentially electron-deficient and therefore can be characterized as a σ^* -orbital. In his model, nucleophiles preferably attack the carbonyl group from the direction such that the σ^* -orbital can interact with the electron-donating orbitals neighboring the carbonyl group. Le Noble and co-workers recently reported that the model developed by Cieplak reasonably explained the stereoselectivity of a series of substituted adamantanones.³⁰⁾ Participation of donor orbitals on the stabilization of polarized carbonyl group of the adamantanones may be supported by the recent X-ray study of the complex, 5-phenyl-2-adamantanone-pentachloroantimony reported by Laube and Stilz.³¹⁾

Application of Cieplak's model to our system gives a satisfactory rationalization. Qualitative transition models are illustrated in **A** for anti-attack and in **B** for syn-attack. In **A**, the transition state is much stabilized



by the large bonding overlap of back side lobe of σ^* -orbital with benzene π -orbital, compared with the transition state in **B**. Thus, increase of electron-donating character of the benzene ring would increase the anti-attack. Furthermore, Cieplak predicts that coordination of metal ions to the carbonyl oxygen would decrease the energy of σ^* -orbital, so that higher stereoselectivity would be observed. This can explain higher anti-attack for **2d** and **2e** in the reduction with diisobutylaluminum hydride and disiamylborane, both of which have a Lewis acid character and would coordinate onto the carbonyl oxygen in the transition state. Lithium ion in THF is also known to coordinate onto carbonyl groups.³²⁾ Thus, Cieplak's model satisfactorily explains our results.

However, similar rationalization is also provided by the contribution of nonclassical carbocation. As Cieplak pointed out that the incipient C-H bond is electron-deficient and polarized in nature, some positive charge remains on the carbonyl carbon to a greater extent than in the ground state. Coordination onto the carbonyl oxygen must assist this polarization. When the benzene ring becomes electron-rich, the transition state for anti-attack would be stabilized as shown in **C**. Thus, the explanations with Cieplak's and nonclassical carbocation models lead to the similar conclusion in this system. We do not have choice of one from the two explanations because of their totally different languages.

It is interesting to compare the results of anti/syn-stereoselectivity in metal hydride reduction of **2a-f** with that in singlet oxygen addition to isopropylidene derivatives **8a-f**. As can be recognized from Tables 2 and 3, higher selectivity of anti-attack for the substrates which have the same substituents on the benzene ring is observed in the reaction with singlet oxygen (e.g. anti/syn-attack for singlet oxygen; 76/24 for **8c**, for LAH reduction with THF; 38/62 for **2c**). High anti-selectivity of addition of other electrophiles to **8** have been reported.^{16,22)} The different selectivity in the two systems is probably related to the difference of the approach of the reagents to the C=C and C=O bond. Electrophiles would attack from the center of C=C in the transition state because of the bonding nature of HOMO of C=C. Whereas nucleophiles would attack the carbonyl group from the side of carbonyl carbon with obtuse angle of Nu-C-O³³⁾ because of the antibonding nature of LUMO of C=O. From this consideration, nucleophilic attack toward 9-benzonorbornenones or 7-norbornenone would involve much severe steric repulsion with H_{2,3}-exo protons in com-

parison with electrophilic addition to the corresponding 9-isopropylidene analogues. High selectivity of syn-attack in the reduction with very bulky tri-*t*-butoxyaluminum hydride for all the substrates may be ascribed to this factor. In this case, the contribution of the electronic factor would be minimized.

Higher syn-selectivity toward **2a** and **2b** for all the metal hydrides may be due to several factors. The expected small electronic contribution via Cieplak's model or nonclassical carbocation as well as steric repulsion with H_{2,3}-exo protons, which would be similar in all the substrates, would suggest more or less syn-attack. However exclusive syn-attack for **2a** may indicate that certain level of special electronic factor such as electrostatic potential field is exerted. Such field calculation in the related isopropylidene system has been reported by Paquette and Gleiter et al.^{16,22)}

In summary, we have demonstrated electronic control of stereoselectivity in the metal hydride reductions of a series of 9-benzonorbornenones: anti-attack prevails when benzene ring becomes electron-rich. Brown's original expectation that anti/syn-stereoselectivity in the nucleophilic addition may reflect the homoconjugation character is realized in this paper. Rationalizations are provided by Cieplak's model or by the contribution of nonclassical carbocation. Since both explanations are related to HOMO-LUMO interaction between *p*-orbital of the polarized carbonyl carbon with benzene π -orbital in the transition state, the observed stereoselectivity must be lined parallel with the homoconjugation interaction which is related to the interaction of weakly polarized C=O and benzene π -orbitals in the ground state. A steric effect of H_{2,3}-exo protons must be also important for the metal hydride reductions. However, such effect is very similar in the series of 9-benzonorbornenones for the given metal hydrides. High syn-selectivity of **2a** is probably due to the special electrostatic potential field effect.

