# Asymmetric Addition of an Electrophile to Naphthalenes Promoted and Stereodirected by Alcohol

**Morifumi Fujita,*,† Hironori Matsushima, Takashi Sugimura,* Akira Tai, and Tadashi Okuyama**

*Contribution from the Faculty of Science, Himeji Institute of Technology, Kouto, Kamigori, Ako-gun, Hyogo 678-1297, Japan*

*Received August 7, 2000*

**Abstract:** 4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) reacts with 1-methoxy-4-methylnaphthalene to give the 1,4-addition product in the presence of methanol; the reaction does not proceed in the absence of the alcohol. Methoxy exchange (with $CD_3OD$) was also observed during the reaction. Reactions of PTAD with 1-(3-hydroxypropoxy)-4-methylnaphthalene and related naphthalenes afford stereoselectively 1,4-adducts (70−98% of the major diastereomer). The stereoface-selective addition of PTAD at C-4 with concurrent formation of an acetal at C-1 takes place in a *syn* manner, which is induced by the hydrogen-bonding interaction between PTAD and the hydroxy group. The α-methyl substitution on the propoxy side chain strongly enhances the stereodifferentiation (90% de) and accelerates the cyclization by the Thorpe−Ingold effect. The alkoxy moiety of the adduct is easily removed to give 4-methyl-4-amino-4*H*-naphthalen-1-one with high enantiomeric excess. The γ-methyl group of the side chain also affects the stereodifferentiation. Thus, the two stereogenic centers of the (1*S*,3*R*)-3-hydroxy-1-methylbutoxy side chain work together to achieve the high stereodifferentiating 1,4-addition from the *Si-Re* face (up to 96% ee). Epimerization of the cyclic acetal of a minor adduct was observed during the reaction of 1-(3-hydroxybutoxy)-4-methylnaphthalene, indicating that the minor component of the final products is derived from the initial minor *syn* adduct formed from the opposite face. The *syn* selectivity of the addition is achieved completely in the initial stage of formation of both the major and the minor adducts.

## Introduction

Hydrogen-bonding interactions play quite important roles in various chemical and biochemical phenomena such as molecular recognition, construction of supramolecular systems, control of chemo-, regio-, and stereoselectivities of chemical reactions, and stabilization of transition states and reaction intermediates.[1−4] An alcohol function contributes to the selectivity, and the promotion of a reaction is not only due to its hydrogen-bond donor ability[5−7] but also to its nucleophilic (hydrogen-bond acceptor) ability.[8−12] The alcohol function may be provided by an external source or more efficiently as an intramolecular functional group. Many synthetic systems successfully employ a hydroxy function to promote a reaction and to achieve high stereoselectivity, but most examples utilize only one of the two capabilities of alcohol.

Asymmetric addition of electrophiles to arenes is still limited[13] in comparison with that to olefins[8,9,14,15] despite the synthetic

† E-mail: fuji@sci.himeji-tech.ac.jp.

(1) For reviews, see: (a) Kirby, A. J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 707−724. (b) Menger, F. M. *Acc. Chem. Res.* **1993**, *26*, 206−212.

(2) (a) Tominaga, M.; Konishi, K.; Aida, T. *J. Am. Chem. Soc.* **1999**, *121*, 7704−7705. (b) Rankin, K. N.; Gauld, J. W.; Boyd, R. J. *J. Am. Chem. Soc.* **2000**, *122*, 5384−5386.

(3) (a) Kelly, T. R.; Bridger, G. J.; Zhao, C. *J. Am. Chem. Soc.* **1990**, *112*, 8024−8034. (b) Jubian, V.; Dixon, R. P.; Hamilton, A. D. *J. Am. Chem. Soc.* **1992**, *114*, 1120−1121. (c) Huc, I.; Pieters, R. J.; Rebeck, J., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 10296−10297. (d) Wintner, E. A.; Conn, M. M.; Rebek, J., Jr. *Acc. Chem. Res.* **1994**, *27*, 198−203. (e) Jubian, V.; Veronese, A.; Dixon, R. P.; Hamilton, A. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1237−1239. (f) Wang, B.; Sutherland, I. O. *Chem. Commun.* **1997**, 1495−1496. (g) Kang, J.; Hilmersson, G.; Santamaría, J.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 3650−3656.

(4) (a) Uno, B.; Okumura, N.; Goto, M.; Kano, K. *J. Org. Chem.* **2000**, *65*, 1448−1455. (b) Kelly, T. R.; Meghani, P.; Ekkundi, V. S. *Tetrahedron Lett.* **1990**, *31*, 3381−3384.

(5) (a) Adam, W.; Nestler, B.; Pastor, A.; Wirth, T. *Tetrahedron Lett.* **1998**, *39*, 2625−2628. (b) Adam, W.; Gläser, J.; Peters, K.; Prein, M. *J. Am. Chem. Soc.* **1995**, *117*, 9190−9193.

(6) (a) Adam, W.; Peters, E. M.; Peters, K.; Prein, M.; von Schnering, H. G. *J. Am. Chem. Soc.* **1995**, *117*, 6686−6690. (b) Adam, W.; Prein, M. *Acc. Chem. Res.* **1996**, *29*, 275−283. (c) Adam, W.; Prein, M. *J. Am. Chem. Soc.* **1993**, *115*, 3766−3767.

(7) (a) Prein, M.; Adam, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 477−494. (b) Adam, W.; Nestler, B. *J. Am. Chem. Soc.* **1992**, *114*, 6549−6550.

(8) For reviews, see: (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370. (b) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321−3408.

(9) (a) Sugimura, T.; Iguchi, H.; Tsuchida, R.; Tai, A.; Nishiyama, N.; Hakushi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1007−1013. (b) Sugimura, T.; Nishiyama, N.; Tai, A.; Hakushi, T. *Tetrahedron: Asymmetry* **1993**, *4*, 43−44. (c) Sugimura, T.; Katagiri, T.; Tai, A. *Tetrahedron Lett.* **1992**, *33*, 367−368. (d) Sugimura, T.; Yoshikawa, M.; Futagawa, T.; Tai, A. *Tetrahedron* **1990**, *46*, 5955−5966.

(10) Stereodifferentiation in electrophilic additions to olefins using an intramolecular nucleophile has been reported: (a) Kang, S. H.; Hwang, T. S.; Kim, W. J.; Lim, J. K. *Tetrahedron Lett.* **1991**, *32*, 4015−4018. (b) Mihelich, E. D.; Hite, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7318−7319. (c) Lipshutz, B. H.; Barton, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 1084−1086. (d) Nishiyama, T.; Kitano, K.; Kishi, H.; Yamada, F. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3822−3824. (e) Barks, J. M.; Knight, D. W.; Weingarten, G. G. *J Chem. Soc., Chem. Commun.* **1994**, 719−720. (f) Barks, J. M.; Knight, D. W.; Seaman, C. J.; Weingarten, G. G. *Tetrahedron Lett.* **1994**, *35*, 7259−7262. (g) Tius, M. A.; Busch-Petersen, J. *Tetrahedron Lett.* **1994**, *35*, 5181−5184.

(11) (a) Tripathy, R.; Carroll, P. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1991**, *113*, 7630−7640. (b) Tripathy, R.; Carroll, P. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 6743−6744.

(12) (a) Bäckvall, J.-E.; Andersson, P. G. *J. Org. Chem.* **1991**, *56*, 2274−2276. (b) Andersson, P. G.; Nilsson, Y. I. M.; Bäckvall, J.-E. *Tetrahedron* **1994**, *50*, 559−572. (c) Itami, K.; Palmgren, A.; Bäckvall, J.-E. *Tetrahedron Lett.* **1998**, *39*, 1223−1226.

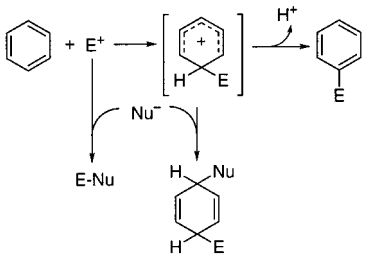
10.1021/ja0029477 CCC: $20.00 
Published on Web 03/08/2001

and biochemical importance of the resulting products.[16−20] Even nonstereocontrolled additions of electrophiles to arenes have limitations due to the facile ensuing eliminations which result in re-aromatization. Nucleophilic trapping[24] of a cationic intermediate[25] is necessary to complete a successful electrophilic addition to arenes (Scheme 1), but a direct mutual reaction of the electrophile and the nucleophile must be avoided.

Adam and co-workers[6] found that reaction of singlet oxygen with a hydroxymethylnaphthalene gave stereoselectively an unstable endoperoxide and showed that hydrogen-bonding interactions of the alcohol function play an important role in stereoselective additions to the arene.

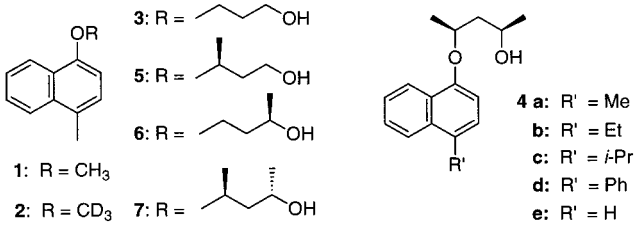
In the present paper, we report that an alcohol function promotes the electrophilic reaction of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD)[5,15,26−32] with 4-substituted 1-alkoxynaphthalenes to give stereospecifically *syn* addition products. Introduction of the (1*S*,3*R*)-3-hydroxy-1-methylbutoxy group to the naphthalene affords an optically active adduct as a stable product. The chiral auxiliary is easily removed from the adduct to give 4-substituted 4-amino-4*H*-naphthalen-1-one in a high enantiomeric excess. Both the hydrogen-bonding and nucleophilic abilities of the alcohol function are involved in this asymmetric addition. The novel role of the alcohol function in this electrophilic addition to arenes is revealed by a stereochemical analysis of the reaction.

**Scheme 1**




## Results

Reactions of PTAD with a series of 1-alkoxynaphthalenes, **1**−**7**, were examined, focusing attention on their stereochemistry. The enantiomerically pure side chain of the substrates **4**−**7** can easily be introduced by the Mitsunobu reaction.[33]




**Addition of PTAD to 1-Methoxy-4-methylnaphthalene in the Presence of Methanol.** The $^1$H NMR spectrum of a mixture

(13) Recently, asymmetric addition of an electrophile to $\eta^2$-pentaamineosmium(II) arene complexes has been reported: (a) Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **2000**, *122*, 2725−2736. (b) Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 5637−5642.

(14) (a) Poli, G.; Scolastico, C. In *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: New York, 1996; Vol. 8, pp 4547−4598. (b) Oehlschlager, A. C. In *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: New York, 1996; Vol. 8, pp 4675−4697.

(15) (a) Adam, W.; Wirth, T.; Pastor, A.; Peters, K. *Eur. J. Org. Chem.* **1998**, 501−506. (b) Adam, W.; Güthlein, M.; Peters, E.-M.; Peters, K.; Wirth, T. *J. Am. Chem. Soc.* **1998**, *120*, 4091−4093.

(16) (a) Winemiller, M. D.; Harman, W. D. *J. Org. Chem.* **2000**, *65*, 1249−1256. (b) Winemiller, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 7835−7840. (c) Kopach, M. E.; Kolis, S. P.; Liu, R.; Robertson, J. W.; Chordia, M. D.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 6199−6204. (d) Kolis, S. P.; Kopach, M. E.; Liu, R.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 6205−6211. (e) Kolis, S. P.; Kopach, M. E.; Liu, R.; Harman, W. D. *J. Org. Chem.* **1997**, *62*, 130−136. (f) Kolis, S. P.; Chordia, M. D.; Liu, R.; Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2218−2226. (g) Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 6581−6592. (h) Kopach, M. E.; Hipple, W. G.; Harman, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 1736−1740.

(17) Murahashi, S.-I.; Naota, T.; Miyaguchi, N.; Noda, S. *J. Am. Chem. Soc.* **1996**, *118*, 2509−2510.

(18) Biochemical asymmetric additions to arenes have been used for preparation of chiral synthons: (a) Gibson, D. T.; Koch, J. R.; Kallio, R. E. *Biochemistry* **1968**, *7*, 2653−2662. (b) Gibson, D. T.; Koch, J. R.; Schuld, C. L.; Kallio, R. E. *Biochemistry* **1968**, *7*, 3759−3802. (c) Hudlicky, T.; Thorpe, A. J. *Chem. Commun*. **1996**, 1993−2000. (d) Hudlicky, T.; Entwistle, D. A.; Pitzer, K. K.; Thorpe, A. J. *Chem. Rev*. **1996**, *96*, 1195−1220. (e) Hudlicky, T.; Tian, X.; Königsberger, K.; Maurya, R.; Rouden, J.; Fan, B. *J. Am. Chem. Soc*. **1996**, *118*, 10752−10765. (f) Carless, H. A. J. *Tetrahedron: Asmmetry* **1992**, *3*, 795−826.

(19) (a) Mander, L. N. *Synlett* **1991**, 134−144. (b) Bach, T. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 729−730.

(20) Asymmetric nucleophilic addition to arenes,[21] arene−metal complexes,[22] and dienones[23] also gave optically active adducts.

(21) (a) Shimano, M.; Meyers, A. I. *J. Org. Chem.* **1995**, *60*, 7445−7455. (b) Tomioka, K.; Shindo, M.; Koga, K. *Tetrahedron Lett*. **1993**, *34*, 681−682.

(22) (a) Kündig, E. P.; Ripa, A.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl*. **1992**, *31*, 1071−1073. (b) Pearson, A. J.; Zhu, P. Y.; Youngs, W. J.; Bradshaw, J. D.; McConville, D. B. *J. Am. Chem. Soc*. **1993**, *115*, 10376−10377. (c) Pearson, A. J.; Milletti, M. C.; Zhu, P. Y. *J. Chem. Soc., Chem. Commun*. **1995**, 853−854.

(23) (a) Wipf, P.; Kim. Y. *J. Am. Chem. Soc.* **1994**, *116*, 11678−11688. (b) Wipf, P.; Jung, J.-K. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 764−767. (c) Wipf, P.; Jung, J.-K. *Chem. Rev*. **1999**, *99*, 1469−1480.

(24) (a) Abramovitch, R. A.; Hawi, A.; Rodrigues, J. A. R.; Trombetta, T. R. *J. Chem. Soc., Chem. Commun.* **1986**, 283−284. (b) Fischer, A.; Fyles, D. L.; Henderson, G. N. *J. Chem. Soc., Chem. Commun*. **1980**, 513−514. (c) Corey, E. J.; Barcza, S.; Klotmann, G. *J. Am. Chem. Soc.* **1969**, *91*, 4782−4786.

