Asymmetric Diels–Alder Reaction of Unsymmetrical Maleates. A Chemical Access to Chiral, Unsymmetrical *cis*-Cyclohexene-1,2-dicarboxylates

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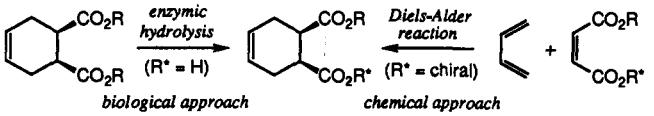
Abstract: A new route to optically active, unsymmetrical *cis*-cyclohexene-1,2-dicarboxylate derivatives has been developed on the basis of the asymmetric Diels–Alder reaction of chiral, unsymmetrical maleates catalyzed by certain Lewis acids. A notably high level of asymmetric induction has been observed in the asymmetric Diels–Alder reaction of unsymmetrical maleates possessing chiral auxiliaries such as α-phenethyl and *trans*-2-phenylcyclohexyl groups. The origin of the chiral outcome using these dienophiles has been elucidated.

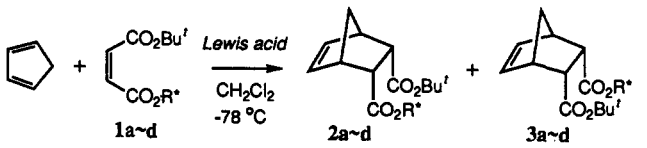
Introduction

Despite numerous studies on the asymmetric Diels–Alder reaction of chiral fumarates, little is known of chiral maleates. This is rather surprising, since chiral, unsymmetric *cis*-cyclohexene-1,2-dicarboxylate derivatives, which are Diels–Alder adducts of chiral unsymmetrical maleates, are versatile chiral building blocks for numerous applications including natural product synthesis. Access to such valuable compounds has so far relied chiefly on biological or biochemical transformations, *e.g.*, enantioselective hydrolysis of *meso*-diesters with hydrolytic enzymes.[1,2] This enzymatic approach has high substrate specificity and hence is not generally applicable.[3] For example, the bicyclic *meso*-diester derived by the Diels–Alder reaction of cyclopentadiene and dimethyl maleate is not susceptible to enzymatic hydrolysis.[2f] Asymmetric Diels–Alder reaction of unsymmetrical maleates is an alternative complementary methodology, and this nonenzymatic approach should have wide applicability and allow easier control of the chiral outcome by the proper choice of chiral auxiliaries. Here we disclose a chemical process that affords unsymmetrical *cis*-cyclohexene-1,2-dicarboxylate derivatives with excellent diastereoselectivity.

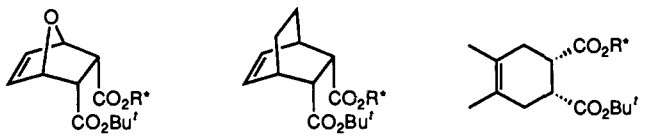


Results and Discussion

Chiral, unsymmetrical maleates of type **1** were conveniently prepared *via* two-step sequences in 50~90% yields by starting from maleic anhydride and various chiral auxiliaries as shown in Scheme 1. We then screened various chiral auxiliaries to obtain high diastereoselectivity in the asymmetric Diels–Alder reaction of the unsymmetrical maleate **1** and cyclopentadiene with several Lewis acids, giving cycloadducts **2** and **3**. These results are



summarized in Table 1. As revealed in the table, α-phenethyl alcohol and *trans*-2-phenylcyclohexanol as the chiral auxiliaries proved to be most effective for the present asymmetric Diels–Alder reaction by stoichiometric or catalytic use of conventional Lewis acids Et_2AlCl and $SnCl_4$ (entries 6 and 8–12). This is in marked contrast to disappointing results for the menthyl and bornyl auxiliaries (entries 1–4). In a similar manner, the asymmetric Diels–Alder reaction of the unsymmetrical *tert*-butyl (1*R*,2*S*)-2-phenylcyclohexyl maleate (**1d**) with several dienes can be effected in the presence of Et_2AlCl as illustrated in Table 2. It should be noted that the 7-oxabicyclo[2.2.1]heptene system, which is readily achievable by cycloaddition of **1d** with furan, can be successfully and convincingly utilized as a key intermediate for the synthesis of important types of natural products.[4,5] A large number of selective transformations of the 7-oxabicyclo[2.2.1]heptene unit endows this nucleus with impressive versatility.[4]



Various cycloadducts from unsymmetrical *tert*-butyl maleates are synthetically quite useful, since the *tert*-butyl ester can be

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(1) Reviews: (a) Whitesides, G. M.; Wong, C.-H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 617. (b) Ohno, M.; Otsuka, M. *Org. React.* **1989**, *37*, 1.

(2) Recent examples: (a) Sabbioni, G.; Shea, M. L.; Jones, J. B. *J. Chem. Soc., Chem. Commun.* **1984**, 236. (b) Schneider, M.; Engel, N.; Honicke, P.; Heinemann, G.; Gorisch, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 67. (c) Kobayashi, S.; Kamiyama, K.; Iimori, T.; Ohno, M. *Tetrahedron Lett.* **1984**, *25*, 2557. (d) Gais, H.-J.; Lukas, K. L. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 142. (e) Laumen, K.; Schneider, M. *Tetrahedron Lett.* **1985**, *26*, 2073. (f) Bloch, R.; Guibe-Jampel, E.; Girard, C. *Ibid.* **1985**, *26*, 4087. (g) Bjorkling, F.; Boutelje, J.; Gatenbeck, S.; Hult, K.; Norin, T. *Appl. Microbiol. Biotechnol.* **1985**, *21*, 16. (h) Adachi, K.; Kobayashi, S.; Ohno, M. *Chimia* **1986**, *40*, 311. (i) Gais, H.-J.; Lukas, K. L.; Ball, W. A.; Braun, S.; Lindner, H. J. *Justus Liebigs Ann. Chem.* **1986**, 687. (j) Guanti, G.; Banfi, L.; Narisano, E.; Riva, R.; Thea, S. *Tetrahedron Lett.* **1986**, *27*, 4639. (k) Sabbioni, G.; Jones, J. B. *J. Org. Chem.* **1987**, *52*, 4565.