Experimental

General. Melting points were measured on a Mettler FP2 apparatus and are uncorrected. IR spectra were recorded with a Hitachi EPI-G3 grating spectrophotometer and wavenumbers were corrected with use of polystyrene film. The wavenumbers of the carbonyl stretching for **2a**–**f** were directly read from the spectrophotometer at their maximum absorptions. ¹H NMR spectra were obtained at 90 MHz on a JEOL FX-90Q, or 100 MHz on a Varian XL-100. ¹³C NMR spectra were taken with a JEOL FX-90Q (22.5 MHz). Mass spectra were measured on a JEOL JMS-01SG-2 mass spectrometer. GLC analyses were performed on a Hitachi 063 gas chromatography with a glass column packed with Silicone OV-17 (3%) on Chromosorb W AW DMCS (1 m). Column chromatography was carried out with Merck Kieselgel 60 or Merck Aluminiumoxide 90 and preparative TLC with Merck Kieselgel GF₂₅₄ (Type 60). Lithium aluminum hydride, sodium borohydride, lithium tri-*t*-butoxyaluminum hydride, and diisobutylaluminum hydride were commercial products and used without purification. Dibo-

rane and disiamylborane were generated in situ prior to use.³⁴⁾ Compounds **2a**,¹⁵⁾ **2b**,¹⁵⁾ **2c**,¹⁵⁾ and **2d**¹⁶⁾ were prepared according to the reported methods. All the solvent were distilled before use.

1,4-Dihydro-9-isopropylidene-6,7-dimethoxy-1,4-methanonaphthalene (7e). In a 300 ml three-necked round bottom flask equipped with a dropping funnel was placed 100 ml of dry THF, 10.0 g (33.9 mmol) of 1,2-dibromo-4,5-dimethoxybenzene (**5**) and 4.70 g (44.3 mmol) of 6,6-dimethylfulvene (**6**). The mixture was flashed with nitrogen, cooled to –50°C, and magnetically stirred while 55 mmol of butyllithium in 34 ml hexane solution (1.63 M; 1 M=1 mol dm^{–3}) was slowly added over 40 min from the dropping funnel. The solution was stirred at –50––34°C for 1 h, and allowed to come up slowly to ambient temperature. After being stirred for 1 h, the mixture was treated dropwise with 80 ml of water and then 60 ml of ether. The separated organic layer was dried, filtered, and concentrated. Chromatography over 50 g silica gel (eluent; hexane:ethyl acetate=10:1) gave 3.08 g (37%) of **7e**. Recrystallization from hexane gave colorless prisms; mp 79–80°C; IR (KBr) 2930, 2900, 1603, 1488, 1462, 1295, 1208, 1086, 1050, 754 cm^{–1}; ¹H NMR (100 MHz, CDCl₃) δ =1.53 (s, 6H), 3.80 (s, 6H), 4.30 (dd, 2H, *J*=1.8, 1.8 Hz), 6.83–6.95 (m, 4H); MS (75 eV) *m/z* (%) 242 (M⁺; 40), 227 (7), 188 (14), 115 (100). Found: C, 79.27; H, 7.49%. Calcd for C₁₆H₁₈O₂: C, 79.31; H, 7.49%.

1,2,3,4-Tetrahydro-9-isopropylidene-6,7-dimethoxy-1,4-methanonaphthalene (8e). To a 50 ml two-necked flask containing 50 mg of 5% Pd on charcoal was added 4.00 g (16.5 mmol) of **7e** dissolved in 20 ml of ethyl acetate. The suspension was flashed with hydrogen (1 atm) and stirred for 3 h at 0°C. Filtration through Celite and evaporation of the solvent produced almost pure **8e**. Recrystallization from hexane gave colorless prisms; mp 82–84°C; IR (KBr) 2945, 2860, 1601, 1499, 1468, 1458, 1323, 1312, 1287, 1252, 1215, 1196, 1110, 1103, 1088, 1020, 794 cm^{–1}; ¹H NMR (100 MHz, CDCl₃) δ =1.18 (m, 2H), 1.59 (s, 6H), 1.86 (m, 2H), 3.69 (dd, 2H, *J*=1.8, 1.8 Hz), 3.80 (s, 6H), 6.75 (s, 2H); ¹³C NMR (CDCl₃) δ =27.34, 43.78, 56.30, 109.74, 139.73, 147.89. Found: C, 78.29; H, 8.21%. Calcd for C₁₆H₂₀O₂: C, 78.65; H, 8.25%.