(25) Ipso attack in aromatic nitration has been reported. For example: (a) Moodie, R. B.; Schofield, K. *Acc. Chem. Res*. **1976**, *9*, 287−292. (b) Banwell, T.; Morse, C. S.; Myhre, P. C.; Vollmar, A. *J. Am. Chem. Soc.* **1977**, *99*, 3042−3051. (c) Fischer, A.; Greig, C. C. *Can. J. Chem*. **1978**, *56*, 1063−1068. (d) Fischer, A.; Henderson, G. N.; RayMahasay, S. *Can. J. Chem*. **1987**, *65*, 1233−1240. (e) Tanaka, M.; Muro, E.; Ando, H.; Xu, Q.; Fujiwara, M.; Souma, Y.; Yamaguchi, Y. *J. Org. Chem*. **2000**, *65*, 2972−2978.

(26) For a recent review, see: Dádl, S. *Adv. Heterocycl. Chem*. **1997**, *67*, 119−205.

(27) Thermal addition of PTAD to naphthalenes has recently been reported to proceed reversibly: Breton, G. W.; Newton, K. A. *J. Org. Chem*. **2000**, *65*, 2863−2869.

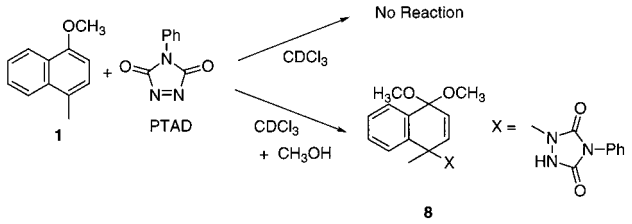
(28) Photochemical reactions of PTAD with arenes have been reported: (a) Hamrock, S. J.; Sheridan, R. S. *J. Am. Chem. Soc*. **1989**, *111*, 9247−9249. (b) Hamrock, S. J.; Sheridan, R. S. *Tetrahedron Lett.* **1988**, *29*, 5509−5512. (c) Kjell, D. P.; Sheridan, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 5368−5370.

(29) (a) Wilson, R. M.; Chantarasiri, N. *J. Am. Chem. Soc*. **1991**, *113*, 2301−2302. (b) Hall, J. H. *J. Org. Chem.* **1983**, *48*, 1708−1712. (c) Hall, J. H.; Kaler, L.; Herring, R. *J. Org. Chem.* **1984**, *49*, 2579−2582.

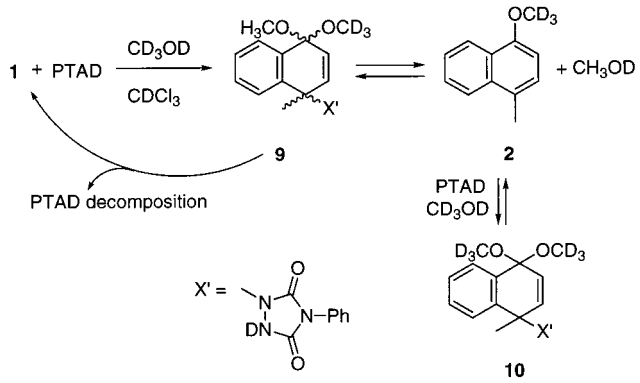
(30) (a) Vassilikogiannakis, G.; Stratakis, M.; Orfanopoulos, M.; Foote, C. S. *J. Org. Chem*. **1999**, *64*, 4130−4139. (b) Chen, J. S.; Houk, K. N.; Foote, C. S. *J. Am. Chem. Soc.* **1998**, *120*, 12303−12309. (c) Stratakis, M.; Orfanopoulos, M.; Foote, C. S. *J. Org. Chem.* **1998**, *63*, 1315−1318. (d) Chen, J. S.; Houk, K. N.; Foote, C. S. *J. Am. Chem. Soc*. **1997**, *119*, 9852−9855. (e) Poon, T. H. W.; Park, S. H.; Elemes, Y.; Foote, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 10468−10473. (f) Zhang, X.; Khan, S. I.; Foote, C. S.; *J. Org. Chem*. **1995**, *60*, 4102−4107. (g) Smonou, I.; Khan, S.; Foote, C. S.; Elemes, Y.; Mavridis, I. M.; Pantidou, A.; Orfanopoulos, M. *J. Am. Chem. Soc.* **1995**, *117*, 7081−7087. (h) Elemes, Y.; Foote, C. S. *J. Am. Chem. Soc*. **1992**, *114*, 6044−6050. (i) Orfanopoulos, M.; Smonou, I.; Foote, C. S. *J. Am. Chem. Soc.* **1990**, *112*, 3607−3614. (j) Jensen, F.; Foote, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6376−6385.

(31) (a) Singleton, D. A.; Hang, C. *J. Am. Chem. Soc.* **1999**, *121*, 11885−11893. (b) Elemes, Y.; Orfanopoulos, M. *Tetrahedron Lett.* **1991**, *32*, 2667−2670. (c) Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136−1144. (d) Adam, W.; Schwarm, M. *J. Org. Chem*. **1988**, *111*, 3129−3130. (e) Clennan, E. L.; Earlywine, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 7104−7110. (f) Orfanopoulos, M.; Foote, C. S.; Smonou, I. *Tetrahedron Lett.* **1987**, *28*, 15−18. (g) Nelsen, S. F.; Kapp, D. L. *J. Am. Chem. Soc*. **1985**, *107*, 5548−5549. (h) Cheng, C.-C.; Seymour, C. A.; Petti, M. A.; Greene, F. D. *J. Org. Chem*. **1984**, *49*, 2910−2916. (i) Seymour, C. A.; Greene, F. D. *J. Am. Chem. Soc*. **1980**, *102*, 6384−6385.

**Scheme 2**




**Scheme 3**




of 1-methoxy-4-methylnaphthalene (**1**) (0.32 M) and PTAD (0.39 M) in $CDCl_3$ solution did not change during 8 h at 298 K in the dark.[27,28] When $CH_3OH$ (1.6 equiv) was added to the mixture, immediate formation of adduct **8** was detected (Scheme 2) while most of the substrate **1** still remained (35% conversion). However, the adduct **8** disappeared in 1 h at 293 K in the dark with accompanying decomposition of PTAD[32] but the unreacted substrate **1** remained. When $CD_3OD$ was employed, a signal due to methanol (3.4 ppm) developed with concomitant decrease of the signal of the methoxy group of **1** (3.96 ppm). The formation of adduct **9** was also observed in addition to the methanol exchange (Scheme 3). Furthermore, formation of the bis(deuteriomethoxy)adduct **10** was also indicated by the loss of the methoxy signal compared with the intensity of the 4-methyl signal.

Time-dependent changes of the substrate and the products are shown in Figure 1. The time course of the reaction suggests that methoxy exchange of **1** occurs with concurrent decomposition of adduct **9**. It is noteworthy that two singlet signals ($\delta = 3.14$ (a) and 3.13 ppm (b)) due to the methoxy group of **9** were observed and the relative peak areas change with the progress of reaction as shown in Table 1. Although the configuration of **9** could not be determined because of its instability, the two signals must correspond to the *cis* and *trans* isomers. This was confirmed by comparison of the $^1$H NMR spectrum of mixture **9** with that of the epimeric mixutre **11**, which was obtained by reaction of the deuterated substrate **2** with PTAD in the presence of $CH_3OH$ (Scheme 4). The chemical shift of the major peak due to the methoxy group of **9** (3.14 ppm) is different from that of **11** (3.13 ppm) as shown in Figure 2.

**Reactions of Hydroxyalkoxynaphthalenes.** When 1-(3-hydroxypropoxy)-4-methylnaphthalene (**3**) was employed for the reaction with PTAD in $CDCl_3$, cyclic acetal **12** was obtained in the absence of methanol as shown in Figure 3. The $^1$H and $^{13}$C NMR spectra showed complete conversion of **3** to **12**.

The reaction of PTAD with **4a** in dichloromethane gave the adduct **13a** as a single diastereomer in 98% isolated yield. The

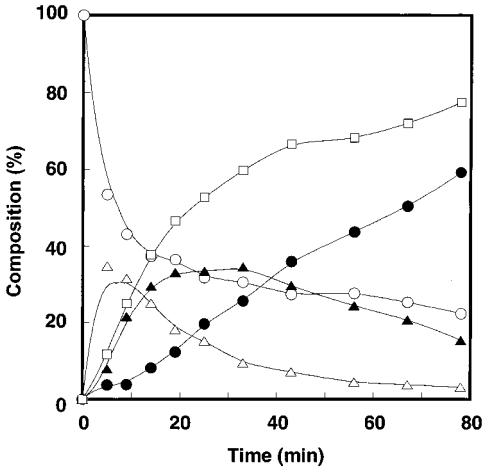



**Figure 1.** Reaction of **1** (80 mM) with PTAD (275 mM) in the presence of $CD_3OD$ (1.0 M) in $CDCl_3$ at 293 K, monitored by $^1$H NMR: **1** (○), **2** (●), **9** (△), **10** (▲), and $CH_3OD$ (□).

**Table 1.** Time Dependence of the Diastereomeric Ratio of the Adduct **9** and Yield of Adducts **9** and **10** in the Electrophilic Addition of PTAD (275 mM) to **1** (80 mM) in the Presence of $CD_3OD$ (1.0 M) in $CDCl_3$

| | **9** | | **10** |
|---|---|---|---|
| time (min) | a:b[a] | yield (%) | yield (%) |
| 5 | >95:5 | 35 | 8 |
| 9 | 84:16 | 32 | 22 |
| 14 | 80:20 | 25 | 30 |
| 19 | 72:28 | 18 | 33 |
| 25 | 69:31 | 15 | 33 |
| 33 | 61:39 | 9 | 35 |
| 43 | 59:41 | 7 | 30 |

[a] Relative peak areas at $\delta = 3.14$ (a) and 3.13 (b) ppm due to the diastereomers.

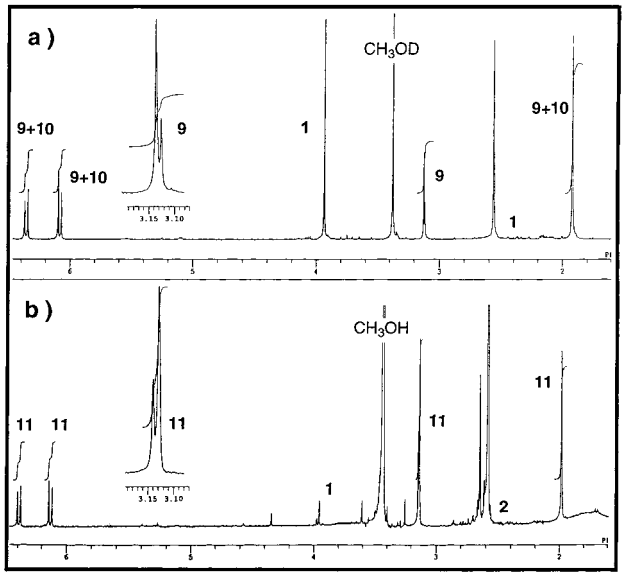



**Figure 2.** $^1$H NMR spectra of reaction mixtures of (a) **1** (80 mM) + $CD_3OD$ (1.0 M) + PTAD (275 mM) in $CDCl_3$ at 19 min and (b) **2** (128 mM) + $CH_3OH$ (254 mM) + PTAD (185 mM) in $CDCl_3$ at 6 min. Assignments of the signals are shown in the spectra.

(32) Decomposition of PTAD by alcohol has been reported: (a) Mackay, D.; Taylor, N. J.; Wigle, I. D. *J. Org. Chem.* **1987**, *52*, 1288−1290. (b) Borhani, D. W.; Greene, F. D. *J. Org. Chem.* **1986**, *51*, 1563−1570. (c) Izydore, R. A.; Johnson, H. E.; Horton, R. T. *J. Org. Chem.* **1985**, *50*, 4589−4595. (d) Nachbaur, E.; Faleschini, G.; Belaj, F.; Janoschek, R. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 701−703.

(33) (a) Fujita, M.; Takarada, Y.; Sugimura, T.; Tai, A. *Chem. Commun.* **1997**, 1631−1632. (b) Sugimura, T.; Yamada, H.; Inoue, S.; Tai, A. *Tetrahedron: Asymmetry* **1997**, *8*, 649−655.

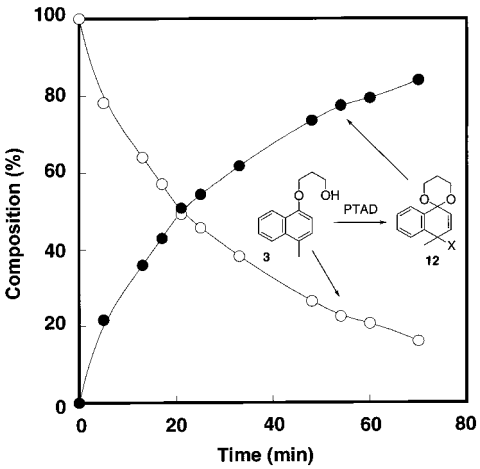
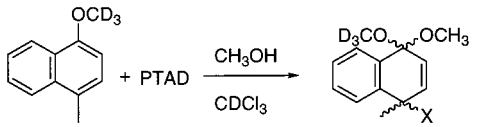
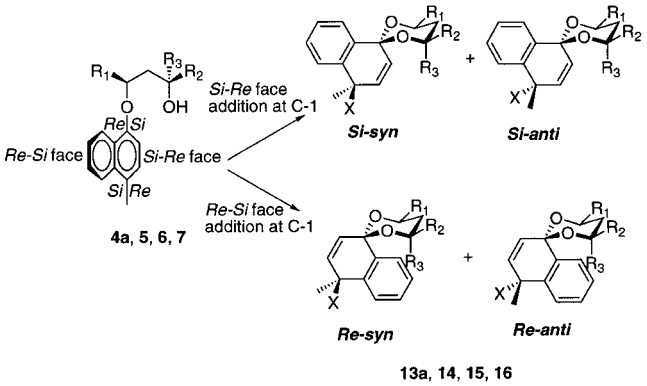



**Figure 3.** Reaction of PTAD (132 mM) with **3** (68 mM) in $CDCl_3$ at 293 K, monitored by $^1$H NMR: **3** (○) and **12** (●).