(3) Bloch, R.; Guibe-Jampel, E.; Girard, C. *Tetrahedron Lett.* **1985**, *26*, 4087.

(4) Review: Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173.

(5) For some key applications of 7-oxabicyclo[2.2.1]heptene derivatives, see: (a) Just, G.; Lim, M. I. *Can. J. Chem.* **1977**, *55*, 427, 2993. (b) Suami, T.; Ogawa, S.; Nakamoto, K.; Kasahara, I. *Carbohydr. Res.* **1977**, *58*, 240. (c) Eggette, T. A.; de Koning., H.; Huisman, H. O. *J. Chem. Soc., Perkins Trans. 1* **1978**, 980. (d) Ogawa, S.; Kasahara, I.; Suami, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 118. (e) Kotsuki, H.; Nishizawa, H. *Heterocycles* **1981**, *16*, 1287. (f) Murai, A.; Takahashi, K.; Taketsuru, H.; Masamune, T. *J. Chem. Soc., Chem. Commun.* **1981**, 221. (g) Ogawa, S.; Iwasawa, Y.; Nose, T.; Suami, T.; Ohba, S.; Ito, M.; Saito, Y. *J. Chem. Soc., Perkin Trans 1* **1985**, 903. (h) Reynord, E.; Reymond, J.-L.; Vogel, P. *Synlett* **1991**, 469.

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Scheme 1

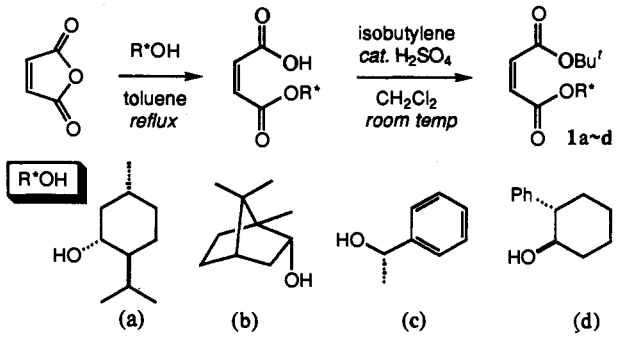
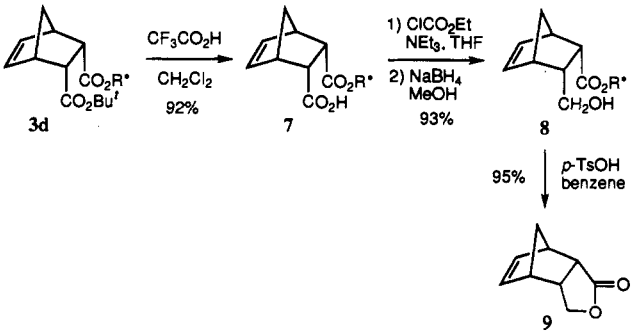


Table 1. Asymmetric Diels–Alder Reaction of Chiral, Unsymmetrical Maleate **1** and Cyclopentadiene[a]

entry	maleate	Lewis acid (equiv)	conditions (°C, h)	yield[b] (%)	ratio of **2**:**3**[c]
1	**1a**	Et_2AlCl (2)	−78, 6.5	97	(54:46)[e]
2		$SnCl_4$ (1)	−78, 6.5	98	(52:48)[e]
3	**1b**	Et_2AlCl (2)	−78, 0.3	99	(56.5:43.5)[e]
4		$SnCl_4$ (1)	−78, 0.3	96	(52:48)[e]
5	**1c**	BF_3-OEt_2 (2)	−78, 1	98	(83.5:16.5)[e]
6		Et_2AlCl (2)	−78, 1	90	(85:15)[e]
7		Et_2AlCl (1) + $LiB(C_6F_5)_4$ (1)[d]	−78, 1	94	(84.5:15.5)[e]
8		$SnCl_4$ (1)	−78, 0.5	87	(84:16)[e]
9	**1d**	Et_2AlCl (1)	−78, 0.1	86	(1:99)[f]
10		Et_2AlCl (2)	−78, 0.1	98	(1:99)[f]
11		$SnCl_4$ (0.2)	−78, 3	95	(2:98)[f]
12		$SnCl_4$ (1)	−78, 0.5	97	(1:99)[f]

[a] The Lewis acid-promoted Diels–Alder reaction of the maleate **1** and cyclopentadiene (2 equiv) was carried out in CH_2Cl_2 under the given reaction conditions. [b] Isolated yields of **2** and **3**. [c] The absolute configurations of the cycloadducts were not assigned in entries 1–4. [d] Reference 9. [e] Determined by capillary GLC and/or 500-MHz ^1H NMR analysis. [f] Determined by HPLC analysis.

selectively cleaved under acidic conditions. For example, treatment of cycloadduct **3d** with CF_3CO_2H in CH_2Cl_2 at room temperature gave ((*trans*-2-phenylcyclohexyl)oxy)carbonyl acid **7**, which was further converted to hydroxy ester **8** and then to the known optically active lactone **9**.[2f,6] Consequently, this synthetic transformation unambiguously establishes the absolute structure of the cycloadduct **3d**.