1,4-Dihydro-6,7-dimethoxy-9-benzylidene-1,4-methanonaphthalene (10). To a solution of 6.00 g (20.3 mmol) of 1,2-dibromo-4,5-dimethoxybenzene (**5**) and 4.70 g (30.5 mmol) of 6-phenylfulvene (**9**) in 60 ml of dry THF cooled to –50°C under nitrogen was added 16.2 ml (26.2 mmol) of a hexane solution of butyllithium (1.62 M) dropwise via syringe over 25 min. After being stirred at –50––60°C for 1 h, the solution was gradually warmed up to room temperature and further stirred for an additional 1 h. Ether (40 ml) and water (50 ml) were added to the mixture. The separated organic layer was dried, filtered, and concentrated under reduced pressure. Column chromatography over 80 g silica gel (eluent; hexane:ethyl acetate=5:1) afforded 1.42 g (24%) of **10**. Recrystallization from ethanol gave colorless prisms; mp 123–125°C; IR (KBr) 3000, 2935, 2900, 2830, 1680, 1603, 1490, 1297, 1219, 1095, 1074, 1054, 853, 771, 712 cm^{–1}; ¹H NMR (100 MHz, CDCl₃) δ =3.81 (s, 3H), 3.82 (s, 3H), 4.20 (m, 1H), 4.70 (m, 1H), 5.49 (s, 1H), 6.89–7.04 (m, 4H), 7.08–7.41 (m, 5H); MS (75 eV) *m/z* (%) 290 (M⁺; 100), 275 (11), 259 (14). Found: C, 82.40; H, 6.31%. Calcd for C₂₀H₁₈O₂: C, 82.73; H, 6.25%.

1,2,3,4-Tetrahydro-6,7-dimethoxy-9-benzylidene-1,4-methanonaphthalene (11). A solution of 1.06 g (3.66 mmol)

of **10** in 10 ml of ethyl acetate in the presence of 100 mg of 1.2% Pd on calcium carbonate³⁵) was stirred under hydrogen (1 atm) at 0°C. During hydrogenation, the absorption of volume of hydrogen was measured. After 16 h, the solution was filtered and evaporated under reduced pressure. Recrystallization of the crude product from ethanol gave 0.977 g (92%) of **11** as colorless needles; mp 56–58°C; IR (KBr) 2930, 2860, 1690, 1610, 1498, 1470, 1327, 1316, 1285, 1220, 1104, 1088, 1020, 793, 706 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.32 (m, 2H), 2.05 (m, 2H), 3.58 (m, 1H), 3.82 (s, 3H), 3.84 (s, 3H), 4.14 (m, 1H), 5.92 (s, 1H), 6.82 (s, 1H), 6.84 (s, 1H), 7.09–7.42 (m, 5H); Found: C, 81.89; H, 6.96%. Calcd for C₂₀H₂₀O₂: C, 82.16; H, 6.90%.

1,2,3,4-Tetrahydro-6,7-dimethoxy-1,4-methanonaphthalen-9-one (2e). To a solution of 450 mg (1.54 mmol) of **11** in 15 ml of dichloromethane was added 5 ml of aqueous sodium hydrogen carbonate (0.5 M) and *m*-chloroperbenzoic acid (310 mg, 1.79 mmol). The mixture was stirred for 2 h at room temperature. The progress of the reaction was followed by TLC. To this mixture was further added 100 mg (0.578 mmol) of *m*-chloroperbenzoic acid. After 1 h of stirring, dichloromethane (15 ml) was added to the mixture and the organic layer was washed with 20 ml of 10% sodium hydrogensulfite solution, 20 ml of saturated sodium hydrogencarbonate solution, and brine prior to drying over magnesium sulfate. After filtration and evaporation of the solvent, the mixture was passed through a short alumina column to give a mixture of epoxides **12** (284 mg; 60%, anti:syn=7:1 from NMR analysis). The mixture of epoxides was used for the next step without separation. To a stirred solution of 230 mg (1.01 mmol) of periodic acid in dry THF (3 ml) at 0°C was added a solution of 284 mg (0.922 mmol) of **12** in 6 ml of dry THF. After 1 h, ether (15 ml) was added to the mixture. The organic layer was washed with saturated sodium hydrogencarbonate, dried and evaporated. Chromatography over 18 g of silica gel (eluent; hexane:ethyl acetate=5:1) of the crude products gave 100 mg (50%) of **2e**. Recrystallization from hexane–benzene gave colorless prisms; mp 142–143°C; IR (CCl₄) 2975, 1778, 1493, 1466, 1321, 1278, 1225, 1078, 1013, 856 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.34 (m, 2H), 2.18 (m, 2H), 3.30 (dd, 2H, *J*=1.8, 1.8 Hz), 3.86 (s, 6H), 6.89 (s, 2H); ¹³C NMR (CDCl₃) δ=23.01, 47.49, 56.35, 106.22, 132.93, 148.69; MS (75 eV) *m/z* (%) 218 (M⁺; 14), 190 (100), 175 (32). Found: C, 71.32; H, 6.44%. Calcd for C₁₃H₁₄O₃: C, 71.54; H, 6.47%.