**Scheme 4**




**Scheme 5**




**4a**: $R_1$ = Me, $R_2$ = Me, $R_3$ = H affords **13a** (2 enantiomeric pairs of diastereomers)

**5**: $R_1$ = Me, $R_2$ = H, $R_3$ = H affords **14** (4 diastereomers)

**6**: $R_1$ = H, $R_2$ = Me, $R_3$ = H affords **15** (4 diastereomers)

**7**: $R_1$ = Me, $R_2$ = H, $R_3$ = Me affords **16** (2 diastereomers)

$^1$H NMR spectrum of **13a** shows that it is diastereomerically pure, and the enantiomeric ratio of **13a** was determined to be 96:4 by chiral HPLC. Possible stereoisomers of **13a** include two enantiomeric pairs of the diastereomers **13a-*Si-syn*/13a-*Si-anti*** and **13a-*Re-syn*/13a-*Re-anti***, as shown in Scheme 5, because **13a-*Si-syn*** and **13a-*Re-syn*** are mirror images of **13a-*Si-anti*** and **13a-*Re-anti***, respectively. The formation of a single diastereomer results from high stereoselectivity at C-1. The enantiomeric ratio also indicates the high stereoselectivity at C-4. The results translate to the product ratio of **13a-*Si-syn*:13a-*Si-anti*:13a-*Re-syn*:13a-*Re-anti*** = 96:4:∼0:∼0 (see below). The stereoselectivities at C-1 and C-4 remain high in benzene and acetonitrile solutions. The electrophilic addition of PTAD to the other substrates **4b**−**e** also gave single diastereomeric adducts with high enantiomeric ratios (Table 2).

The reaction of **5** in $CH_2Cl_2$ gave **14** (91% yield) with a high diastereomeric ratio (**14-*Si-syn*:14-*Si-anti*:14-*Re-syn*:14-*Re-anti*** = 95:5:∼0:∼0).[34] Other substrates **6** and **7** gave similar results.

**Table 2.** Isolated Yields and Enantiomeric Ratios of the Product **13** in Stereodifferentiating Addition of PTAD to **4** at 293 K[a]

| substrate | solvent | yield (%)[b] | enantiomeric ratio[c] |
|---|---|---|---|
| **4a** | benzene | 98 | 97:3 |
| **4a** | $CH_2Cl_2$ | 98 | 96:4 |
| **4a** | $CH_3CN$ | 81 | 96:4 |
| **4b** | $CH_2Cl_2$ | 96 | 98:2 |
| **4c** | $CH_2Cl_2$ | 93 | 95:5 |
| **4d** | $CH_2Cl_2$ | 94 | 95:5 |
| **4e** | $CH_2Cl_2$ | 71 | 91:9 |

[a] The adduct **13** is obtained as a single diastereomer (de > 98%) determined by $^1$H NMR. [b] Product yield isolated by column chromatography. [c] Enantiomeric ratio was determined by HPLC with a chiral column (Daicel CHIRALPAK AD).

**Table 3.** Stereoselectivity in the Reaction of **5**−**7** with PTAD at 293 K

| PTAD (equiv) | solvent | time (min) | yield (%) | diastereomeric ratio[a] |
|---|---|---|---|---|
| | | **5** | | |
| 1.7 | $C_6H_6$ | 180 | 95[b] | 95:5 |
| 1.2 | $CH_2Cl_2$ | 60 | 91[b] | 95:5 |
| 2.1 | $CH_3CN$ | 60 | 94[b] | 95:5 |
| 1.9 | $C_6D_6$ | 344 | 88 | 94:6 |
| 1.9 | $CDCl_3$ | 37 | 97 | 96:4 |
| | | **6** | | |
| 1.7 | $C_6H_6$ | 340 | 63[b,c] | 74:26 |
| 1.2 | $CH_2Cl_2$ | 120 | 85[b] | 72:28 |
| 6.9 | $C_6D_6$ | 68 | 27 | 82:18[d] |
| 6.9 | $C_6D_6$ | 123 | 44 | 79:21[d] |
| 6.9 | $C_6D_6$ | 240 | 70 | 76:24[d] |
| 6.9 | $C_6D_6$ | 432 | 92 | 73:27 |
| 7.1 | $CDCl_3$ | 9 | 27 | 85:15[d] |
| 7.1 | $CDCl_3$ | 34 | 71 | 76:24[d] |
| 7.1 | $CDCl_3$ | 91 | 97 | 70:30 |
| | | **7** | | |
| 1.7 | $CDCl_3$ | 74 | 84 | 95:5 |

[a] **14-*Si-syn*/14-*Si-anti*** for **5**, **15-*Si-syn*/15-*Si-anti*** for **6**, and **16-*Si-syn*/16-*Si-anti*** for **7**. [b] Isolated yield. [c] Substrate **6** was recovered (18%). [d] Transient product **19** was also detected. Yields and ratios were the values excluding **19**.

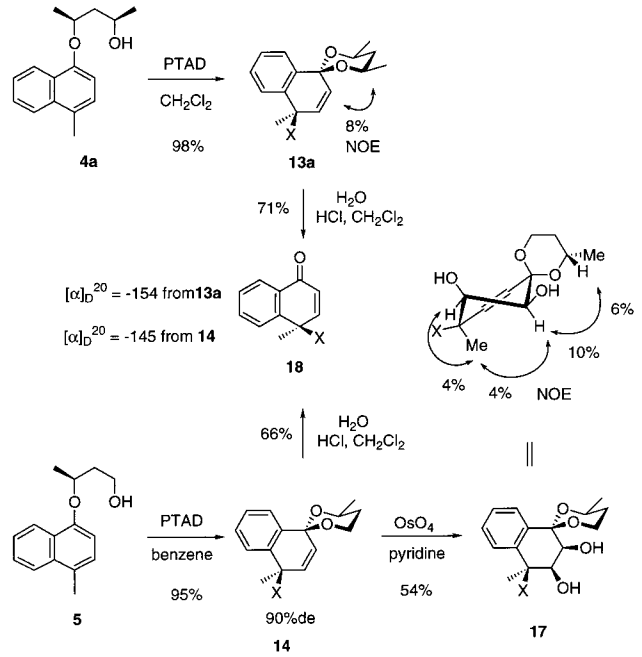
The diastereomeric ratio of adducts **14**−**16** obtained under various conditions are summarized in Table 3. In the case of **6**, the diastereomeric ratio of the adduct **15** (85% isolated yield) obtained in $CH_2Cl_2$ was **15-*Si-syn*:15-*Si-anti*:15-*Re-syn*:15-*Re-anti*** = 72:28:∼0:∼0.[34] The diastereomeric ratio of **15** decreased with the progress of the reaction. Substrate **7**, a stereoisomer of **4a**, also gave a high diastereomeric ratio (**16-*Si-syn*:16-*Si-anti*** = 95:5).[34]

**Stereochemistry of the Products. (1) Stereochemistry of 14.** The configuration of the major isomer of **14** was determined on the basis of chemical transformations in conjunction with the NOE measurements as illustrated in Scheme 5. The NOE's observed for the diol **17**, which was derived from **14** by $OsO_4$ oxidation,[14a,35] establish the configurations of the major isomer of **14** as depicted in Scheme 6, **14-*Si-syn***. Acid hydrolysis of **14** gave levorotatory enone **18**. Thus, (−)-enone **18** has the *R* configuration at C-4. The minor diastereomer of **14** has the same $^1$H NMR spectrum as that of the major isomer of adduct **15** obtained from **6**. The major isomer of **15** is **15-*Si-syn*** (see

(34) The adducts **14** and **15** possibly consist of four diastereomers **14-*Si-syn*/14-*Si-anti*** /**14-*Re-syn*/14-*Re-anti*** and **15-*Si-syn*/15-*Si-anti*/15-*Re-syn*/15-*Re-anti***, respectively. In the case of **16**, the possible isomers are only two diastereomers, because **16-*Si-syn*** and **16-*Si-anti*** are identical to **16-*Re-anti*** and **16-*Re-syn***, respectively. The ratios were determined by the measurement of the peak area of the olefinic protons obtained by $^1$H NMR.

(35) (a) Trost, B. M.; Kuo, G.-H.; Benneche, T. *J. Am. Chem. Soc.* **1988**, *110*, 621−622. (b) Poli, G. *Tetrahedron Lett.* **1989**, *30*, 7385−7388.

**Scheme 6**




below), which is the enantiomer of **14-*Si-anti***. Proton NMR signals other than those due to **14-*Si-syn*** and **14-*Si-anti*** were not observed for **14** either when isolated or in the reaction mixture. Thus, the diastereomeric ratio **14-*Si-syn***:**14-*Si-anti***:**14-*Re-syn***:**14-*Re-anti*** was determined as 95:5:∼0:∼0.

**(2) Stereochemistry of 13a.** The NOE between the olefinic proton and the methine protons of **13a** indicates that the hydroxy group of the side chain attacks C-1 from the *Si-Re* face of the naphthalene core (**13a** = **13a-*Si-syn*** and **13a-*Si-anti***). Hydrolysis of **13a** also gave (*R*)-(−)-enone **18**, indicating that the addition of PTAD at C-4 proceeds from the *Si-Re* face preferentially. From these results, the configration of the major isomer of **13a** is determined to be **13a-*Si-syn*.** The $^1$H NMR spectrum of **13a** indicates that it consists of a single diastereomer, and the chiral HPLC indicates that the enantiomeric ratio of **13a** is 96:4. In summary, the isomeric ratio is **13a-*Si-syn***:**13a-*Si-anti***:**13a-*Re-syn*:13a-*Re-anti*** = 96:4:∼0:∼0.

**(3) Stereochemistry of 15.** The minor diastereomer of **15** has the same $^1$H NMR spectrum as that of the major adduct of **14** (= **14-*Si-syn***), which is the enantiomer of **15-*Si-anti***. The major isomer of **15** also shows an NOE between the olefinic proton and the methine proton of the acetal ring. This indicates that the major isomer of **15** is formed by attack of the alcohol at C-1 from the *Si-Re* face (**15-*Si-syn*** or **15-*Si-anti***). Hydrolysis of the diastereomeric mixture of **15** gave (*R*)-(−)-enone **18**, indicating that the addition of PTAD at C-4 proceeds preferentially from the *Si-Re* face. The optical rotation of **18** obtained from **15** of 48% de ($[\alpha]^{20}_D = -82$) is lower than that obtained from **13a** ($[\alpha]^{20}_D = -154$). The smaller optical rotation is consistent with the lower diastereomeric purity of **15**, **15-*Si-syn***:**15-*Si-anti*** = 74:26. Thus, the major isomer of **15** is **15-*Si-syn***. Diastereomeric signals other than those of **15-*Si-syn*** and **15-*Si-anti*** were not observed in the $^1$H NMR of **15** isolated. Thus, the diastereomeric ratio of **15** in benzene is determined to be **15-*Si-syn***:**15-*Si-anti***:**15-*Re-syn***:**15-*Re-anti*** = 74:26:∼0:∼0 by $^1$H NMR.

**(4) Stereochemistry of 16.** The $^1$H NMR spectrum of **16** shows that it is a mixture of two diastereomers, and its hydrolysis gave again (*R*)-(−)-enone **18**. Thus, the diastereomeric ratio **16-*Si-syn***:**16-*Si-syn*** is determined to be 95:5. Here, it should be noted that **16-*Si-syn*** = **16-*Re-anti*** and **16-*Si-anti*** = **16-*Re-syn***; that is, there are only two possible diastereomers of **16**.

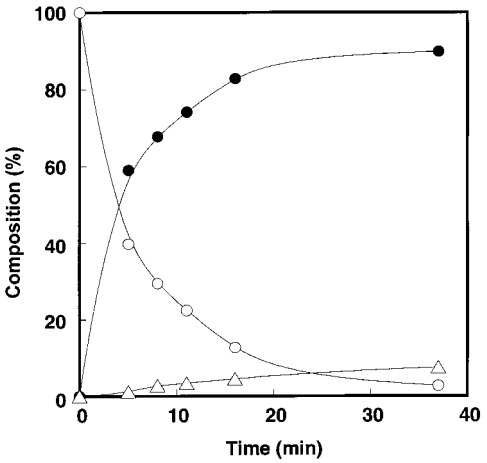



**Figure 4.** Reaction of PTAD (148 mM) with **5** (78 mM) in $CDCl_3$ at 293 K, monitored by $^1$H NMR: **5** (○), **14-*Si-syn*** (●), and **14-*Si-anti*** (△).

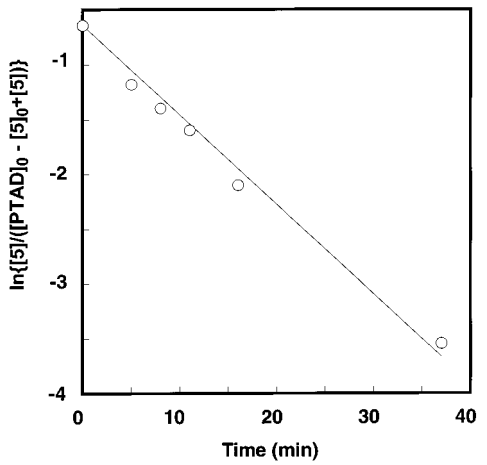



**Figure 5.** Plot of $\ln\{[\mathbf{5}]/([\mathrm{PTAD}]_0 - [\mathbf{5}]_0 + [\mathbf{5}])\}$ vs time for the electrophilic addition of PTAD (148 mM) to **5** (78 mM) in $CDCl_3$ at 293 K.

**Kinetic Determinations.** The electrophilic addition of PTAD to **5** was monitored by $^1$H NMR at 293 K, and its time course is shown in Figure 4. The decrease in [**5**] obeys second-order kinetics,[36] first order to both [**5**] and [PTAD], as shown by the linear plot of $\ln\{[\mathbf{5}]/([\mathrm{PTAD}]_0 - [\mathbf{5}]_0 + [\mathbf{5}])\}$ vs time[37a] in Figure 5. From the slope of the linear plot and initial concentrations of **5** and PTAD ($[\mathbf{5}]_0$ and $[\mathrm{PTAD}]_0$), the second-order rate constant $k$ was determined to be $2.1 \times 10^{-2}$ $M^{-1}$ $s^{-1}$. The rate constants $k$ for the reaction of **3**−**7** are summarized in Table 4.

The ratio **14-*Si-syn*/14-*Si-anti*** is constant during the reaction of **5**, indicating that these isomers are formed by parallel kinetically controlled processes. Thus, the rate constant $k$ for the decrease of the substrate is resolved into the rate constants for the formations of isomeric products ($k_1$ and $k_2$) using the product ratio.