To elucidate the chiral outcome using the effective chiral auxiliaries c and d, we compared the diastereoselectivities of **2** and **3** with those of cycloadducts **12** and **13** derived from the corresponding acrylates **10** and fumarates **11**, respectively. Selected data are indicated in Scheme 2. Apparently, transition states of cycloaddition with maleates **1c,d** are markedly different from those with acrylates **10** and fumarates **11**, suggesting different coordination patterns of the Lewis acids for the former dienophiles. Since Lewis acids coordinate to acrylate and

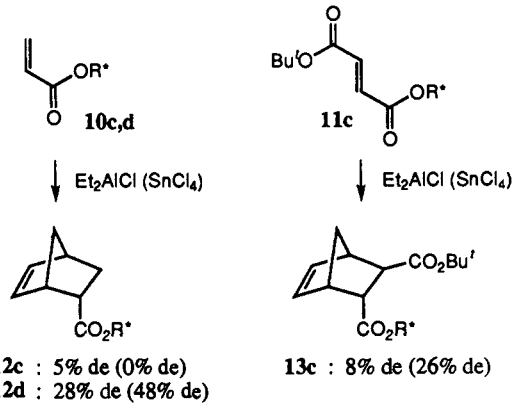
(6) Lok, K. P.; Jakovac, I. J.; Jones, J. B. *J. Am. Chem. Soc.* **1985**, *107*, 2521.

Table 2. Asymmetric Diels–Alder Reaction of Unsymmetrical Maleate **1d** and Several Dienes[a]

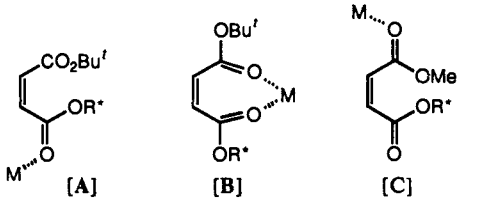
entry	diene	conditions (°C, h)	major adduct	% yield[b]	% de[c]
1	cyclopentadiene	−78, 0.5	**3d**	95	98
2	furan	−20, 13	**4d**	47	98
3	1,3-cyclohexadiene	−40, 5.5	**5d**	98	98
4	2,3-dimethylbutadiene	−78, 43	**6d**	52	82

[a] The Diels–Alder reaction of the maleate **1d** and diene (2~4 equiv) was carried out in the presence of Et_2AlCl (2 equiv) in CH_2Cl_2. [b] Isolated yield. [c] Determined by HPLC and/or 500-MHz ^1H NMR analysis.

Scheme 2



fumarate carbonyls *anti* to alkoxy moieties,[7] the observed higher diastereoselectivities with maleates **1c,d** compared to those with **10** and **11** excludes the possibility of a transition state A for



maleate–Lewis acid complexes. This inference is further supported by low-temperature ^{13}C NMR spectroscopy. Thus, the 125 MHz ^{13}C NMR measurement of the 1:1 maleate **1c**–$SnCl_4$ complex in $CDCl_3$ at −50 °C showed that the original signals of (α-phenethyloxy)carbonyl and *tert*-butoxycarbonyl at δ 164.47 and 164.65 shifted downfield to δ 166.73 and 167.77. A similar tendency was observed for the 1:1 maleate **1d**–$SnCl_4$ complex. These findings imply the existence of the chelation complex B for the dienophiles **1c,d** rather than the nonchelation complex A, which is normally seen in the coordination complexes of acrylates and fumarates with Lewis acids. In contrast, the ^{13}C NMR spectrum of the 1:1 maleate **1c**–MAD complex under similar conditions showed an upfield shift for *tert*-butoxycarbonyl at δ 162.44 and a downfield shift for (α-phenethyloxy)carbonyl at δ 176.40, suggesting the intervention of a nonchelation complex A.[8] Diethylaluminum cation, generated from Et_2AlCl and $LiB(C_6F_5)_4$ (entry 7 in Table 1),[9,10] forms the chelation complex B with unsymmetrical maleate **1c** as evident from its diastereoselectivity similar to those with Et_2AlCl and $SnCl_4$ (entries 6 and 8 in Table 1). *Hence, the high diastereoselectivity in the Lewis acid-promoted Diels–Alder reaction of the unsymmetrical*

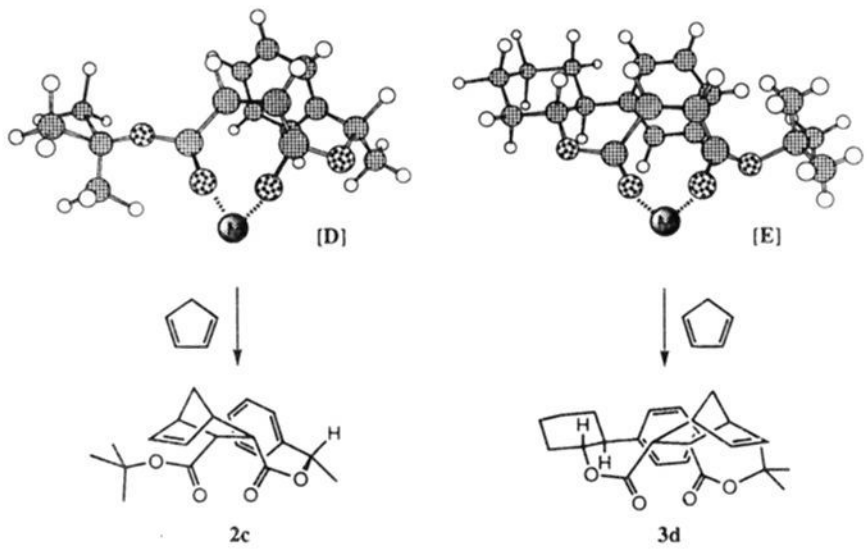
(7) (a) Lewis, F. D.; Oxman, J. D. *J. Am. Chem. Soc.* **1984**, *106*, 466. (b) Loncharich, R. J.; Schwartz, T. R.; Houk, K. N. *Ibid.* **1987**, *109*, 14.