1,4-Dihydro-9-isopropylidene-5,6,7,8-tetramethoxy-1,4-methanonaphthalene (7f). To a stirred solution of 3.36 g (9.44 mmol) of 1,2-dibromo-3,4,5,6-tetramethoxybenzene (**13**) and 2.00 g (18.8 mmol) of 6,6-dimethylfulvene (**6**) in 25 ml of dry THF cooled at –50°C under nitrogen was added dropwise butyllithium (12 mmol) in 7.6 ml of hexane solution (1.62 M) over 10 min via syringe. The mixture was stirred for 1 h at –50––44°C and slowly allowed to come up to room temperature. After 1 h of stirring, water (20 ml) and ether (20 ml) was added. The separated organic layer was dried and evaporated under reduced pressure. Chromatography over 70 g silica gel (eluent; hexane:ethyl acetate=15:1) afforded 1.38 g (48%) of **7f**. Recrystallization from hexane gave colorless prisms; mp 51–53°C; IR (KBr) 2990, 2965, 2925, 1471, 1451, 1409, 1402, 1350, 1262, 1190, 1116, 1071, 1027, 1020, 973, 959, 751 cm⁻¹. ¹H NMR (90 MHz, CDCl₃) δ=1.55 (s, 6H), 3.86 (s, 12H), 4.60 (dd, 2H, *J*=1.8, 1.8 Hz), 6.90 (dd, 2H, *J*=1.8, 1.8 Hz); MS (75 eV) *m/z* (%) 302

(M⁺; 100), 287 (50). Found: C, 71.39; H, 7.33%. Calcd for C₁₈H₂₂O₄: C, 71.50; H, 7.33%.

1,2,3,4-Tetrahydro-9-isopropylidene-5,6,7,8-tetramethoxy-1,4-methanonaphthalene (8f). According to the similar procedure with the preparation of **11**, 1.00 g (3.31 mmol) of **7f** was converted to the hydrogenated **8f** (936 mg, 3.08 mmol, 93%). Recrystallization from ethanol–water gave as colorless plates; mp 55–59°C; IR (KBr) 2980, 2950, 2920, 1471, 1449, 1410, 1360, 1291, 1268, 1120, 1108, 1081, 1060, 1025, 1007, 966 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) δ=1.32 (m, 2H), 1.63 (s, 6H), 1.86 (m, 2H), 3.87 (s, 12H), 3.97 (dd, 2H, *J*=1.8, 1.8 Hz); ¹³C NMR (CDCl₃) δ=19.89, 27.10, 40.43, 61.23, 61.28, 110.09, 135.15, 142.73, 144.30. Found: C, 70.87; H, 8.00%. Calcd for C₁₈H₂₄O₄: C, 71.03; H, 7.95%.

1,2,3,4-Tetrahydro-5,6,7,8-tetramethoxy-1,4-methanonaphthalen-9-one (2f). A solution of 702 mg (4.18 mmol) of 2,3-dimethoxy-1,4-benzoquinone (**14**) and 1.60 g (6.06 mmol) of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (**15**) in 5 ml of xylene was refluxed for 20 h with stirring under nitrogen. After evaporation of the solvent under reduced pressure, the mixture was separated with chromatography over 40 g silica gel (eluent; hexane:ethyl acetate=2:1) to give 1.76 g (97%) of the endo adduct **16**. Recrystallization from hexane–benzene gave colorless prisms; mp 121–122°C; IR (KBr) 2950, 2845, 1698, 1680, 1594, 1458, 1330, 1294, 1259, 1247, 1189, 1148, 1121, 1044, 1015, 1009, 979, 957, 910, 815, 623 cm⁻¹. ¹H NMR (100 MHz, CDCl₃) δ=3.57 (s, 5H), 3.66 (s, 3H), 3.97 (s, 6H); MS (75 eV) *m/z* (%) 434 (M⁺+4, 4), 432 (M⁺+2, 8), 430 (M⁺, 5), 401 (5), 399 (34), 397 (95), 395 (100). Found: C, 41.80; H, 3.29; Cl, 32.61%. Calcd for C₁₅H₁₄O₆Cl₄: C, 41.70; H, 3.27; Cl, 32.82%. A solution of 800 mg (1.85 mmol) of **16** and 0.3 ml (3.7 mmol) of pyridine in 10 ml dry methanol was refluxed for 20 h. To the cooled solution were added 30 ml of dichloromethane and 20 ml of hydrochloric acid (1 M). The separated organic layer was washed with brine, dried, and concentrated. Separation with chromatography over 30 g silica gel (eluent; hexane:ethyl acetate=2:1) gave 625 mg (78%) of **17**. Recrystallization from hexane–benzene gave colorless plates; mp 144–145°C; IR (KBr) 3490, 3390, 2950, 2845, 1603, 1477, 1438, 1305, 1260, 1190, 1131, 1078, 1007, 950, 781, 763, 699, 682, 664 cm⁻¹. ¹H NMR (100 MHz, CDCl₃) δ=3.52 (s, 3H), 3.64 (s, 3H), 3.91 (s, 6H), 5.67 (s, 2H). Found: C, 42.01; H, 3.32; Cl, 32.73%. Calcd for C₁₅H₁₄O₆Cl₄: C, 41.70; H, 3.27; Cl, 32.82%. A solution of 460 mg (1.06 mmol) of **17** in 10 ml of dry acetone containing 0.20 ml (2.1 mmol) of dimethyl sulfate and 3.1 g (22 mmol) of anhydrous potassium carbonate was refluxed for 15 h with vigorous stirring. The cooled solution was treated with 20 ml of water and stirred for 30 min at room temperature. The mixture was extracted with 20 ml of ether twice, and the ethereal layer was washed with brine and dried. Evaporation of ether afforded almost pure **18**. Recrystallization from hexane gave colorless prisms; mp 99–100°C; IR (KBr) 2930, 2820, 1607, 1471, 1410, 1348, 1273, 1184, 1100, 1026, 1004, 987, 964, 940, 822, 771, 693, 682, 653 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=3.50 (s, 3H), 3.66 (s, 3H), 3.82 (s, 6H), 3.92 (s, 6H). Found: C, 44.41; H, 3.91; Cl, 30.96%. Calcd for C₁₇H₁₈O₆Cl₄: C, 44.37; H, 3.94; Cl, 30.82%. A solution of 2.43 g (5.28 mmol) of **18** in a mixture of triethylamine (25 ml) and ethanol (50 ml) containing 300 mg of 5% palladium on charcoal was stirred for 3 h under hydrogen (1 atm) at room temperature. Filtration through Celite and evaporation of the solvent gave almost pure **19** (1.88 g,