(36) The reaction of **5** was too fast to determine $k$ accurately under the pseudo-first-order reaction conditions ([PTAD] ≫ [**5**]) by $^1$H NMR. In the case of **6**, $k$ values were determined at various concentrations of PTAD. The $10^3k$ ($M^{-1}$ $s^{-1}$) values were 4.9, 5.0, and 5.0 when $[\mathrm{PTAD}]_0/[\mathbf{6}]_0$ = 4.2, 7.1, and 13, respectively.

(37) Moore, J. W.; Pearson, R. G. In *Kinetics and Mechanism, third eddition*; John Wiley & Sons: New York, 1981; (a) pp 22−25, (b) pp 290−296. The integrated kinetic equations are modified for the parallel reaction.

**Table 4.** Second-Order Rate Constants ($k$) for Electrophilic Addition of PTAD to Several Substrates in Various Solvents at 293 K

| | $10^3k$ ($M^{-1}s^{-1}$)[a] | | | |
|---|---|---|---|---|
| substrate | $C_6D_6$ | $CDCl_3$ | $CD_2Cl_2$ | $CD_3CN$ |
| **4a** | 1.0 | 15 | 26 | 2.9 |
| **4b** | | 47 | | |
| **4c** | | 10 | | |
| **4d** | | 0.067 | | |
| **4e** | | >300[b] | | |
| **5** | 2.1 | 21 | 26 | 2.2 |
| **6** | 0.68 | 5.0 | 2.0 | |
| **7** | | 10 | | |
| **3** | | 4.7 | | |

[a] The experimental errors are ±10%. [b] Too fast to be determined accurately by $^1$H NMR.

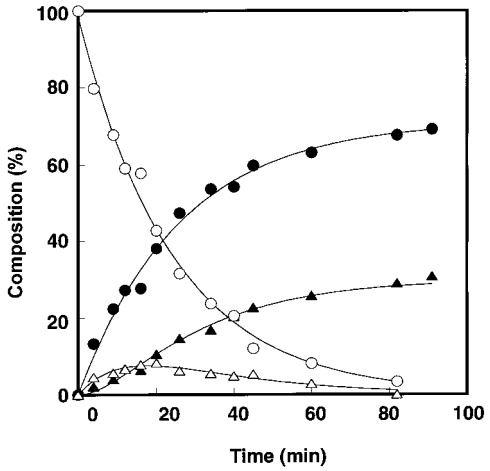



**Figure 6.** Reaction of PTAD (135 mM) with **6** (19 mM) in $CDCl_3$ at 293 K, monitored by $^1$H NMR: **6** (○), **15-*Si-syn*** (●), **15-*Si-anti*** (△), and **19** (▲). Solid lines show theoretical curves calculated from the rate constants given in Table 5.

In the case of **6**, the product ratio **15-*Si-syn*/15-*Si-anti*** changes with time and the reaction does not consist of simple parallel processes (Table 3 and Figure 6). The curvatures of the plots for the conversion of **6** and formation of **15-*Si-syn*** are smooth and follow pseudo-first-order kinetics with the same half-life. However, the increase in **15-*Si-anti*** follows an S-shaped curve. The $^1$H NMR spectra show formation of a third transient intermediate **19**. Although **19** could not be isolated from the reaction mixture to allow full structural characterization, the $^1$H NMR spectrum of the reaction mixture shows olefinic protons at 6.35 and 6.15 ppm and a high-field shift of the 4-methyl group (2.03 ppm) for **19**; this suggests that **19** is a product of 1,4-addition to the naphthalene ring. The sum of **15-*Si-anti*** and **19** fits well the first-order curve with the same half-life as that for **6** and **15-*Si-syn***. These results strongly suggest that the minor diastereomer **15-*Si-anti*** is formed via **19** as an intermediate (Scheme 7). The curvatures for **19** and **15-*Si-anti*** can be treated as a typical consecutive reaction, **6** → **19** → **15-*Si-anti***. Integrated forms of the kinetic equations for time-dependent changes of [**19**] and [**15-*Si-anti***][37b] were simulated by a nonlinear least-squares method on a personal computer to give reasonable rate constants $k_3$ (Table 5). Typical simulation curves are shown in Figure 6.

The rate constant for conversion of **19** to **15-*Si-anti***, $k_3$, is decreased by added pyridine (Figure 7). Although the other rate constants, $k_1$ and $k_2$, also become slightly smaller,[38] the lifetime of the transient product **19** is clearly prolonged by a base.

**Scheme 7**

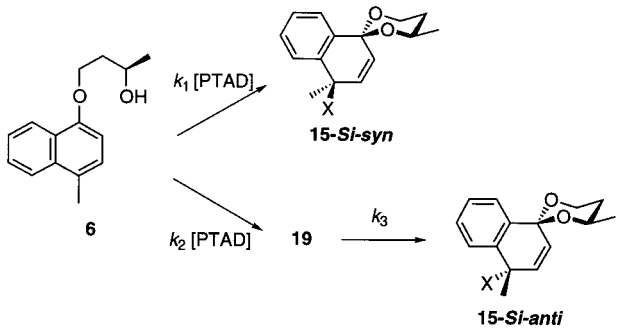



**Table 5.** Rate Constants for the Elementary Steps in the Reaction of **6** with PTAD at 293 K

| solvent | $k_1$ ($M^{-1}s^{-1}$) | $k_2$ ($M^{-1}s^{-1}$) | $k_3$ ($s^{-1}$) |
|---|---|---|---|
| $C_6D_6$ | $4.9 \times 10^{-4}$ | $1.9 \times 10^{-4}$ | $3.0 \times 10^{-4}$ |
| $CDCl_3$ | $3.5 \times 10^{-3}$ | $1.5 \times 10^{-3}$ | $1.7 \times 10^{-3}$ |
| $CDCl_3$[a] | $1.5 \times 10^{-3}$ | $5.4 \times 10^{-4}$ | $2.8 \times 10^{-4}$ |
| $CD_2Cl_2$ | $1.4 \times 10^{-3}$ | $5.7 \times 10^{-4}$ | $8.3 \times 10^{-4}$ |

[a] In the presence of pyridine (48 mM).

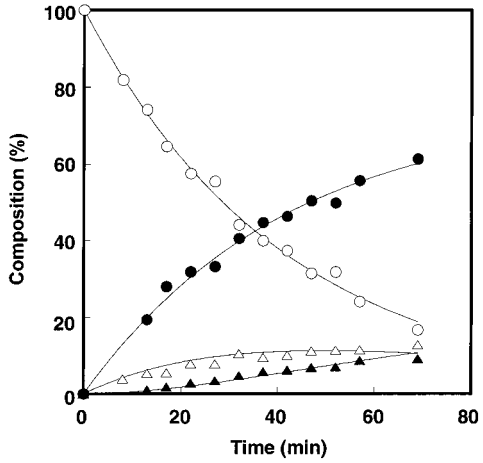


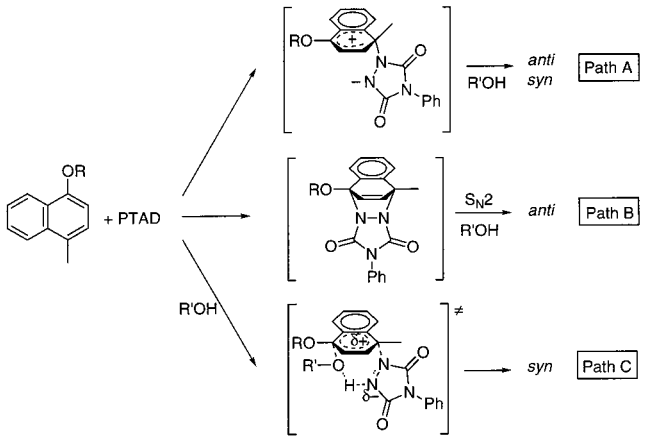

**Figure 7.** Reaction of PTAD (194 mM) with **6** (26 mM) in the presence of pyridine (48 mM) in $CDCl_3$ at 293 K, monitored by $^1$H NMR: **6** (○), **15-*Si-syn*** (●), **15-*Si-anti*** (△), and **19** (▲). Solid lines show theoretical curves calculated from the rate constants given in Table 5.

## Discussion

**Stereochemistry of the Electrophilic Addition.** Methanol promotes the addition of PTAD to **1** to give adduct **8** rapidly, but the reaction does not proceed to completion because of the instability of **8**. Adduct **8** decomposes back to **1**, but the reaction is not fully reversible due to the decay of PTAD. This was confirmed by the methoxy exchange with $CD_3OD$ and accompanying loss of **8**(**9**). The adduct **9** initially formed from **1** and PTAD in the presence of $CD_3OD$ is a single diastereomer despite the possibility of the *cis* and *trans* isomers (Scheme 3). However, epimerization of the adduct was observed as the reaction progresses probably due to the secondary reaction of **2** with $CH_3OD$ generated by the methoxy exchange. The bis-(deuteriomethoxy)adduct **10** was also formed. These results indicate that subsequent decomposition of the adduct lowers not only the chemical yield of the adduct but also the stereoselectivity. Although the configuration of the first-formed diastereomeric adduct **9** could not be determined due to its instability and facile epimerization, the high stereoselectivity

(38) The decrease in $k_1$ and $k_2$ in the presence of pyridine are ascribed to interference by pyridine with the hydrogen-bonding interactions.

**Scheme 8**



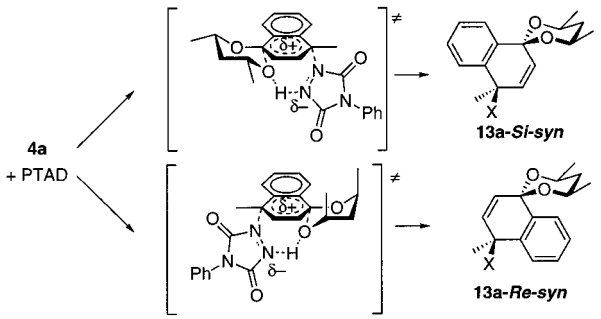

of the addition of PTAD and methanol to **1** is evident from results obtained in the initial stages of the reaction (Table 1).

Among the three conceivable pathways for the electrophilic addition illustrated in Scheme 8, a simple trapping of the naphthalenium intermediate by a free methanol molecule (Path A) cannot explain the stereoselectivity.[39] Immediate trapping of a transient Diels−Alder adduct by methanol via the $S_N2$ pathway should result in *anti* stereoselectivity (Path B).[39] In contrast, the *syn* adduct should be formed by a concerted process of electrophilic addition of PTAD at C-4, proton transfer from alcohol to PTAD, and nucleophilic attack at C-1 of the naphthalene core by the alcohol (Path C). Thus, the relative configuration (*cis* or *trans*) of the adduct is key evidence regarding the role of alcohol in the electrophilic addition of PTAD to naphthalene. It is reasonable that the electrophilic addition and nucleophilic trapping by methanol proceed in a *syn* fashion (Path C) by analogy with the *syn* addition observed for the internal alcohols **4**−**6** (see below). Moreover, promotion of the reaction by methanol is compatible with Path C.

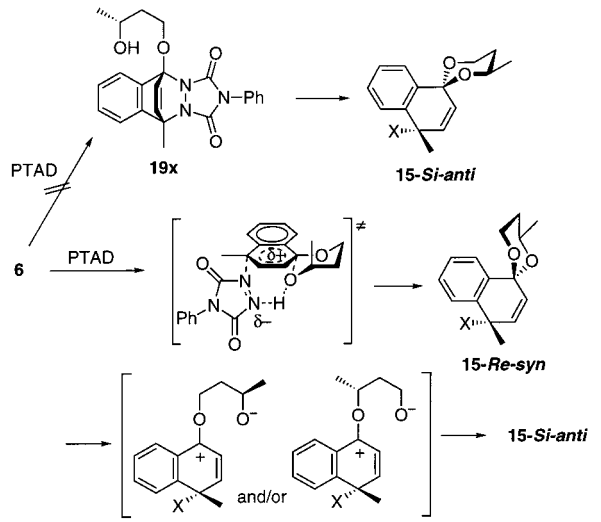
When an internal alcohol function is introduced to the alkoxy side chain of the substrate, quantitative formation of the adduct is observed in the absence of an external alcohol. The adducts obtained from **4**−**6** are stable enough to be isolated in 71−98% yield. The electrophilic addition of PTAD to **4a** yields **13a-*Si-syn***, **13a-*Si-anti*** **13a-*Re-syn***, and **13a-*Re-anti*** in a ratio of 96:4:∼0:∼0. The major isomer **13a-*Si-syn*** is formed by the *syn* attack of PTAD and the internal alcohol from the *Si-Re* face. This mode of reaction is preferred in all the electrophilic additions of PTAD to **4a**, **5**, and **6**.

The *syn* selectivity can reasonably be explained by the concerted addition mechanism (Path C in Scheme 8). The transition states for concerted formation of **13a** are illustrated in Scheme 9. The *Si-Re* face preference may be attributed to the steric repulsion between the *peri*-hydrogen of the naphthalene core and the cyclic acetal moiety in the alternative mode, *Re-Si* face attack.[40] When the steric repulsion is avoided in the transition state for the *Re-Si* face attack, the methyl groups of the side chain are forced to the axial positions (Scheme 9). In fact, the acetal **15-*Re-syn*** formed by the *Re-Si* attack to **6** is unstable and easily isomerizes to **15-*Si-anti***, whose acetal moiety corresponds to the adduct obtained by the *Si-Re* attack (see below in Scheme 10). Adam and co-workers[5] have reported the

**Scheme 9**




**Scheme 10**




directing ability of an alcohol in [4 + 2] addition and ene reactions of PTAD to alkenes. The directing ability of an alcohol has also been shown in endoperoxide formation from naphthalenes and singlet oxygen.[6] Singlet oxygen and PTAD are suggested to have a similar electrophilic reactivity.[26] In these addition reactions, it was suggested that the stereoselectivities are achieved by the hydrogen-bonding interactions between the alcohol and the electrophile.

If the electrophilic addition of PTAD to **4**−**6** proceeds via stereocontrolled [4 + 2] addition followed by the nucleophilic substitution by the internal alcohol, the *anti* adduct should be formed preferentially by the $S_N2$ pathway (Scheme 8, Path B). Formation of the *syn* adduct is only possible via the stereocontrolled [4 + 2] addition if the retention of configuration occurs in the nucleophilic substitution step. This possibility is not strictly excluded; the retained substitution by the alcohol may be achieved when proton transfer from the alcohol to the PTAD moiety of the [4 + 2] adduct acts as a driving force for the substitution and the concerted nucleophilic trapping by the same alcohol. Furthermore, the formation of the [4 + 2] addition should have been in the equilibrium lying toward the substrate if it occurred, since the reaction of **1** with PTAD was not observed in the absence of alcohol.