(8) Methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) forms a nonchelation complex with dicarbonyl substrates: Maruoka, K.; Oishi, M.; Yamamoto, H. *Synlett* **1993**, 683.

(9) Castellino, S.; Dwight, W. J. *J. Am. Chem. Soc.* **1993**, *115*, 2986.

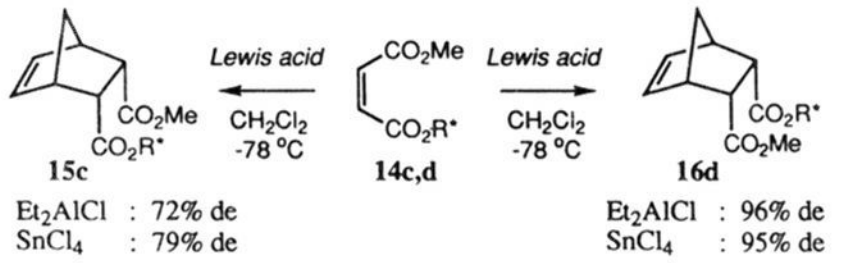
(10) $LiB(C_6F_5)_4$ was kindly provided by Toso-Akzo Chemical Co., Ltd.

Scheme 3



maleates **1c,d** *may be interpreted as being the attractive π–π interaction between the maleate C=C bond and phenyl groups of the chiral auxiliaries as depicted in D and E, in which cyclopentadiene approaches from the front side preferentially, leading to* **2c** *and* **3d**, *respectively, in accord with the experimental findings (Scheme 3).*

The asymmetric Diels–Alder reaction of chiral, unsymmetrical maleates of type **14** gave similar diastereoselectivity to that of *tert*-butyl maleates **1c,d**, again implying the intervention of the chelation complex B, since a nonchelation complex C would afford different diastereoselectivity. Indeed, the attempted Diels–Alder reaction of methyl (*S*)-phenethyl maleate (**14c**) and cyclopentadiene with bulky Lewis acid MAD in CH_2Cl_2 at –20 °C gave, *via* coordination complex C, Diels–Alder adduct **15c** in only 30% de.[11]



Experimental Section

Preparation of *tert*-Butyl *l*-Menthyl Maleate (1a). A mixture of maleic anhydride (2.94 g, 30 mmol) and *l*-menthol (3.12 g, 20 mmol) in toluene (25 mL) was heated to reflux for 7 h. After being cooled to room temperature, the reaction was quenched with 4 N HCl and extracted with ether. The combined organic layers were dried over Na_2SO_4, concentrated, and chromatographed (ether:hexane = 5:1 to 10:1) to give maleic acid, mono-*l*-menthyl ester almost quantitatively. This half ester was dissolved in CH_2Cl_2 (20 mL) in a sealed tube, and excess isobutylene was introduced at –78 °C. Then, 5 drops of concentrated H_2SO_4 was added at –78 °C. The mixture was allowed to warm to room temperature in a closed system and stirred there for 2 days. Then it was recooled to –78 C, the sealed tube was opened, and the mixture was poured into aqueous $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, concentrated, and chromatographed (ether:hexane = 1:10) to furnish the title compound (5.09 g, 78% yield): $[\alpha]_D^{23}$ –50.6° (*c* 0.37, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.18 (1H, d, *J* = 11.8 Hz, CH=), 6.09 (1H, d, *J* = 11.8 Hz, CH=), 4.80 (1H, td, *J* = 4.4, 11 Hz, CH—O), 2.03–2.17 (1H, m, CH), 1.77–2.00 (1H, m, CH), 1.61–1.71 (2H, m, CH_2), 1.51 (9H, s, *t*-Bu), 0.91 (3H, d, *J* = 7 Hz, CH_3), 0.89 (3H, d, *J* = 7 Hz, CH_3), 0.78 (3H, d, *J* = 7 Hz, CH_3); IR (liquid film) 2957, 2872, 2359, 1728, 1644, 1456, 1397, 1370, 1256, 1215, 1148, 986 cm^{-1}. Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.70; H, 9.79.

***l*-Bornyl *tert*-Butyl Maleate (1b):** $[\alpha]_D^{23}$ –30.4° (*c* 0.80, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.07–6.25 (2H, m, 2CH=), 4.93–5.03 (1H, m, CH—O), 2.29–2.47 (1H, m, CH), 1.62–2.00 (3H, m, CH and CH_2), 1.50 (9H, s, *t*-Bu), 0.92 (3H, s, CH_3), 0.88 (3H, s, CH_3), 0.86 (3H, s, CH_3); IR (liquid film) 2977, 2361, 1728, 1644, 1393, 1368, 1258, 1230, 1217, 1150 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.02; H, 9.29.

***tert*-Butyl (*S*)-α-Phenethyl Maleate (1c):** $[\alpha]_D^{23}$ –50.04° (*c* 0.86, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.25–7.42 (5H, m, Ph—H), 6.16 (2H, s, 2CH=), 6.02 (1H, q, *J* = 6.6 Hz, CH—O), 1.59 (3H, d, *J* = 6.6 Hz, CH_3), 1.47 (9H, s, *t*-Bu); IR (liquid film) 2982, 2936, 2361, 1717, 1647, 1456, 1370, 1298, 1260, 1148, 1065, 978, 849, 762, 700 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.29. Found: C, 69.29; H, 7.35.