91%). Recrystallization from hexane afforded colorless prisms; mp 113–115 °C; IR (KBr) 2925, 2820, 1470, 1410, 1359, 1291, 1253, 1189, 1105, 1067, 1040, 997, 977, 933, 842, 810, 710, 620 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.77 (m, 2H), 2.50 (m, 2H), 3.53 (s, 3H), 3.73 (s, 3H), 3.83 (s, 6H), 3.92 (s, 6H). Found: C, 51.87; H, 5.64; Cl, 18.16%. Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_6\text{Cl}_2$: C, 51.92; H, 5.64; Cl, 18.03%. To a solution of 2.00 g (15.6 mmol) of naphthalene in 30 ml dry DME under nitrogen at 0 °C was added sodium (290 mg, 12.6 mmol). To this sodium naphthalenide solution was added dropwise at 0 °C a solution of 1.00 g (2.54 mmol) of **19** in 10 ml of dry DME. After 30 min, the mixture was slowly treated with 10 ml of ethanol, 60 ml of water, and extracted with 70 ml of ether twice. The ether layer was washed with brine and dried. Purification with chromatography over 30 g silica gel (eluent; hexane:ethyl acetate=6:1) afforded 750 mg (91%) of acetal **19**. Recrystallization from hexane gave colorless prisms; mp 69–70 °C; IR (KBr) 2945, 2825, 1472, 1413, 1369, 1302, 1277, 1179, 1138, 1089, 1064, 1031, 958, 801 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.16 (m, 2H), 2.12 (m, 2H), 3.12 (s, 3H), 3.29 (s, 3H), 3.50 (dd, 2H, J =1.8, 1.8 Hz), 3.83 (s, 6H), 3.88 (s, 6H). Found: C, 62.92; H, 7.45%. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_6$: C, 62.95; H, 7.46%. To a solution of 666 mg (2.06 mmol) of **19** in 10 ml of dioxane was added a solution of 20% aqueous sulfuric acid (20 ml) at 0 °C. After 11 h of stirring at 50 °C, the solution was cooled, poured into 30 ml of water, and extracted with 50 ml of ether twice. The combined ether layer was washed with brine, dried, and concentrated. Purification with chromatography over 10 g silica gel (eluent; hexane:ethyl acetate=5:1) afforded 485 mg (85%) of **2f**. Recrystallization from hexane gave colorless prisms; mp 92–94 °C; IR (CCl_4) 2925, 1785, 1481, 1420, 1410, 1360, 1302, 1272, 1121, 1084, 1063, 1032, 1012 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.43 (m, 2H), 2.24 (m, 2H), 3.54 (dd, 2H, J =1.8, 1.8 Hz), 3.86 (s, 6H), 3.90 (s, 6H); ^{13}C NMR (CDCl_3) δ =22.59, 44.02, 61.38, 61.49, 127.50, 144.16, 145.65; MS (75 eV) m/z (%) 278 (M^+ ; 23), 250 (100), 235 (80), 207 (16). Found: C, 64.70; H, 6.52%. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_5$: C, 64.73; H, 6.52%.