In contrast to these less likely possibilities, a direct concerted process is most reasonable for the *syn* selectivity (Scheme 8, Path C). In the rate-determining step, the three events take place in concert: (1) the electrophilic addition of PTAD, (2) proton transfer from alcohol to PTAD, and (3) nucleophilic addition of the alcohol. In other words, an anionic part of the zwitterionic intermediate[41] is stabilized by hydrogen-bonding interactions with alcohol and the cationic part receives the nucleophilic addition of the alcohol. The hydrogen-bonding interaction must

(39) Stereochemical considerations on 1,2-addition of PTAD and methanol to olefin have been reported in ref 30g.

(40) Similar reactions have been reported: (a) Fujita, M.; Ohshiba, M.; Yamasaki. Y.; Sugimura, T.; Tai, A. *Chem. Lett.* **1999**, 139−140. (b) Fujita, M.; Ohshiba, M.; Shioyama. S.; Sugimura, T.; Tai, A. *Chem. Commun.* **1998**, 2243−2244.

exist before the formation of the C−N bond and act as a driving force for the addition, judging from the directing ability of the alcohol in the electrophilic addition. The hydrogen-bonding interaction in the transition state will be stronger than that in [4 + 2] cycloadditions[5,6] due to the polar transition state of electrophilic addition.

**Mechanism for Formation of the Minor Diastereomer.** It was found from the time course of electrophilic addition to **6** that the minor product **15-*Si-anti*** is formed via the transient product **19**. Two alternative structures are possible for the intermediate **19**: [4 + 2] cycloadduct **19x** and the epimer (**15-*Re-syn***) of **15-*Si-anti*** (Scheme 10). The cycloadduct **19x** can be formed by the [4 + 2] addition of PTAD from the *Re-Si* face and then undergo an intramolecular attack of the hydroxy group to give **15-*Si-anti***. However, the [4 + 2] adduct of PTAD to **1** could not be detected at all in the absence of methanol. This result excludes **19x** as a candidate for the transient product **19**.

On the other hand **15-*Re-syn*** is formed by the *syn* attack of PTAD and the internal alcohol from the *Re-Si* face. The conversion of **15-*Re-syn*** to **15-*Si-anti*** can be achieved by the intramolecular acetal exchange that causes epimerization at the spiro carbon (C-1). The stabilization of **19** by pyridine conforms to this mechanism of conversion of **15-*Re-syn*** to **15-*Si-anti***. Thus, the transient product **19** is presumably the epimer **15-*Re-syn***, which is generated by the *syn* addition of PATD and the intramolecular alcohol of **6** from the *Re-Si* face. This implies that the *syn* selectivity of the PTAD addition to **6** is achieved completely in the initial stage of both major and minor pathways, the former from the *Si-Re* face attack to give **15-*Si-syn*** and the latter from the *Re-Si* face attack to give **15-*Re-syn*** which is then converted to **15-*Si-anti***. Thus, the *syn* relationship between the alcohol and PTAD is a key feature of the promotion of the addition to the naphthalene. In other words, when the stereodifferentiation of the nucleophilic attack is achieved, PTAD is guided by the nucleophile to the same stereoface to result in the stereoface-differentiating addition of PTAD.

Minor products also seem to be formed in the *anti* addition of PTAD and the internal alcohol in the reactions of **4** and **5**. A similar mechanism involving an initial *syn* addition from the *Re-Si* face followed by epimerization to give the final minor product is most reasonable,[42] although the isomerization pathway could not be observed during the electrophilic addition to **4** and **5** because of the low yield of the minor adduct.

The degree of the stereoface differentiation of *Si-Re* vs *Re-Si* is controlled by the side chain. The α-methyl group of the alkoxy side chain largely dictates the stereodifferentiation, since both **5** and **7** show stereoselectivity comparable to **4a**. The γ-methyl group of **6** also helps the preferential addition from the *Si-Re* face. In this case, stereodifferentiating addition occurs at C-4 which is as remote as 7 bonds from the stereogenic center. Thus, both stereogenic centers of the (1*S*,3*R*)-3-hydroxy-1-methylbutoxy side chain work together to achieve highly stereodifferentiating addition from the *Si-Re* face.

**Comparison of the Reaction Rate Constants.** The rate constants summarized in Table 4 show the effects of substituents at C-4 and the alkoxy side chain as well as the effect of the solvent. 4-Alkyl-substituted **4a**−**c** undergo a slow addition compared with **4e** despite the electron-donating ability of alkyl groups. These results indicate an important steric contribution to the rate of the electrophilic addition. The reactivity of 4-phenyl-substituted substrate **4d** is very small, probably due to the steric effects of the phenyl group perpendicular to the naphthalene ring as well as the electron-withdrawing effect of the phenyl group.

A lower reactivity is observed for the substrate with a primary alkoxy side chain (**3** and **6**) compared with **4a**, **5**, and **7**. This indicates that the α-methyl group effectively accelerates cyclization by the Thorpe−Ingold effect,[43] i.e., the alkyl substitution in the side chain makes the entropy change in ring closure more favorable.

The rates in chloroform and dichloromethane are larger than those in benzene. Polar solvents can promote generation of an ionic or zwitterionic intermediate. The decrease in reactivity in acetonitrile may be due to interference with the hydrogen-bonding interactions at the transition state by the hydrogen-bond-accepting ability of the solvent. The moderate solvation needed to stabilize the polar transition state without interference with the hydrogen-bonding interactions appears to afford the highest reactivity.

In conclusion, the dual properties of an alcohol as a proton donor and a nucleophile not only effectively promote the electrophilic addition of PTAD to naphthalenes but also stereochemically dictate *syn* addition. The asymmetric variant for the electrophilic addition was also successfully achieved by using a chiral side chain.

## Experimental Section

**General.** Proton and $^{13}C$ NMR spectra were measured on a JEOL EXcalibur-400 spectrometer as solutions in $CDCl_3$. $^1H$ NMR spectra at 400 MHz were recorded using the residual $CHCl_3$ as an internal reference (7.24 ppm), and $^{13}C$ NMR spectra at 100 MHz were recorded using $CDCl_3$ as an internal reference (77.00 ppm). Optical rotations were measured on a Perkin-Elmer 243B polarimeter. Melting points were measured on a Yanaco micro-melting-point apparatus and are uncorrected. Infrared spectra were recorded on a Jasco IR-810 or FT/IR-410 spectrometer. A JEOL JMS-AX505HA mass spectrometer was used for MS. HPLC were conducted on a Hitachi L-6200 intelligent pump with a chiral column (Daicel CHIRALPAK AD, 0.46 $\phi$ × 25 cm) and were monitored using a Shimadzu SPD-10A UV−vis detector and a Jasco OR-990 chiral detector. 4-Phenyl-1,2,4-triazoline-3,5-dione

(41) (a) Fatiadi, A. J. *Synthesis* **1987**, 749−789. (b) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl*. **1980**, *19*, 779−807. (c) Sustmann, R.; Lücking, K.; Kopp, G.; Rese, M. *Angew. Chem., Int. Ed. Engl*. **1989**, *28*, 1713−1715. (d) Drexler, J.; Lindermayer, R.; Hassan, M. A.; Sauer, J. *Tetrahedron Lett*. **1985**, *26*, 2559−2562. (e) Kataoka, F.; Shimizu, N.; Nishida, S. *J. Am. Chem. Soc*. **1980**, *102*, 711−716. (f) Yamago, S.; Ejiri, S.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 5344−5345.

(42) Alternative conceivable mechanisms for the formation of the minor diastereomers in these cases are (A) direct formation via zwitterionic intermediate, (B) [4 + 2] cycloaddition followed by immediate $S_N2$ reaction, (C) *syn* addition from the *Re-Si* face followed by epimerization of the acetal, and (D) isomerization of the substrate followed by the *syn* addition. Mechanism A is unlikely from the observed independence of the stereoselectivity of the solvent, since the ionic intermediate would be strongly influenced by the medium. On the basis of the methoxy exchange results, decomposition of the adduct possibly leads the isomerization of the substrate (from **4** to enantiomer of **4**, from **5** to the enantiomer of **6**, and from **6** to the enantiomer of **5**) to result in the fall of the stereoselectivity of the adduct (mechanism D). If the isomerization of **5** to the enantiomer of **6** occurred during the electrophilic addition of PTAD to **5**, formation of the enantiomer of **6** should have been observed because the reaction of **6** is slower than that of **5**. Failure to observe isomerization of the substrate during the reaction of **5** excludes mechanism D. Although it is difficult to exclude mechanism B completely, mechanism C is more reasonable on the analogy of the reaction of **6,** which affords a relatively large amount of the minor diastereomer.

(43) (a) Kirby, A. J. In *Advances in Physical Organic Chemistry*; Gold, V., Bethell, D., Eds.; Academic Press: London, 1980; Vol. 17, pp 183−278. (b) Jager, J.; Graafland, T.; Schenk, H.; Kirby, A. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc*. **1984**, *106*, 139−143. (c) DeTar, D. F.; Luthra, N. P. *J. Am. Chem. Soc*. **1980**, *102*, 4505−4512. (d) Sternbach, D. D.; Rossana, D. M.; Onan, K. D. *Tetrahedron Lett*. **1985**, *26*, 591−594.

(Aldrich) was used without further purification. 1-Methoxy-4-methylnaphthalene (**1**) was prepared according to the literature procedure.[44] 1-(Methoxy-$d_3$)-4-methylnaphthalene (**2**) was prepared from 4-methyl-1-naphthol and dimethyl-$d_6$ sulfate (Aldrich). Acetonitrile and dichloromethane were distilled from calcium hydride. Benzene was purified by distillation from sodium. Acetonitrile-$d_3$, dichloromethane-$d_2$, benzene-$d_6$, methanol-$d_4$, and chloroform-*d* were obtained from Aldrich.

**1-(3-Hydroxypropoxy)-4-methylnaphthalene (3).** A solution of 4-methyl-1-naphthol (1.05 g, 6.6 mmol) and 3-bromo-1-propanol (1.8 mL) in acetone (10 mL) was refluxed in the presence of $K_2CO_3$ (4.9 g) for 4 h. The solution was cooled to room temperature, quenched by $H_2O$, and extracted with $CH_2Cl_2$. The combined organic extract was dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 30% EtOAc in hexane) to give **3** as a white solid (1.4 g, 100% yield): mp 94−97 °C (EtOAc); $^1$H NMR ($CDCl_3$) $\delta$ 8.24 (d, 1H, $J$ = 8.3 Hz), 7.90 (d, 1H, $J$ = 8.3 Hz), 7.52 (t, 1H, $J$ = 8.3 Hz), 7.47 (t, 1H, $J$ = 8.3 Hz), 7.17 (d, 1H, $J$ = 7.8 Hz), 6.72 (d, 1H, $J$ = 7.8 Hz), 4.26 (t, 2H, $J$ = 5.9 Hz), 3.96 (t, 2H, $J$ = 5.9 Hz), 2.59 (s, 3H), 2.17 (quint, 2H, $J$ = 5.9 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 153.3, 133.5, 126.3, 126.1, 126.0, 124.8, 124.0, 122.3, 104.9, 65.9, 60.5, 32.5, 18.7; IR (KBr) 3350, 2900, 1580, 1500, 1460, 1420, 1380, 1350, 1280, 1250, 1150, 1080, 1050, 800 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 216 (53, M$^+$), 158 (100); HRMS (EI) calcd for $C_{14}H_{16}O_2$ (M) 216.1150, found 216.1153.

**Typical Procedure for the Mitsunobu Reaction To Give (1′*S*,3′*R*)-1-(3-Hydroxy-1-methylbutoxy)-4-methylnaphthalene (4a).** To a solution of 4-methyl-1-naphthol (4.0 g, 25 mmol), $Ph_3P$ (6.6 g, 25 mmol), and (2*R*, 4*R*)-2,4-pentanediol (3.0 g, 28 mmol) in THF (15 mL) was added diethyl azodicarboxylate (4.0 mL, 25 mmol) dropwise at 0 °C. The mixture was stirred overnight, quenched by a small amount of $H_2O$, and concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 40% EtOAc in hexane) to give **4a** (5.5 g, 90% yield): $[\alpha]^{20}_D$ = +83 (*c* 1.05 $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.23 (d, 1H, $J$ = 8.3 Hz), 7.91 (d, 1H, $J$ = 7.8 Hz), 7.51 (t, 1H, $J$ = 7.6 Hz), 7.45 (t, 1H, $J$ = 7.6 Hz), 7.18 (d, 1H, $J$ = 7.8 Hz), 6.80 (d, 1H, $J$ = 7.8 Hz), 4.87−4.74 (m, 1H), 4.15−4.08 (m, 1H), 2.59 (s, 3H), 2.11 (dt, 1H, $J$ = 14.7, 7.1 Hz), 1.79 (ddd, 1H, $J$ = 14.7, 4.4, 3.4 Hz), 1.36 (d, 3H, $J$ = 5.9 Hz), 1.23 (d, 3H, $J$ = 6.3 Hz); $^{13}$C NMR ($CDCl_3$) 151.1, 133.4, 126.6, 126.5, 126.1, 125.9, 125.0, 124.0, 122.3, 106.7 (Ar), 74.0, 67.1, 45.7, 23.9, 20.0, 19.0; IR (film) 3370, 3070, 2970, 2930, 1630, 1590, 1520, 1460, 1430, 1390, 1340, 1280, 1250, 1210, 1160, 1120, 1080, 1020, 960, 920, 820, 760 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 244 (33, M$^+$), 158 (100); HRMS (EI) calcd for $C_{16}H_{20}O_2$ (M) 244.1463, found 244.1472.