***tert*-Butyl (1*R*,2*S*)-2-Phenylcyclohexyl Maleate (1d):** $[\alpha]_D^{24}$ –15.87° (*c* 1.39, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.10–7.35 (5H, m, Ph—H), 6.02 (1H, d, *J* = 12 Hz, —CH=), 5.81 (1H, d, *J* = 12 Hz, —CH=), 5.08 (1H, td, *J* = 4.6, 10.4 Hz, CH—O), 2.70 (1H, td, *J* = 3.8, 10.4 Hz, Ph—CH), 1.20–2.34 (8H, m, $4CH_2$), 1.48 (9H, s, *t*-Bu); IR (liquid film) 2936, 1725, 1644, 1495, 1397, 1370, 1256, 1210, 1152, 1015, 849, 756, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.69; H, 8.02.

Typical Procedure for Asymmetric Diels–Alder Reaction of Maleate 1. To a solution of maleate **1** (1 mmol) in CH_2Cl_2 (5 mL) was added a Lewis acid (1 mmol) or a 1 M CH_2Cl_2 or hexane solution of a Lewis acid (1 mmol) followed by cyclopentadiene (163 μL, 2 mmol) at –78 °C. The resulting mixture was stirred under the conditions indicated in Table 1. The solution was then poured into 1 N HCl and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether/hexane as the eluant) to furnish Diels–Alder *endo*-adducts **2** and **3**. The diastereomeric ratio (*i.e.*, the ratio of **2** to **3**) was determined by capillary GLC (0.25- × 25 000-mm PEG-HT column), HPLC (4.6- × 250-mm Jasco Finepak Sil column), and/or 500-MHz ^1H NMR analyses by comparison with authentic samples which were prepared by the thermal Diels–Alder reactions.

Diels–Alder Adducts 2a and 3a: ^1H NMR ($CDCl_3$) δ 6.28 and 6.37 (1H, dd, *J* ≈ 2.8, 5.5 Hz, diastereomeric CH=), 6.13 and 6.20 (1H, dd, *J* = 2.8, 5.5 Hz, diastereomeric CH=), 4.61 and 4.67 (1H, dt, *J* = 4.4, 10.6 Hz, diastereomeric CH—O), 3.01–3.30 (4H, m, 2CH—C=O and 2CH—C=), 1.81–2.10 (2H, m, CH_2), 1.56–1.76 (2H, m, CH_2), 1.40 (9H, s, *t*-Bu), 0.89 (6H, d, *J* = 7 Hz, $2CH_3$), 0.76 (3H, d, *J* = 7 Hz, CH_3); IR (liquid film) 2959, 2930, 2872, 1732, 1456, 1370, 1343, 1256, 1210, 1180, 1150, 1080, 779, 766, 737 cm^{-1}. Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.37; H, 9.64. Found: C, 73.27; H, 9.34.

Diels–Alder Adducts 2b and 3b: ^1H NMR ($CDCl_3$) δ 6.14–6.23 (1H, m, CH=), 6.24–6.36 (1H, m, CH=), 4.75 and 4.86 (1H, ddd, *J* = 3.4, 3.6, 10 Hz, diastereomeric CH—O), 3.18–3.25 (2H, m, 2CH), 3.10–3.17 (2H, m, 2CH), 2.18–2.36 (1H, m, CH), 1.59–1.98 (3H, m, 3C—H), 1.40 (9H, s, *t*-Bu), 0.88 (3H, s, CH_3), 0.86 (3H, s, CH_3), 0.81 and 0.83 (3H, s, diastereomeric CH_3); IR ($CHCl_3$) 2959, 1732, 1456, 1368, 1345, 1256, 1210, 1186, 1152, 785, 669 cm^{-1}. Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.81; H, 9.34.

Diels–Alder Adduct 2c: $[\alpha]_D^{23}$ –45.17° (*c* 0.83, THF); ^1H NMR ($CDCl_3$) δ 7.20–7.43 (5H, m, Ph—H), 6.27 (1H, dd, *J* = 2.8, 5.4 Hz, CH=), 6.13 (1H, dd, *J* = 2.8, 5.4 Hz, CH=), 5.85 (1H, q, *J* = 6.8 Hz, CH—O), 3.29 (1H, dd, *J* = 3.4, 10 Hz, CH—C=), 3.18 (1H, dd, *J* = 3.4, 10 Hz, CH—C=), 3.04–3.28 (2H, m, 2CH—C=O), 1.49 (3H, d, *J* = 6.6 Hz, CH_3), 1.43 (9H, s, *t*-Bu); IR (liquid film) 2979, 1740, 1497, 1368, 1343, 1254, 1208, 1177, 1150, 1076, 700 cm^{-1}. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.72; H, 7.83. The isomeric ratio was determined by capillary GLC analysis: t_R(**3c**) = 49.5 min, t_R(**2c**) = 54.0 min (column temperature of 180 °C).

Diels–Alder Adduct 3d: $[\alpha]_D^{23}$ +13.49° (*c* 0.81, THF); ^1H NMR ($CDCl_3$) δ 7.17–7.32 (5H, m, Ph—H), 6.17 (1H, dd, *J* = 2.5, 5.6 Hz, CH=), 5.44 (1H, dd, *J* = 3, 5.6 Hz, CH=), 4.95 (1H, dt, *J* = 4.4, 10.7 Hz, CH—O), 2.89–3.02 (3H, m, 3CH), 2.63 (1H, dt, *J* = 3.8, 11.5 Hz, Ph—CH), 2.41 (1H, s, CH), 2.06–2.16 (1H, m, CH), 1.72–1.97 (3H, m, CH and CH_2), 1.38 (9H, s, *t*-Bu), 1.06–1.62 (6H, m, $3CH_2$); IR ($CHCl_3$) 2938, 1732, 1451, 1370, 1340, 1256, 1210, 1181, 1154, 1078, 779, 750 cm^{-1}. Anal. Calcd for $C_{25}H_{32}O_4$: C, 75.73; H, 8.13. Found: C, 75.74; H, 8.15. The isomeric ratio was determined by HPLC analysis (ether:hexane = 1:20, flow rate = 1 mL/min): t_R(**3d**) = 13.7 min, t_R(**2d**) = 15.7 min.