Prototypical Procedure for Reductions with Lithium Aluminum Hydride. To a suspension of 28 mg (0.74 mmol) of lithium aluminum hydride in 5 ml of dry ether under nitrogen at 0 °C was added dropwise a solution of 100 mg (0.63 mmol) of **2c** in 5 ml of dry ether. After 30 min, the reaction was quenched by addition of 0.1 ml of water. The ether layer was dried over magnesium sulfate and directly subjected to GLC analysis (**3c**:**4c**=81:19). Separation with preparative TLC gave 80 mg (0.50 mmol) of **3c** and 20 mg (0.13 mmol) of **4c** in total yield of 99%. The yields for other derivatives were as follows; in ether: 96% for **2a**, 79% for **2b**, 99% for **2d**, 89% for **2e**, and 80% for **2f**, in THF: 98% for **2a**, 71% for **2b**, 97% for **2c**, 99% for **2d**, 91% for **2e**, and 90% for **2f**. The anti/syn ratio of the alcohols are listed in Table 3. A large volume (80–100 ml) of solvents were used to dissolve 100 mg of **2b**. Physical data for the alcohols **3a–f** and **4b–f** are as follows; **3a**: colorless prisms from hexane; mp 122–124 °C; IR (KBr) 3300, 2905, 1500, 1482, 1301, 1139, 1032, 951, 888, 777 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.22 (m, 2H), 1.90–2.38 (m, 3H), 3.42 (m, 2H), 3.82 (m, 1H). Found: C, 56.79; H, 3.43%. Calcd for $\text{C}_{11}\text{H}_8\text{OF}_4$: C, 56.90; H, 3.47%. **3b**: colorless needles from hexane; mp 133–135 °C; IR (KBr) 3255, 2920, 1371, 1294, 1101, 1065, 678 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.23 (m, 2H), 2.02 (br s, 1H), 2.24 (m, 2H), 3.46 (m, 2H), 3.92 (m, 2H). **4b**: colorless needles from hexane;

mp 162–165 °C; IR (KBr) 3260, 2945, 1374, 1309, 1132, 1122, 1070 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.18 (m, 2H), 1.76 (br s, 1H), 2.08 (m, 2H), 3.52 (m, 2H), 4.20 (br s, 1H). Found: C, 44.14; H, 2.72; Cl, 47.41%. Calcd for $\text{C}_{11}\text{H}_{18}\text{OCl}_4$: C, 44.34; H, 2.71; Cl, 47.59%. **3c**:^{13,24} colorless needles from hexane; mp 103–105 °C; IR (KBr) 3250, 2970, 1350, 1337, 1105, 1080, 747 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.18 (m, 2H), 1.87 (br s, 1H), 2.10 (m, 2H), 3.11 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.80 (br s, 1H), 7.06 (s, 4H). **4c**:^{13,23,24} colorless needles from hexane; mp 114–115 °C; IR (KBr) 3250, 2970, 1458, 1370, 1271, 1151, 1124, 1068, 750 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.11 (m, 2H), 1.58 (br s, 1H), 1.96 (m, 2H), 3.16 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 4.10 (br s, 1H), 6.99–7.30 (m, 4H). **3d**: colorless needles from hexane; mp 107–108 °C; IR (KBr) 3560, 3530, 2950, 2835, 1508, 1468, 1459, 1446, 1298, 1260, 1165, 1093, 1065, 969, 811, 800, 717 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.17 (m, 2H), 1.95–2.21 (m, 3H), 3.11 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.72 (s, 6H), ca 3.7 (m, 1H), 6.54 (s, 2H). Found: C, 70.69; H, 7.28%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.88; H, 7.32%. **4d**: colorless needles from hexane; mp 68–70 °C; IR (KBr) 3945, 3920, 2945, 2880, 1502, 1463, 1302, 1259, 1168, 1075, 1032, 961, 794, 715 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.12 (m, 2H), 1.63 (br s, 1H), 1.92 (m, 2H), 3.40 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.73 (s, 6H), 4.06 (t, 1H, J =1.8), 6.61 (s, 2H). Found: C, 70.83; H, 7.28%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.88; H, 7.32%. **3e**: colorless needles from hexane; mp 118–119 °C; IR (KBr) 3520, 2930, 1499, 1463, 1331, 1248, 1216, 1097, 1069, 771 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.14 (m, 2H), 1.97–2.23 (m, 3H), 3.07 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.81 (m, 1H), 3.82 (s, 6H), 6.77 (s, 2H). Found: C, 71.00; H, 7.41%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.88; H, 7.32%. **4e**: colorless prisms from hexane–benzene; mp 107–108 °C; IR (KBr) 3325, 2965, 1500, 1491, 1461, 1328, 1282, 1121, 1092, 1074, 1039, 783 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.08 (m, 2H), 1.72 (br d, 1H, J =ca. 9.0 Hz), 1.94 (m, 2H), 3.11 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.86 (s, 6H), 4.11 (m, 1H), 6.89 (s, 2H). Found: C, 70.82; H, 7.38%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C, 70.88; H, 7.32%. **3f**: colorless needles from hexane; mp 105–106 °C; IR (KBr) 3315, 2970, 2940, 1478, 1417, 1319, 1295, 1126, 1065, 1027, 1005 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.03 (m, 2H), 1.93–2.27 (m, 2H), 3.34 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.82 (m, 1H), 3.83 (s, 6H), 3.86 (s, 6H). Found: C, 63.96; H, 7.14%. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_5$: C, 64.27; H, 7.19%. **4f**: colorless needles from hexane; mp 121–124 °C; IR (KBr) 3320, 2935, 1472, 1413, 1364, 1309, 1089, 1068, 1032, 1020, 973 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3) δ =1.18 (m, 2H), 1.58 (d, 1H, J =9.0 Hz), 2.00 (m, 2H), 3.42 (ddd, 2H, J =1.8, 1.8, 1.8 Hz), 3.85 (s, 6H), 3.90 (s, 6H), 4.11 (dt, 1H, J =9.0, 1.8 Hz); Found: C, 64.00; H, 7.17%. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_5$: C, 64.27; H, 7.19%.