**(1′*S*,3′*R*)-1-(3-Hydroxy-1-methylbutoxy)-4-ethylnaphthalene (4b).** The Mitsunobu reaction using 4-ethyl-1-naphthol (3.08 g) gave **4b** (3.53 g, 76% yield): $[\alpha]^{24}_D$ = +92 (*c* 1.02 $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.26 (d, 1H, $J$ = 7.8 Hz), 7.98 (d, 1H, $J$ = 7.8 Hz), 7.51 (t, 1H, $J$ = 7.8 Hz), 7.45 (t, 1H, $J$ = 7.8 Hz), 7.21 (d, 1H, $J$ = 7.8 Hz), 6.84 (d, 1H, $J$ = 7.8 Hz), 4.81−4.76 (m, 1H), 4.14−4.08 (m, 1H), 3.02 (q, 2H, $J$ = 7.5 Hz), 2.55 (s, 1H), 2.12 (dt, 1H, $J$ = 14.4, 8.6 Hz), 1.79 (dt, 1H, $J$ = 14.4, 3.7 Hz), 1.37 (d, 3H, $J$ = 5.7 Hz), 1.34 (t, 3H, $J$ = 7.5 Hz), 1.23 (d, 3H, $J$ = 6.3 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 151.2, 132.7, 132.6, 126.8, 126.1, 124.8, 124.4, 123.6, 122.5, 106.7, 73.8, 67.0, 45.7, 25.5, 23.8, 20.0, 15.2; IR (film) 3400, 2970, 2940, 2880, 1740, 1590, 1520, 1465, 1380, 1275, 1220, 1120, 820, 770 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 258 (58, M$^+$), 172 (100), 157 (76); HRMS (EI) calcd for $C_{17}H_{22}O_2$ (M) 258.1620, found 258.1642.

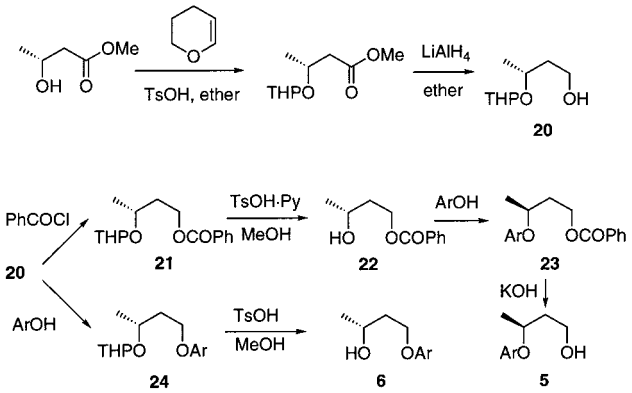
**(1′*S*,3′*R*)-1-(3-Hydroxy-1-methylbutoxy)-4-isopropylnaphthalene (4c).** The Mitsunobu reaction using 4-isopropyl-1-naphthol (2.85 g) gave **4c** (2.17 g, 52% yield): $[\alpha]^{20}_D$ = +87 (*c* 1.08 $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.31 (d, 1H, $J$ = 8.3 Hz), 8.09 (d, 1H, $J$ = 8.3 Hz), 7.53 (t, 1H, $J$ = 8.3 Hz), 7.47 (t, 1H, $J$ = 8.3 Hz), 7.31 (d, 1H, $J$ = 7.8 Hz), 6.90 (d, 1H, $J$ = 7.8 Hz), 4.85−4.77 (m, 1H), 4.16−4.09 (m, 1H), 3.68 (sept, 1H, $J$ = 6.8 Hz), 2.69 (s, 1H), 2.14 (dt, 1H, $J$ = 14.4, 8.6 Hz), 1.79 (dt, 1H, $J$ = 14.4, 3.7 Hz), 1.399 (d, 3H, $J$ = 6.8 Hz), 1.399 (d, 3H, $J$ = 6.8 Hz), 1.39 (d, 3H, $J$ = 5.9 Hz), 1.26 (d, 3H, $J$ = 5.9 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 150.9, 136.8, 132.3, 126.7, 126.0, 124.7, 123.1, 122.5, 121.3, 106.6, 73.8, 67.0, 45.8, 28.2, 23.9, 23.7, 23.7, 20.0; MS (EI) *m*/*z* (relative intensity, %) 272 (25, M$^+$), 186 (73), 171 (100); HRMS (EI) calcd for $C_{18}H_{24}O_2$ (M) 272.1776, found 272.1783.

**(1′*S*,3′*R*)-1-(3-Hydroxy-1-methylbutoxy)-4-phenylnaphthalene (4d).** The Mitsunobu reaction using 4-phenyl-1-naphthol (0.51 g) gave **4d** (0.60 g, 85% yield): $[\alpha]^{22}_D$ = +66 (*c* 1.00 $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.39 (d, 1H, $J$ = 8.6 Hz), 7.83 (d, 1H, $J$ = 8.6 Hz), 7.54−7.42 (m, 7H), 7.37 (d, 1H, $J$ = 7.8 Hz), 7.00 (d, 1H, $J$ = 7.8 Hz), 4.94−4.87 (m, 1H), 4.21−4.13 (m, 1H), 2.67 (br, 1H), 2.23 (dt, 1H, $J$ = 14.6, 8.4 Hz), 1.85 (dt, 1H, $J$ = 14.6, 4.2 Hz), 1.48 (d, 3H, $J$ = 6.3 Hz), 1.31 (d, 3H, $J$ = 5.9 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.3, 140.7, 132.9, 132.7, 130.1, 128.1, 126.8, 126.7, 126.5, 126.4, 125.8, 125.1, 122.1, 106.2, 73.6, 66.8, 45.7, 23.9, 20.0; IR (film) 3400, 2980, 2930, 1720, 1580, 1510, 1460, 1380, 1240, 1110, 1070, 770, 700 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 306 (19, M$^+$), 220 (100), 122 (44); HRMS (EI) calcd for $C_{21}H_{22}O_2$ (M) 306.1620, found 306.1649.

**(1′*S*,3′*R*)-1-(3-Hydroxy-1-methylbutoxy)naphthalene (4e).** The Mitsunobu reaction using 1-naphthol (0.70 g) gave **4e** (0.83 g, 74% yield): $[\alpha]^{22}_D$ = +107 (*c* 1.01 $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.20 (dd, 1H, $J$ = 6.8, 2.0 Hz), 7.78 (dd, 1H, $J$ = 6.8, 2.0 Hz), 7.46−7.33 (m, 4H), 6.90 (d, 1H, $J$ = 7.3 Hz), 4.86−4.78 (m, 1H), 4.15−4.08 (m, 1H), 2.43 (d, 1H, $J$ = 2.9 Hz, OH), 2.13 (ddd, 1H, $J$ = 14.1, 8.8, 5.8 Hz), 1.80 (dt, 1H, $J$ = 14.1, 3.9 Hz), 1.39 (d, 3H, $J$ = 5.9 Hz), 1.24 (d, 3H, $J$ = 5.7 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.8, 134.6, 127.5, 126.4, 126.3, 125.7, 125.3, 121.9, 120.5, 106.7, 73.7, 66.9, 45.7, 23.9, 19.9; IR (film) 3400, 3050, 2970, 2930, 1730, 1510, 1460, 1400, 1270, 1240, 1100, 800, 780 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 230 (14, M$^+$), 144 (100); HRMS (EI) calcd for $C_{15}H_{18}O_2$ (M) 230.1307, found 230.1328.

**(1′*S*)-1-(3-Hydroxy-1-methylpropoxy)-4-methylnaphthalene (5).** Substrates, **5** and **6** were prepared according to Scheme 11. Methyl (*R*)-3-hydroxybutanoate (5.1 g, 43 mmol) purchased from Kanto Chemicals was treated with 3,4-dihydropyrane (4.3 g, 51 mmol) in $Et_2O$ (15 mL) in the presence of a catalytic amount of TsOH. The mixture was quenched by saturated $NaHCO_3$ and extracted with ether (×3). The combined organic extract was washed with brine, dried ($Na_2SO_4$), and concentrated in vacuo to give the THP ether (10 g) as a crude oil. The crude THP ether was reduced with $LiAlH_4$ in ether. The mixture was quenched by a small amount of $H_2O$. The salt formed was removed by filtration through a Celite pad and washed with ether. The filtrate was concentrated in vacuo to give alcohol **20** (7.2 g, 41 mmol, 97% yield) as an oil. To a solution of **20** (2.24 g, 12.9 mmol) in $CH_2Cl_2$ (10 mL) containing pyridine (2.1 mL) was added PhCOCl (2.2 mL) at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with $H_2O$ and extracted with ether (×3). The combined extract was washed with saturated $CuSO_4$ and brine and then dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 30% EtOAc in hexane) to give the benzoate **21** (3.54 g, 99% yield). To a solution of **21** (3.54 g) in MeOH was added TsOH−pyridine, and the solution was stirred for 3 h. The solution was concentrated in vacuo, and the residue was purified by chromatography ($SiO_2$, eluent 20−40% EtOAc in hexane, gradient) to give recovered **21** and alcohol **22** (1.37 g, 56% yield). The Mitsunobu reaction using **22** and 4-methyl-1-naphthol was performed in a similar manner to that described for **4a** to give **23** in 84% yield. The benzoate **23** (2.4 g, 7.2

**Scheme 11**




(44) Buu-Hoï, N. P.; Lavit, D. *J. Chem. Soc.* **1955**, 2776−2779.

mmol) was hydrolyzed in EtOH (50 mL) in the presence of KOH (0.2 g) and $H_2O$ (2 mL). The mixture was quenched with $H_2O$ and extracted with $CH_2Cl_2$ after evaporation of EtOH. The combined organic extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 35% EtOAc in hexane) to give the title compound **5** as a colorless oil (1.31 g, 79% yield): $[\alpha]^{20}_D = +89$ (*c* 0.78 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 8.25 (d, 1H, $J = 8.4$ Hz), 8.10 (d, 1H, $J = 8.4$ Hz), 7.52 (ddd, 1H, $J = 8.4$, 6.8, 1.5 Hz), 7.46 (ddd, 1H, $J = 8.4$, 6.8, 1.5 Hz), 7.18 (d, 1H, $J = 7.8$ Hz), 6.80 (d, 1H, $J = 7.8$ Hz), 4.82−4.76 (m, 1H), 3.90−3.86 (m, 2H), 2.59 (s, 3H), 2.16−2.09 (m, 1H), 2.01−1.95 (m, 1H), 1.80 (br, 1H), 1.39 (d, 3H, $J = 5.9$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.2, 133.8, 127.0, 126.3, 126.1, 126.1, 124.8, 124.0, 122.6, 106.9, 72.7, 60.0, 39.7, 20.0, 18.6; IR (film) 3350, 2950, 1720, 1580, 1380, 1280 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 230 (39, $M^+$), 158 (100); HRMS (EI) calcd for $C_{15}H_{18}O_2$ (M) 230.1307, found 230.1316. Racemic **5** was also prepared using racemic methyl 3-hydroxybutanoate by the same procedure.

**(3′*R*)-1-(3-Hydroxybutoxy)-4-methylnaphthalene (6).** Using the alcohol **20** (1.0 g) prepared above, the Mitsunobu reaction of 4-methyl-1-naphthol was carried out to give **24** (1.1 g, 58% yield). Compound **24** (0.22 g, 0.7 mmol) was hydrolyzed in MeOH in the presence of TsOH. The mixture was concentrated in vacuo and purified by chromatography ($SiO_2$, 25% EtOAc in hexane) to give **6** as a white solid (0.16 g, 97% yield): mp 74.5−75.0 °C; $[\alpha]^{20}_D = -14.9$ (*c* 1.07 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 8.23 (d, 1H, $J = 7.8$ Hz), 7.91 (d, 1H, $J = 7.8$ Hz), 7.52 (ddd, 1H, $J = 7.8$, 7.3, 1.5 Hz), 7.46 (ddd, 1H, $J = 7.8$, 7.3, 1.5 Hz), 7.18 (d, 1H, $J = 7.8$ Hz), 6.72 (d, 1H, $J = 7.8$ Hz), 4.32−4.18 (m, 3H), 2.59 (s, 3H), 2.15−1.99 (m, 2H), 1.31 (d, 3H, $J = 6.3$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 153.4, 133.6, 126.4, 126.2, 126.1, 124.9, 124.0, 122.4, 105.1, 105.0, 66.2, 66.2, 38.8, 23.9, 18.6; IR (KBr) 3300, 3060, 2900, 1800, 1590, 1280, 1090 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 230 (94, $M^+$), 158 (100); HRMS (EI) calcd for $C_{15}H_{18}O_2$ (M) 230.1307, found 230.1304. Racemic **6** was also prepared by the same procedure.

**(1′*S*,3′*S*)-1-(3-Hydroxy-1-methylbutoxy)-4-methylnaphthalene (7).** To a solution of **4a** (2.0 g, 8.3 mmol), $Ph_3P$ (2.6 g, 9.8 mmol), and benzoic acid (1.24 g, 10.1 mmol) in THF (12 mL) was added diethyl azodicarboxylate (1.8 mL, 11.5 mmol) dropwise at 0 °C. The mixture was stirred overnight, quenched by a small amount of $H_2O$, and concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 30% EtOAc in hexane) to give (2*S*,4*S*)-2-benzoyloxy-4-(4-methyl-1-naphthoxy)pentane (2.16 g, 74.8% yield): $^1$H NMR ($CDCl_3$) $\delta$ 8.25 (d, 1H, $J = 8.8$ Hz), 7.98 (d, 2H, $J = 7.3$ Hz), 7.87 (d, 1H, $J = 8.3$ Hz), 7.54−7.46 (m, 2H), 7.42−7.37 (m, 3H), 7.09 (d, 1H, $J = 7.8$ Hz), 6.66 (d, 1H, $J = 7.8$ Hz), 5.43−5.38 (m, 1H), 4.74−4.70 (m, 1H), 2.55 (s, 3H, Me), 2.24−2.11 (m, 2H), 1.43 (d, 3H, $J = 6.4$ Hz), 1.39 (d, 3H, $J = 5.9$ Hz). The benzoate (2.16 g, 6.19 mmol) was hydrolyzed in aqueous methanol containing KOH at 35 °C for 8 h. The reaction mixture was extracted with $CH_2Cl_2$, and the organic extracts were evaporated in vacuo. The resulting residue was purified by chromatography ($SiO_2$, eluent 30% EtOAc in hexane) to give **7** as a white solid (1.27 g, 84.2% yield): $[\alpha]^{20}_D = +87$ (*c* 1.02 $CHCl_3$); mp 51.3−53.0 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.24 (d, 1H, $J = 8.3$ Hz), 7.90 (d, 1H, $J = 8.3$ Hz), 7.51 (t, 1H, $J = 7.1$ Hz), 7.45 (t, 1H, $J = 6.8$ Hz), 7.18 (d, 1H, $J = 7.8$ Hz), 6.80 (d, 1H, $J = 7.8$ Hz), 4.87−4.82 (m, 1H), 4.19−4.18 (m, 1H), 2.59 (s, 3H, Me), 1.98 (ddd, 1H, $J = 14.7$, 8.8, 2.9 Hz), 1.85−1.79 (m, 2H), 1.38 (d, 3H, $J = 5.9$ Hz), 1.25 (d, 3H, $J = 6.4$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.0, 133.5, 126.5, 126.1, 126.0, 124.8, 124.0, 122.4, 106.2, 71.7, 64.8, 45.9, 24.2, 20.0, 18.9; IR (KBr) 3300, 2690, 2920, 1590, 1520, 1470, 1430, 1380, 1340, 1280, 1250, 1230, 1160, 1110, 1080, 1040, 020, 820, 770, 740 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 244 (61, $M^+$), 158 (100); HRMS (EI) calcd for $C_{16}H_{20}O_2$ (M) 244.1463, found 244.1480. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.53; H, 8.26.