Diels–Alder Adduct 4d: $[\alpha]_D^{23}$ +30.21° (*c* 0.58, THF); ^1H NMR ($CDCl_3$) δ 7.18–7.37 (5H, m, Ph—H), 6.43 (1H, dd, *J* = 1.6, 5.8 Hz, CH=), 5.41 (1H, dd, *J* = 1.6, 5.8 Hz, CH=), 4.82–4.95 (2H, m, O—CH—C= and CH—O), 4.42 (1H, d, *J* = 4.1 Hz, O—CH—C=), 3.06–3.17 (2H, m, 2CH—C=O), 2.65 (1H, dt, *J* = 1.6, 10 Hz, Ph—CH), 2.03–2.12 (1H, m, CH), 1.21–1.98 (8H, m, $4CH_2$), 1.38 (9H, s, *t*-Bu);

(11) An exceptionally bulky Lewis acid, MAD, coordinates to the less hindered ester carbonyls preferentially: Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1992**, *114*, 1089.

IR ($CHCl_3$) 3031, 3011, 2938, 1734, 1370, 1223, 1210, 1183, 1154, 787, 776, 766, 743, 729, 668 cm^{-1}. Anal. Calcd for $C_{24}H_{30}O_5$: C, 72.34; H, 7.59. Found: C, 72.34; H, 7.52. The isomeric ratio was determined by comparison with the integration of the olefinic hydrogens by 500-MHz ^1H NMR analysis: δ 6.58 (dd, J = 1.6, 5.8 Hz, diastereomeric CH=), 6.20 (dd, J = 1.6, 5.8 Hz, diastereomeric CH=).

Diels–Alder Adduct 5d: $[\alpha]_D^{23}$ +18.71° (*c* 1.04, THF); ^1H NMR ($CDCl_3$) δ 7.10–7.35 (5H, m, Ph—H), 6.23 (1H, t, J = 7 Hz, CH=), 5.60 (1H, t, J = 7 Hz, CH=), 4.99 (1H, td, J = 4.5, 10 Hz, CH—O), 2.55–2.83 (4H, m, 2CH—C=O, Ph—CH, and CH—C=), 1.66–2.15 (5H, m, CH and $2CH_2$), 1.38 (9H, s, *t*-Bu), 0.95–1.65 (8H, m, $4CH_2$); IR ($CHCl_3$) 3001, 2940, 1736, 1370, 1221, 1215, 1186, 1152, 765, 740 cm^{-1}. Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.35. Found: C, 76.10; H, 8.40. The isomeric ratio was determined by HPLC analysis (ether: hexane = 1:20, flow rate = 2 mL/min): t_R(**5d**) = 7.8 min, t_R(diastereomer of **5d**) = 8.2 min.

Diels–Alder Adduct 6d: $[\alpha]_D^{23}$ −27.14° (*c* 1.03, THF); ^1H NMR ($CDCl_3$) δ 7.09–7.32 (5H, m, Ph—H), 5.00 (1H, dt, J = 4.6, 10.4 Hz, CH—O), 2.50–2.78 (3H, m, 2CH—C=O and Ph-CH), 1.68–2.40 (9H, m, CH and $4CH_2$), 1.51 (3H, s, CH_3—C=), 1.41 (9H, s, *t*-Bu), 1.34 (3H, s, CH_3—C=); IR (liquid film) 2932, 1732, 1495, 1451, 1368, 1200, 1159, 1119, 1022, 851, 754, 700 cm^{-1}. Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80. Found: C, 75.69; H, 9.05. The isomeric ratio was determined by HPLC analysis (ether:hexane = 1:20, flow rate = 1 mL/min): t_R(**6d**) = 8.7 min, t_R(diastereomer of **6d**) = 9.4 min.

Chemoselective Transformation of 3d to Lactone 9. A solution of **3d** (793 mg, 2 mmol) in CH_2Cl_2 (10 mL) was treated with CF_3CO_2H (0.46 mL, 6 mmol) at room temperature for 40 h. The reaction was quenched with diluted $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and chromatographed (ether: hexane = 2:1 to ether as the eluant) to furnish a monoacid **7** (626 mg, 92% yield).