Prototypical Procedure for Reductions with Diisobutylaluminum Hydride. To a solution of 100 mg (0.633 mmol) of **2c** in 10 ml of dry ether under nitrogen at 0 °C was added dropwise a 1.43 ml hexane solution of diisobutylaluminum hydride (2.50 mmol). After being stirred for 30 min at 0 °C, the mixture was treated with 2 ml of ethanol and 8 ml of aqueous hydrochloric acid (2 M). The separated ether layer was washed with brine and dried over magnesium sulfate. GLC analysis of the mixture gave the ratio of **3c**:**4c**=43:57. The products were separated with preparative TLC to give 35 mg (0.22 mmol) of **3c** and 47 mg (0.29 mmol) of **4c** in total yield of 81%. Yields for other derivatives were 86% for **2a**, 83% for **2b**, 76% for **2d**, 92% for **2e**, and 80% for **2f**.

Prototypical Procedure for Reductions with Lithium Tri-

***t*-butoxyaluminum Hydride.** To a suspension of 640 mg (2.52 mmol) of lithium tri-*t*-butoxyaluminum hydride in 5 ml of dry ether under nitrogen at 0 °C was added a solution of 100 mg (0.633 mmol) of **2c** in 5 ml of dry ether. After 30 min of stirring at 0 °C, the mixture was treated with 3 ml of ethanol and 8 ml of aqueous hydrochloric acid (2 M). The separated ether layer was washed with brine, dried over magnesium sulfate, and subjected to GLC analysis (**3c**: **4c**=93:7). The products were purified with preparative TLC to give 92 mg (0.58 mmol) of **3c** and 7 mg (0.04 mmol) of **4c** in total yield of 98%. The yields for other derivatives were 99% for **2a**, 79% for **2b**, 97% for **2d**, 99% for **2e**, and 97% for **2f**.

Prototypical Procedure for Reductions with Sodium Borohydride. To a solution of 26 mg (0.69 mmol) of sodium borohydride in 5 ml of dry ethanol at 0 °C was added a solution of 100 mg (0.633 mmol) of **2c** in 8 ml of dry ethanol. After being stirred for 30 min at 0 °C, the mixture was treated with 30 ml of water and extracted with 20 ml of ether twice. The ether layer was washed with brine and dried over magnesium sulfate. GLC analysis afforded the anti/syn ratio (**3c**: **4c**=81:19). Separation with preparative TLC gave 76 mg (0.48 mmol) of **3c** and 19 mg (0.12 mmol) of **4c** in 94% total yield. The yields for other derivatives were 99% for **2a**, 77% for **2b**, 94% for **2d**, 89% for **2e**, and 88% for **2f**.

Prototypical Procedure for Reductions with Diborane. To a suspension of 48 mg (1.3 mmol) of sodium borohydride in 10 ml of anhydrous THF under nitrogen at 15–18 °C was added dropwise 0.21 ml (1.7 mmol) of boron trifluoride etherate. After being stirred for 30 min, a solution of 100 mg (0.633 mmol) of **2c** in 5 ml of THF was added to the mixture at 0 °C. After 30 min, the mixture was treated with 3 ml of ethanol and 8 ml of aqueous hydrochloric acid (2 M) and extracted with 15 ml of ether twice. The organic layer was washed with brine and dried over magnesium sulfate. GLC analysis provided the anti/syn ratio (**3c**: **4c**=75:25). The products were separated with preparative TLC to give 68 mg (0.43 mmol) of **3c** and 23 mg (0.14 mmol) of **4c** in total yield of 90%. The yields for other derivatives were 91% for **2a**, 81% for **2b**, 92% for **2d**, 96% for **2e**, and 82% for **2f**. For the reduction of **2b**, **2b** was added as solids.