**Reaction of 1 with PTAD in the Absence of $CH_3OH$.** A solution of **1** (0.32 M) and PTAD (0.39 M) in $CDCl_3$ was prepared by mixing. After 8 h at 293 K in the dark, most of the substrate **1** remained, although a trace amount of enone **18** and methanol were detected (<5% yield) presumably from $H_2O$ in the $CDCl_3$.

**Reaction of 1 with PTAD in the Presence of $CH_3OH$.** To a solution of **1** (0.30 M) and PTAD (0.66 M) in $CDCl_3$ was added $CH_3OH$ (0.49 M). The reaction was monitored at 293 K in the dark by $^1$H NMR. Formation of adduct **8** (35% yield) was observed with an accompanying decrease of **1** after 10 min. **8**: $^1$H NMR ($CDCl_3$) $\delta$ 8.20−6.94 (m, 9H), 6.39 (d, 1H, $J = 10.4$ Hz), 6.14 (d, 1H, $J = 10.4$ Hz), 3.15 (s, 3H), 3.11 (s, 3H), 1.98 (s, 3H).

**Reaction of 1 with PTAD in the Presence of $CD_3OD$.** To a solution of **1** (80 mM) and PTAD (275 mM) in $CDCl_3$ was added $CD_3OD$ (1.0 M). The reaction was monitored at 293 K in the dark by $^1$H NMR. Formation of adducts **9**/**10**, **2**, and $CH_3OD$ was observed with an accompanying decrease of **1.** The ratio of **1**/**2** was determined by comparison of the peak areas due to the methoxy group (3.96 ppm) and the 4-methyl group (2.59 ppm). The ratio of **9**/**10** was determined by comparison of the peak areas due to the methoxy group (3.14 and 3.13 ppm) and methyl group (1.98 ppm). Formation of the dimethoxy adduct **8** was neglected. The diastereomeric ratio of **9** was determined by comparison of the peak areas due to the methoxy group (3.14 and 3.13 ppm). Determination of the composition of the naphthalenes and the adducts was performed by comparison of the peak areas due to the 4-methyl groups of the **1**/**2** (2.59 ppm) and **9**/**10** (1.98 ppm). The amount of $CH_3OD$ was determined by the peak area at 3.4 ppm. A time course of the reaction is shown in Figure 1 and Table 1. **9**: $^1$H NMR ($CDCl_3$) $\delta$ 8.20−6.94 (m, 9H), 6.39 (d, 1H, $J = 10.4$ Hz), 6.14 (d, 1H, $J = 10.4$ Hz), 3.14 and 3.13 (s, 3H), 1.98 (s, 3H).

**Reaction of 2 with PTAD in the Presence of $CH_3OH$.** To a solution of **2** (128 mM) and PTAD (185 mM) in $CDCl_3$ was added $CH_3OH$ (254 mM). The reaction was monitored at 293 K in the dark by $^1$H NMR. Formation of adduct **11** (15% yield) was observed after 6 min. The ratio of peaks at 3.14 and 3.13 ppm was 29:71 at 6 min. The diastereomeric ratio of **11** decreased with reaction time to be 43:57 at 25 min (23% yield).

**Electrophilic Addition of PTAD to 3.** To a solution of **3** (7.6 mg, 0.035 mmol, 68 mM) in $CDCl_3$ (0.52 mL) in an NMR tube was added PTAD (12 mg, 0.068 mmol, 132 mM). The mixture was allowed to stand for 70 min at 293 K in the dark to give adduct **12** in 80% yield. The product **12** was characterized by $^1$H and $^{13}$C NMR spectroscopy: $^1$H NMR ($CDCl_3$) $\delta$ 7.89 (d, 1H, $J = 6.9$ Hz), 7.54−7.27 (m, 8H), 7.03 (d, 1H, $J = 10.8$ Hz), 6.22 (d, 1H, $J = 10.8$ Hz), 4.30−4.20 (m, 2H), 4.03−3.91 (m, 2H), 2.35−2.27 (m, 1H), 2.03 (s, 3H), 1.54 (d, 1H, $J = 13.2$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.7, 152.1, 137.0, 136.6, 131.0, 129.8, 129.3, 128.9, 128.7, 127.4, 125.6, 124.7, 123.9, 123.6, 91.0, 61.2, 61.0, 61.0, 28.0, 25.5.

**General Procedure of Electrophilic Addition of PTAD to Naphthalenes 4a−e.** A sample of PTAD (36 mg, 0.21 mmol, 1.3 equiv) was added to a solution of **4a** (40 mg, 0.16 mmol) in $CH_2Cl_2$ (2 mL). After stirring at room temperature for 30 min, the solution was concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 60% EtOAc in hexane) to give **13a** (67 mg, 98% yield). No other diastereomeric isomer of **13a** was detected in the $^1$H NMR spectrum of the isolated sample or of the crude mixture. $^1$H NMR monitoring of the reaction of **4a** with PTAD in $CDCl_3$ also indicates formation of the single diastereomer of **13a**. The enantiomeric ratio was determined by HPLC with a chiral column using both UV−vis and polarimetric detectors. A mixed solvent of hexane and 2-propanol (95:5 v/v) was used as an eluent at a flow rate of 0.5 mL/min. Peak areas were measured at 260 nm. The peaks were confirmed to be due to the enantiomeric products by optical rotation and by the co-injection of the enantiomeric adduct prepared from the enantiomeric substrate, which was obtained from (2*S*,3*S*)-2,4-pentandiol. The retention times of the major (**13a**-***Si*-*syn***) and minor (**13a**-***Si*-*anti***) enantiomers of **13a** were 38.9 and 35.8 min, respectively, and the ratio of peak areas was 96:4. **13a**: mp 96−98 °C; $[\alpha]^{20}_D = -98$ (*c* 1.02 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.89 (d, 1H, $J = 6.8$ Hz), 7.57 (d, 1H, $J = 6.8$ Hz), 7.48−7.40 (m, 6H), 7.34 (t, 1H, $J = 6.8$ Hz), 6.96 (d, 1H, $J = 10.8$ Hz), 6.20 (d, 1H, $J = 10.8$ Hz), 4.31−4.25 (m, 2H), 2.02 (s, 3H), 1.66 (d, 1H, $J = 13.2$ Hz), 1.44 (q, 1H, $J = 13.2$ Hz), 1.24 (d, 3H, $J = 5.8$ Hz), 1.22 (d, 3H, $J = 6.4$ Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 152.3, 151.8, 137.5, 136.5, 131.6, 131.1, 129.4, 128.9, 128.8, 127.9, 127.4, 125.5, 125.4, 124.7, 91.8, 66.8, 66.4, 60.9, 40.4, 27.8, 22.3, 22.3; IR (film) 3200, 2980, 1780, 1700, 1600, 1500, 1420, 1300, 1250 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 419 (0.3, $M^+$), 244 (20, M −

PTAD$^+$), 158 (100). Anal. Calcd for $C_{24}H_{25}O_4N_3$: C, 68.78; H, 6.01; N, 10.02. Found: C, 68.99; H, 6.00; N, 10.11.

**13b.** A similar procedure to that used for the electrophilic addition using **4b** (51 mg, 0.20 mmol) and PATD (52 mg, 0.30 mmol, 1.5 equiv) gave **13b** (83 mg, 96% yield) as a single diastereomer. The retention times of the major and minor enantiomers of **13b** were 34.9 and 31.0 min, respectively, when 95:5 hexane−2-propanol was used as the eluent. The enantiomeric ratio was 98:2: mp 86−88 °C; $[\alpha]^{20}_D = -74$ (*c* 1.19 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 7.88 (d, 1H, $J$ = 7.3 Hz), 7.52 (d, 1H, $J$ = 7.3 Hz), 7.47−7.37 (m, 6H), 7.33 (t, 1H, $J$ = 7.3 Hz), 7.04 (d, 1H, $J$ = 10.7 Hz), 6.09 (d, 1H, $J$ = 10.7 Hz), 4.30−4.25 (m, 2H), 2.71 (quint, 1H, $J$ = 7.3 Hz), 2.62 (quint, 1H, $J$ = 7.3 Hz), 1.69 (d, 1H, $J$ = 12.7 Hz), 1.43 (q, 1H, $J$ = 12.7 Hz), 1.22 (d, 3H, $J$ = 7.3 Hz), 1.21 (d, 3H, $J$ = 6.4 Hz), 0.67 (t, 3H, $J$ = 7.3 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.1, 151.8, 139.0, 134.3, 131.2, 130.0, 129.3, 128.9, 128.8, 127.9, 127.5, 126.9, 125.6, 124.7, 91.9, 66.8, 66.3, 65.2, 40.4, 31.4, 22.3, 22.3, 8.7; IR (film) 3200, 3000, 1700, 1600, 1500, 1420, 1150 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 433 (0.6, M$^+$), 258 (26, M − PTAD$^+$), 172 (100), 157 (94).

**13c.** A similar procedure to that used for the electrophilic addition using **4c** (45 mg, 0.17 mmol) and PATD (50 mg, 0.29 mmol, 1.7 equiv) gave **13c** (69 mg, 93% yield) as a single diastereomer. The retention times of the major and minor enantiomers of **13c** were 38.5 and 32.6 min, respectively, when 95:5 hexane−2-propanol was used as the eluent. The enantiomeric ratio was 95:5: mp 104−106 °C; $[\alpha]^{20}_D = +45$ (*c* 1.07 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 7.83 (d, 1H, $J$ = 6.4 Hz), 7.63 (d, 1H, $J$ = 6.4 Hz), 7.48−7.29 (m, 7H), 7.06 (d, 1H, $J$ = 10.8 Hz), 6.10 (d, 1H, $J$ = 10.8 Hz), 4.24−4.21 (m, 2H), 3.42 (qq, 1H, $J$ = 6.8, 6.4 Hz), 1.63 (d, 1H, $J$ = 12.7 Hz), 1.40 (q, 1H, $J$ = 12.7 Hz), 1.18 (d, 3H, $J$ = 5.9 Hz), 1.14 (d, 3H, $J$ = 4.4 Hz), 1.13 (d, 3H, $J$ = 6.4 Hz), 0.69 (d, 3H, $J$ = 6.8 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.0, 151.0, 138.3, 135.7, 131.2, 129.0, 128.4, 127.7, 127.5, 127.5, 127.2, 126.9, 125.4, 123.9, 91.6, 67.6, 66.5, 66.0, 40.3, 34.2, 22.2, 18.2, 17.6; IR (film) 3200, 3000, 1700, 1600, 1420, 1120 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 447 (0.3, M$^+$), 272 (23, M − PTAD$^+$), 186 (61), 171 (100).

**13d.** A similar procedure to that used for the electrophilic addition using **4d** (15 mg, 0.049 mmol) and PATD (28 mg, 0.16 mmol, 3.3 equiv) gave **13d** (22 mg, 94% yield) as a single diastereomer. The retention times of the major and minor enantiomers of **13d** were 25.9 and 21.4 min, respectively, when 80:20 hexane−2-propanol was used as the eluent. The enantiomeric ratio was 95:5: mp 105−106 °C; $[\alpha]^{20}_D = -69$ (*c* 2.5 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 7.86 (d, 1H, $J$ = 7.8 Hz), 7.43 (d, 1H, $J$ = 8.3 Hz), 7.39−7.18 (m, 12H), 7.01 (d, 1H, $J$ = 10.4 Hz), 6.46 (d, 1H, $J$ = 10.4 Hz), 4.29−4.23 (dqd, 1H, $J$ = 12.7, 5.8, 2.4 Hz), 4.23−4.16 (dqd, 1H, $J$ = 12.7, 5.8, 2.4 Hz), 1.63 (dt, 1H, $J$ = 12.7, 2.4 Hz), 1.38 (q, 1H, $J$ = 12.7 Hz), 1.18 (s, 3H), 1.12 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.5, 152.4, 140.6, 138.2, 135.2, 131.1, 130.1, 128.9, 128.8, 128.5, 128.0, 127.7, 127.1, 126.9, 126.6, 126.0, 126.0, 125.3, 92.2, 66.8, 66.5, 66.4, 40.4, 22.3; IR (film) 3200, 1720, 1600, 1420, 1110, 700 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 481 (0.1, M$^+$), 306 (17, M − PTAD$^+$), 220 (100).

**13e.** A similar procedure to that used for the electrophilic addition using **4e** (86 mg, 0.37 mmol) and PATD (80 mg, 0.46 mmol, 1.2 equiv) in $CH_2Cl_2$ (3 mL) for 30 min gave **13e** (108 mg, 71% yield) as a single diastereomer. The retention times of the major and minor enantiomers of **13e** were 28.9 and 24.6 min when 85:15 hexane−2-propanol was used as the eluent. The enantiomeric ratio was 91:9: $[\alpha]^{20}_D = -56$ (*c* 0.56 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 8.27 (d, 1H, $J$ = 8.3 Hz), 7.89−7.32 (m, 8H), 7.11 (d, 1H, $J$ = 10.3 Hz), 6.22 (dd, 1H, $J$ = 10.7, 4.9 Hz), 5.94(d, 1H, $J$ = 4.9), 4.35 (dqd, 1H, $J$ = 11.7, 5.9, 2.4 Hz), 4.25 (dqd, 1H, $J$ = 11.7, 5.9, 2.4 Hz), 1.71(dt, 1H, $J$ = 11.7, 2.4 Hz), 1.46 (q, 1H, $J$ = 11.7 Hz), 1.29 (d, 3H, $J$ = 5.9 Hz), 1.23 (d, 3H, $J$ = 5.9 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 151.7, 151.1, 139.4, 131.3, 131.2, 130.6, 129.2, 129.1, 128.9, 127.9, 127.4, 126.4, 126.1, 125.3, 92.3, 67.7, 66.4, 51.1, 40.1, 22.1; IR (KBr) 3460, 1770, 1706, 1503, 1420, 1108, 1044, 766 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 405 (41, M$^+$), 319 (100); HRMS (EI) calcd for $C_{23}H_{23}O_4N_3$ (M) 405.1689, found 405.1653.