The acid **7** and NEt_3 (0.28 mL, 2 mmol) were dissolved in THF (8 mL) and cooled to −15 °C. Ethyl chlorocarbonate (0.2 mL, 2 mmol) was added at −15 °C. The entire mixture was stirred at this temperature for 15 min. The solid (Et_3N·HCl) which appeared was removed by filtration and washed with THF. The combined filtrates were treated with $NaBH_4$ (76 mg, 2 mmol), and then MeOH (0.5 mL) was carefully added dropwise to this mixture at −20 °C.[2f] The resulting mixture was stirred at −20 °C for 1.5 h. The reaction was quenched by the addition of saturated NH_4Cl and extracted with ether. The combined extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether:hexane = 1:1 to 2:1 as the eluant) to furnish hydroxy ester **8** (558 mg, 93% yield): $[\alpha]_D^{20}$ +41.1° (*c* 0.75, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.18–7.34 (5H, m, Ph—H), 5.74 (1H, dd, J = 3, 5.7 Hz, CH=), 5.12 (1H, dd, J = 3, 5.7 Hz, CH=), 5.00 (1H, dt, J = 4.4, 10.6 Hz, CH—O—C=O), 3.29–3.39 (1H, m, CH—O), 3.07–3.15 (1H, m, CH), 2.98–3.07 (1H, m, CH), 2.93 (1H, dd, J = 3.5, 9.5 Hz, CH—C=O), 2.77 (1H, s, CH), 2.70 (1H, s, CH), 2.63–2.76 (1H, m, CH), 2.45–2.57 (1H, m, CH), 2.07–2.15 (1H, m, CH), 1.74–1.98 (3H, m, 3CH), 1.30–1.58 (4H, m, $2CH_2$), 1.17–1.26 (2H, m, CH_2); IR (liquid film) 3415, 3064, 3028, 2936, 2861, 1728, 1495, 1451, 1339, 1250, 1181, 1152, 1105, 1059, 1032, 756, 733, 700 cm^{-1}.

The hydroxy ester **8** in benzene (10 mL) was treated with catalytic *p*-TsOH·H_2O under reflux for 30 min to furnish the desired lactone **9** (244 mg, 95% yield):[2f,6] $[\alpha]_D^{20}$ +150.1° (*c* 0.82, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.23–6.35 (2H, m, 2CH=), 4.29 (1H, dd, J = 8.4, 9.6 Hz, CH—O), 3.80 (1H, dd, J = 3.2, 9.6 Hz, CH—O), 3.31–3.38 (1H, m, CH—C=), 3.25 (1H, dd, J = 4.6, 9.3 Hz, CH—C=O), 3.05–3.16 (2H, m, 2CH), 1.65 (1H, d, J = 9.6 Hz, CH), 1.47 (1H, d, J = 9.6 Hz, CH); IR ($CHCl_3$) 3021, 2979, 1759, 1480, 1381, 1343, 1221, 1184, 1048, 1003, 760, 706, 669 cm^{-1}.

Since the optical rotation value of the authentic, optically pure lactone **9** is reported to be $[\alpha]_D^{25}$ +143.2° (*c* 5.2, $CHCl_3$),[6] the absolute structure of the Diels–Alder adduct should be **3d**.

(*S*)-α-Phenethyl Acrylate (10c): $[\alpha]_D^{23}$ −85.6° (*c* 1.06, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.25–7.42 (5H, m, Ph—H), 6.43 (H, dd, J = 1.6, 17.3 Hz, CH=), 6.15 (1H, dd, J = 10.3, 17.3 Hz, C*H*H=), 5.97 (1H, q, J = 6.6 Hz, PhCH—O), 5.83 (1H, dd, J = 1.6, 10.3 Hz, CH*H*=), 1.58 (3H, d, J = 6.6 Hz, CH_3); IR (liquid film) 3036, 2984, 2934, 1727, 1638, 1619, 1497, 1455, 1406, 1377, 1294, 1269, 1194, 1065, 1044, 1030, 986, 924, 810, 762, 700 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.00; H, 6.87.

(1*R*,2*S*)-2-Phenylcyclohexyl Acrylate (10d): $[\alpha]_D^{23}$ −29.0° (*c* 0.92, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.12–7.30 (5H, m, Ph—H), 6.16 (H, dd, J = 1.5, 17.3 Hz, CH=), 5.89 (1H, dd, J = 10.4, 17.3 Hz, C*H*H=), 5.63 (1H, dd, J = 1.5, 10.4 Hz, CH*H*=), 5.03 (1H, td, J = 4.4, 10.7 Hz, CH—O), 2.71 (1H, td, J = 4.1, 12.1 Hz, PhCH), 2.12–2.33 (1H, m, CH), 1.76–2.01 (3H, m, CH and CH_2), 1.20–1.67 (4H, m, $2CH_2$); IR (liquid film) 3031, 2936, 2859, 1721, 1495, 1451, 1406, 1318, 1294, 1269, 1196, 1055, 1019, 808, 756, 700 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.21; H, 8.00.

***tert*-Butyl (*S*)-α-Phenethyl Fumarate (11c):** $[\alpha]_D^{23}$ −10.86° (*c* 0.75, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.24–7.41 (5H, m, Ph—H), 6.78 (2H, s, CH=), 5.98 (1H, q, J = 6.6 Hz, CH—O), 1.59 (3H, d, J = 6.6 Hz, CH_3), 1.50 (9H, s, *t*-Bu); IR (liquid film) 2982, 2936, 2361, 1717, 1647, 1456, 1370, 1298, 1260, 1148, 1065, 978, 849, 762, 700 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.29. Found: C, 69.60; H, 7.36.

Diels–Alder Adduct 12c: ^1H NMR ($CDCl_3$) δ 7.25–7.39 (5H, m, Ph—H), 6.12 and 6.20 (1H, dd, J = 3.2, 5.4 Hz, diastereomeric CH=), 5.66 and 5.94 (1H, dd, J = 2.7, 5.4 Hz, diastereomeric CH=), 5.83 (1H, dq, J = 2.2, 6.6 Hz, CH—O), 3.24 (1H, d, J = 12 Hz, CH), 2.98 (1H, ddd, J = 3.9, 5, 8.2 Hz, CH), 2.90 (1H, m, CH), 1.89 (1H, ddd, J = 3.8, 9.1, 11.5 Hz, CH), 1.23–1.55 (3H, m, 3CH), 1.51 (3H, d, J = 6.6 Hz, CH_3); IR (liquid film) 3068, 2979, 2944, 2870, 1732, 1453, 1337, 1271, 1188, 1173, 1067, 760, 712, 698 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.40; H, 7.57.