Prototypical Procedure for Reductions with Disiamylborane. To a suspension of 48 mg (1.3 mmol) of sodium borohydride and 0.35 ml (3.3 mmol) of 2-methyl-2-butene in 10 ml of dry diglyme under nitrogen at 0 °C was added 0.21 ml (1.7 mmol) of boron trifluoride etherate. The mixture was stirred for 30 min at 0 °C. To this suspension was added a solution of 100 mg (0.633 mmol) of **2c** in diglyme (5 ml) at 0 °C. After 3 h, 13 ml of aqueous sodium hydroxide (3 M) and 10 ml of 30% aqueous hydrogen peroxide were added to the mixture. After being stirred for overnight at room temperature, the mixture was poured into ice-water and extracted with 25 ml of ether twice. The ether layer was washed with brine, dried over magnesium sulfate, and subjected to GLC analysis (**3c**: **4c**=57:43). Separation with preparative TLC gave 56 mg (0.35 mmol) of **3c** and 38 mg (0.24 mmol) of **4c** in total yield of 93%. The yields for other derivatives were 86% for **2a**, 92% for **2d**, 89% for **2e**, and 72% for **2f**. Under similar conditions, **2b** was inert, resulting in 70–95% of recovery.

Prototypical Procedure for Singlet Oxygen Reactions. A water cooled solution of 200 mg (0.820 mmol) of **8e** and rose bengal (10 mg) in 50 ml of methanol was irradiated with

sodium lamp (55 W×4) while oxygen was bubbled through the solution. After 8 h, the solvent was concentrated under reduced pressure to ca. 10 ml. The mixture was treated with 310 mg (8.20 mmol) of sodium borohydride and stirred at room temperature for 12 h. After addition of 30 ml of water, the products was extracted with 30 ml of ether twice. The ether layer was washed with brine and dried over magnesium sulfate. The mixture was carefully separated with preparative TLC to give 7 mg (0.03 mmol) of the recovered **8e**, 176 mg (0.677 mmol) of **21e**, and 18 mg (0.069 mmol) of **22e**. The anti/syn ratio was 91/9. **21e**: Colorless prisms; mp 110–112 °C; IR (KBr) 3590, 2940, 1492, 1467, 1422, 1330, 1286, 1250, 1222, 1116, 1098, 1078, 1007, 901 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.19 (m, 2H), 1.71 (m, 4H), 2.30 (m, 2H), 3.19 (dd, 2H, *J*=1.8, 1.8 Hz), 3.82 (s, 6H), 4.75 (m, 1H), 4.88 (m, 1H), 6.71 (s, 2H). Found: C, 73.63; H, 7.76%. Calcd for C₁₆H₂₀O₃: C, 73.82; H, 7.74%. **22e**: colorless prisms from hexane; mp 112–115 °C; IR (KBr) 3540, 2950, 1490, 1465, 1328, 1285, 1248, 1222, 1167, 1120, 1099, 1062 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.09 (m, 2H), 1.65–2.11 (m, 6H), 3.27 (dd, 2H, *J*=1.8, 1.8 Hz), 3.87 (s, 6H), 5.08 (m, 1H), 5.16 (m, 1H), 6.91 (s, 2H). Found: C, 73.54; H, 7.73%. Calcd for C₁₆H₂₀O₃: C, 73.82; H, 7.74%. Under similar conditions **21c** and **22c** were obtained from **8c** in total yield of 95% with the ratio of **21c**: **22c**=80:20. Similarly, **21f** and **22f** were produced in total yield of 85% with the ratio of **21f**: **22f**=72:28. **21f**: colorless prisms from hexane. mp 81–82 °C; IR (KBr) 3585, 2925, 1476, 1460, 1416, 1368, 1301, 1271, 1123, 1077, 1068, 1017, 1006, 900 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.27 (m, 2H), 1.67–1.81 (m, 4H), 2.34 (m, 2H), 3.46 (dd, 2H, *J*=1.8, 1.8 Hz), 3.83 (s, 6H), 3.86 (s, 6H), 4.76 (m, 1H), 4.93 (m, 1H). Found: C, 67.37; H, 7.57%. Calcd for C₁₈H₂₄O₅: C, 67.48; H, 7.55%. **22f**: oil; IR (CCl₄) 3550, 2935, 1475, 1418, 1369, 1299, 1276, 1132, 1093, 1071, 1035, 1021, 908 cm⁻¹; ¹H NMR (100 MHz, CDCl₃) δ=1.16 (m, 2H), 1.79 (br s, 1H), 1.90–2.16 (m, 5H), 3.54 (dd, 2H, *J*=1.8, 1.8 Hz), 3.88 (s, 6H), 3.91 (s, 6H), 5.10 (m, 1H), 5.18 (m, 1H). Found: C, 67.21; H, 7.58%. Calcd for C₁₈H₂₄O₅: C, 67.48; H, 7.55%.

NMR Shift Reagent Study. The Eu(fod)₃ used was taken directly from a fresh bottle of commercial product. The purified alcohols (**3a**–**f**, **4b**–**f**) were each dissolved in CDCl₃ (25–30 mg/0.3 ml) in a NMR tube. The shift reagent, Eu(fod)₃, was weighed out and added into the solution five times in about 5 mg portions, and ¹H NMR spectrum was measured each time. The plots of the observed relative shift of each proton of the alcohol vs. the amount of added Eu(fod)₃ gave fairly good straight lines. From the slope of each proton, the relative shift value was calculated.

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