**Hydrolysis of 13a To Give Enone 18.** To a solution of **13a** (72 mg, 0.17 mmol) in $CH_2Cl_2$ (3 mL) was added 2 M aqueous HCl (2 $\mu$L). After 2 h of reaction at room temperature, the solvent was evaporated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 75% EtOAc in hexane) to give **18** (39 mg, 71% yield). Although the enantiomeric ratio of **18** could not be determined by chiral HPLC analysis, the optical rotation value and comparison of it with the value obtained from **14**−**16** suggest retention of stereochemical purity at C-4 after the hydrolysis: $[\alpha]^{20}_D = -154$ (*c* 0.76 $CH_2Cl_2$); $^1$H NMR ($CDCl_3$) $\delta$ 8.18 (d, 1H, $J$ = 7.3 Hz), 7.71 (d, 1H, $J$ = 7.3 Hz), 7.66 (t, 1H, $J$ = 7.3 Hz), 7.51−7.35 (m, 6H), 7.05 (d, 1H, $J$ = 10.2 Hz), 6.54 (d, 1H, $J$ = 10.2 Hz), 2.07 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 153.4, 153.4, 146.3, 142.9, 133.7, 130.8, 130.6, 130.0, 129.0, 128.8, 128.4, 127.4, 125.6, 125.5, 61.2, 27.6; IR (film) 3400, 2950, 1700, 1600, 1500, 1420, 1300 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 333 (18, M$^+$), 177 (43), 158 (100); HRMS (EI) calcd for $C_{19}H_{15}O_3N_3$ (M) 333.1113, found 333.1118.

**Electrophilic Addition of PTAD to 5 To Give 14.** A sample of PTAD (180 mg, 1.03 mmol, 1.2 equiv) was added to a solution of **5** (192 mg, 0.84 mmol) in $CH_2Cl_2$ (4 mL). After stirring at room temperature for 1 h, the solution was concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 75% EtOAc in hexane) to give **14** (308 mg, 91% yield). No products other than **14-*Si-syn*** and **14-*Si-anti*** were detected by NMR either in the isolated sample or the crude mixture. The diastereomeric ratio of compound **14** was determined by measurement of peak areas for the olefinic protons in the 6.2 ppm region of the $^1$H NMR spectrum as 95:5. The $^1$H NMR of the minor diastereomer **14-*Si-anti*** was the same as that of the major product (**15-*Si-syn***) from **6**. The diastereomeric mixture of **14** (**14-*Si-syn***:**14-*Si-anti*** = 95:5) had an optically rotation of $[\alpha]^{20}_D = -83$ (*c* 0.96 $CH_2Cl_2$). **14-*Si-syn***: $^1$H NMR ($CDCl_3$) $\delta$ 7.87 (d, 1H, $J$ = 7.8 Hz), 7.52 (d, 1H, $J$ = 7.8 Hz), 7.46−7.32 (m, 7H), 6.97 (d, 1H, $J$ = 10.8 Hz), 6.19 (d, 1H, $J$ = 10.8 Hz), 4.30−4.24 (m, 1H), 4.23−4.18 (m, 1H), 3.98 (dd, 1H, $J$ = 12.5, 5.2 Hz), 2.03 (s, 3H), 1.87 (qd, 1H, $J$ = 12.5, 5.2 Hz), 1.63−1.57 (m, 1H), 1.20 (d, 3H, $J$ = 5.9 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.6, 152.1, 137.2, 136.5, 131.5, 131.1, 129.4, 128.9, 128.7, 128.0, 127.5, 125.5, 124.6, 124.3, 91.5, 66.4, 61.2, 61.1, 32.9, 27.9, 22.5; IR (film) 3450, 2950, 1700, 1600, 1500, 1400, 1300, 1250, 1100, 1020, 770, 660 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 230 (18, M − PTAD$^+$), 158 (100).

**Hydrolysis of 14 to Give Enone 18.** The procedure for the hydrolysis of **13a** was applied to **14** (90% de, 83 mg, 0.20 mmol) to give **18** (45 mg, 66% yield) having $[\alpha]^{20}_D = -145$ (*c* 0.90 $CH_2Cl_2$). The optical rotation of **18** agrees with that calculated from the diastereomeric ratio of **14**.

**Electrophilic Addition of PTAD to 6 To Give 15.** A sample of PTAD (150 mg, 0.86 mmol, 1.2 equiv) was added to a solution of **6** (166 mg, 0.72 mmol) in $CH_2Cl_2$ (4 mL). After stirring at room temperature for 2 h, the solution was concentrated in vacuo. The residue was purified by chromatography ($SiO_2$, eluent 75% EtOAc in hexane) to give **15** (248 mg, 85% yield). No products other than **15-*Si-syn*** and **15-*Si-anti*** were detected in the NMR spectrum of the isolated sample. The diastereomeric ratio of **15** was determined by measurement of peak areas for the olefinic protons in the 6.2 ppm region of the $^1$H NMR spectrum as 72:28. The $^1$H NMR spectrum of the minor diastereomer **15-*Si-anti*** was the same as that of the major product (**14-*Si-syn***) from **5**. The diastereomeric mixture of **15** (**15-*Si-syn***:**15-*Si-anti*** = 72:28) had an optical rotation of $[\alpha]^{20}_D = -65$ (*c* 0.80 $CH_2Cl_2$). **15-*Si-syn***: $^1$H NMR ($CDCl_3$) $\delta$ 7.88 (d, 1H, $J$ = 7.8 Hz), 7.56−7.32 (m, 8H), 6.9*8* (d, 1H, $J$ = 10.5 Hz), 6.21 (d, 1H, $J$ = 10.5 Hz), 4.36−4.28 (m, 1H), *4*.24−4.16 (m, 1H), 3.96 (dd, 1H, $J$ = 11.7, 3.9 Hz), 2.05 (s, 3H), 1.89 (qd, 1H, $J$ = 12.7, 5.4 Hz), 1.63−1.60 (m, 1H), 1.24 (d, 3H, $J$ = 6.4 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 152.5, 151.9, 137.3, 136.5, 131.9, 131.1, 129.5, 128.9, 128.8, 128.0, 127.3, 125.6, 124.7, 124.6, 91.5, 66.8, 61.0, 32.9, 27.9, 22.4; IR (film) 3400, 3000, 1770, 1700, 1600, 1500, 1430, 1300, 1220, 1160, 1080, 750, 660 cm$^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 230 (18, M − PTAD$^+$), 158 (100).

**Time-Course Monitoring of Electrophilic Addition of PTAD to 6.** A solution of **6** (19 mM) and PTAD (135 mM) in $CDCl_3$ was prepared by mixing, and the reaction was immediately monitored by $^1$H NMR at 293 K in the dark. Formation of three adducts **15-*Si-syn*** **15-*Si-anti***, and **19** was observed with the decrease of substrate **6**. The signals due to **15-*Si-syn*** and **15-*Si-anti*** agree with the assigned signals from the isolated adducts. No signals other than those due to the three adducts and the substrate **6** were detected. The composition of the

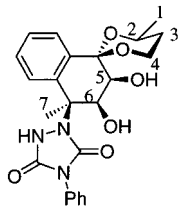
reaction mixture was determined by comparison of the peak areas for the olefinic protons of the three adducts in the 6.2 ppm region and the aromatic proton of **6** at 6.72 ppm. The time-course of the reaction is shown in Figure 6. **19**: $^1$H NMR ($CDCl_3$) $\delta$ 8.2−7.0 (m, 9H), 6.35 (d, 1H, $J$ = 10.2 Hz), 6.15 (d, 1H, $J$ = 10.2 Hz), 4.46−3.94 (m, 3H), 2.03 (s, 3H), 1.95−1.55 (m, 2H), 1.21 (d, 3H, $J$ = 5.9 Hz).

**Hydrolysis of 15 To Give Enone 18.** Hydrolysis of **15** (48% de, 120 mg, 0.29 mmol) by the same procedure as that for **13a** gave **18** (92 mg, 96% yield) having $[\alpha]^{20}_D = -84$ (*c* 0.92 $CH_2Cl_2$). The optical rotation of **18** agrees with that calculated from the diastereomeric ratio of **15**.

**Electrophilic Addition of PTAD to 7 To Give 16.** A solution of **7** (46 mM) and PTAD (78 mM) in $CDCl_3$ was prepared in an NMR tube, and the reaction was immediately monitored by $^1$H NMR at 293 K in the dark. After 74 min, 84% conversion of **7** to **16** was observed. The conversion and diastereomeric ratio were calculated by the peak areas at 6.80 ppm for **7** and those at 6.13 and 6.18 ppm for **16**. The major diastereomer of **16**: $^1$H NMR ($CDCl_3$) $\delta$ 7.83−7.81 (m, 1H), 7.71−7.68 (m, 1H), 7.55−7.30 (m, 7H), 6.56 (d, 1H, $J$ = 10.2 Hz), 6.13 (d, 1H, $J$ = 10.2 Hz), 4.38−4.29 (m, 1H), 4.25−4.16 (m, 1H), 2.16 (s, 3H), 1.88−1.76 (m, 2H), 1.33 (d, 3H, $J$ = 6.3 Hz), 1.24 (d, 3H, $J$ = 5.92 Hz). The minor diastereomer of **16**: $^1$H NMR ($CDCl_3$) $\delta$ 7.9−7.2 (m, 9H), 6.49 (d, 1H, $J$ = 10.2 Hz), 6.18 (d, 1H, $J$ = 10.2 Hz), 4.4−4.1 (m, 2H), 2.15 (s, 3H), 1.9−1.7 (m, 2H), 1.33−1.30 (m, 3H), 1.24−1.21 (m, 3H).

**Hydrolysis of 16 To Give Enone 18.** A sample of PTAD (23 mg, 0.13 mmol, 1.4 equiv) was added to a solution of **7** (23 mg, 0.094 mmol) in $CH_2Cl_2$ (1.5 mL). After stirring at room temperature for 30 min, 2 M HCl aqueous (2 $\mu$L) was added to the reaction mixture. After 4 h reaction at room temperature, the solvent was evaporated in vacuo and the residue was purified by chromatography ($SiO_2$, eluent 75% EtOAc in hexane) to give **18** (31 mg, 98% yield): $[\alpha]^{20}_D = -145$ (*c* 0.62 $CH_2Cl_2$).

**$OsO_4$ Oxidation of 14 To Give Diol 17.** To a solution of racemic **14** (90% de, 60 mg, 0.15 mmol) in pyridine (0.7 mL) was added $OsO_4$ (151 mg, 0.59 mmol). After the mixture was stirred for 4 h at room temperature, THF (6 mL), $H_2O$ (0.18 mL), Florisil (1.2 g), and sodium hydrogensulfite (0.5 g) were added to the mixture, and stirring was continued for 39 h. The resulting mixture was purified by column chromatography ($SiO_2$, eluent $CH_2Cl_2$/THF = 8/1) to give diol **17** (35 mg, 54% yield) as a single diastereomer. The purified diol was analyzed by $^1$H NMR spectroscopy. The $^1$H NMR signals of **17** were assigned by using decoupling and NOE measurements: $^1$H NMR ($CDCl_3$) $\delta$ 7.94




**17**

(t, 1H, $J$ = 7.9 Hz), 7.62 (d, 1H, $J$ = 7.9 Hz), 7.51 (t, 2H, $J$ = 6.9 Hz), 7.42−7.09 (m, 5H), 5.18 (d, 1H, $J$ = 2.4 Hz, 6-H), 5.08 (d, 1H, $J$ = 2.4 Hz, 5-H), 4.28 (dqd, 1H, $J_{2,3ax}$ = 10.8 Hz, $J_{1,2}$ = 6.4 Hz, $J_{2,3eq}$ = 2.4 Hz, 2-H), 4.13 (ddd, 1H, $J_{3ax,4ax}$ = 11.8 Hz, $J_{4ax,4eq}$ = 10.2 Hz, $J_{3eq,4ax}$ = 2.0 Hz, $4_{ax}$-H), 3.99 (ddd, 1H, $J_{4ax,4eq}$ = 10.2 Hz, $J_{3eq,4eq}$ = 3.4 Hz, $J_{3ax,4eq}$ = 2.0 Hz, $4_{eq}$-H), 2.39 (s, 3H, 7-H), 1.85 (dddd, 1H, $J_{3ax,3eq}$ = 13.2 Hz, $J_{3ax,4ax}$ = 11.8 Hz, $J_{2,3ax}$ = 10.8 Hz, $J_{4eq,2ax}$ = 2.0 Hz, $3_{ax}$-H), 1.62 (dddd, 1H, $J_{3ax,3eq}$ = 13.2 Hz, $J_{3eq,4eq}$ = 3.4 Hz, $J_{2,3eq}$ = 2.4 Hz, $J_{3eq,4ax}$ = 2.0 Hz, $3_{eq}$-H), 1.33 (d, 3H, $J_{1,2}$ = 6.4 Hz, 1-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 148.1, 140.8, 133.2, 132.7, 129.6, 128.4, 127.8, 127.5, 126.7, 126.5, 126.4, 125.6, 97.9, 82.9, 67.5, 67.4, 65.6, 61.1, 32.5, 29.9, 22.4; IR (film) 3400, 3000, 1700, 1400, 1100, 840, 760 $cm^{-1}$; MS (EI) *m*/*z* (relative intensity, %) 187 (26), 149 (49), 79 (100); HRMS (FAB) calcd for $C_{23}H_{26}O_6N_3$ ($MH^+$) 440.4822, found 440.1831.

**Kinetic Measurements.** The reaction was started by mixing the naphthalene compound (80−40 mM) and PTAD (8−2 equiv) in $CDCl_3$ in an NMR tube and monitored by $^1$H NMR at 293 K in the dark. The composition of products was calculated from the peak area for olefinic protons in the 6.2 ppm region of the $^1$H NMR. For the reactions of **6**, a large excess of PTAD was employed to overcome the slow reaction. The curve fitting was carried out by using KaleidaGraph ver. 3.08d (Synergy Software).

**Acknowledgment.** We are very grateful to Dr. Howard Maskill (Newcastle upon Tyne) for reading the munscript and invaluable comments.

**Supporting Information Available:** Detailed spectral data. This material is available free charge via the Internet at http://pubs.acs.org.

JA0029477