Diels–Alder Adduct 12d: ^1H NMR ($CDCl_3$) δ 7.13–7.33 (5H, m, Ph—H), 5.91 and 5.92 (1H, dd, J = 3.1, 5.8 Hz, diastereomeric CH=), 4.60 and 5.66 (1H, dd, J = 3, 5.6 Hz, diastereomeric CH=), 4.90 (1H, dq, J = 4.6, 10.5 Hz, CH—O), 2.61–3.07 (4H, m, 2CH—C=, CH—C=O, and Ph—CH), 2.02–2.16 (1H, m, CH), 1.06–1.96 (11H, m, CH and $5CH_2$); IR ($CHCl_3$) 3034, 2942, 2863, 1721, 1451, 1337, 1273, 1192, 1109, 1030, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.93; H, 8.20.

Asymmetric Diels–Alder Reaction of Fumarate 11c. Asymmetric Diels–Alder reaction of fumarate **11c** with Et_2AlCl or $SnCl_4$ gave rise to four isomeric mixtures, *i.e.*, diastereomeric **13c** with *tert*-butoxycarbonyl *endo* and their regioisomers with *tert*-butoxycarbonyl *exo*: ^1H NMR ($CDCl_3$) δ 7.25–7.38 (5H, m, Ph—H), 6.19 and 6.27 (1H, dd, J = 3, 5.6 Hz, isomeric CH=), 5.76 and 6.07 (1H, dd, J = 2.4, 5.6 Hz, isomeric CH=), 5.81 and 5.84 (1H, dq, J = 2.3, 6.5 Hz, isomeric CH—O), 3.03–3.38 (3H, m, 2CH—C=, CH—C=O), 2.57–2.70 (1H, m, CH—C=O), 1.48–1.57 (3H, m, isomeric CH_3), 1.39, 1.41, 1.43, and 1.45 (9H, s, isomeric *t*-Bu); IR (liquid film) 2980, 1725, 1456, 1368, 1308, 1267, 1156, 1113, 1063, 760, 698 cm^{-1}. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.69; H, 7.83. The diastereomeric ratio of **13c** was determined on the basis of the integration of two *tert*-butoxy signals (*i.e.*, δ 1.43 and 1.45). The authentic **13c** was prepared by the asymmetric Diels–Alder reaction of fumarate **11c** with MAD in CH_2Cl_2 at −40 °C.

Diels–Alder Adduct 13c: ^1H NMR ($CDCl_3$) δ 7.25–7.38 (5H, m, Ph—H), 6.18 and 6.26 (1H, dd, J = 3.3, 5 Hz, diastereomeric CH=), 5.76 and 6.07 (1H, dd, J = 3, 5 Hz, diastereomeric CH=), 5.81 (1H, dq, J = 3, 6.5 Hz, CH—O), 3.03–3.38 (3H, m, 2CH—C=, CH—C=O), 2.59 (1H, dd, J = 1.4, 4.4 Hz, CH—C=O), 1.49 and 1.51 (3H, d, J = 7 Hz, diastereomeric CH_3), 1.43 and 1.45 (9H, s, diastereomeric *t*-Bu).

Low-Temperature ^{13}C NMR Spectroscopy of the Acrylate 1–$SnCl_4$ Complex. To a solution of maleate **1** (0.3 mmol) in $CDCl_3$ (1 mL) in a 5-mm NMR tube was added $SnCl_4$ (0.3 mmol) at −78 °C, and the 125-MHz ^{13}C NMR spectra were taken at −50 °C. The coordination pattern of the maleate **1**–$SnCl_4$ complex was measured by low-temperature 125-MHz ^{13}C NMR analysis of carbonyl carbons of the coordinated maleate **1**.

tert-Butyl (*S*)-α-phenethyl maleate (**1c**): ^{13}C NMR ($CDCl_3$) δ 164.47 and 164.65 (*tert*-butoxy C=O and α-phenethyloxy C=O), 141.18 (C= of Ph), 131.71 (CH=), 128.62 (*m*-C= of Ph), 128.33 (*p*-C= of Ph), 128.02 (CH=), 126.29 (*o*-C= of Ph), 82.05 (O–*C*Me$_3$), 72.96 (O*C*HMe), 27.67 (C(*C*H$_3$)$_3$), 21.69 (CH–*C*H$_3$).

Maleate **1c**–$SnCl_4$ (1:1) complex: ^{13}C NMR ($CDCl_3$) δ 166.73 and 167.77 (*tert*-butoxy C=O··Sn and α-phenethyloxy C=O··Sn), 136.45 (C= of Ph), 135.52 (CH=), 132.53 (CH=), 93.59 (O*C*HMe), 81.72 (O—*C*Me$_3$), 27.49 (C(*C*H$_3$)$_3$), 21.03 (CH—*C*H$_3$).

tert-Butyl (1*R*,2*S*)-2-phenylcyclohexyl maleate (**1d**): ^{13}C NMR ($CDCl_3$) δ 164.52 and 164.52 (*tert*-butoxy C=O and (*trans*-2-phenylcyclohexyl)oxy C=O), 142.97 (C= of Ph), 131.48 (CH=), 128.34 (*m*-C= of Ph), 128.10 (*p*-C= of Ph), 127.53 (*o*-C= of Ph), 126.49 (CH=), 81.84 (O–*C*Me$_3$), 70.58 (O–CH), 49.36 (Ph–*C*H), 39.76 (CH_2), 31.77 (CH_2), 27.75 (C(*C*H$_3$)$_3$), 25.55 (CH_2), 24.47 (CH_2).

Maleate **1d**–$SnCl_4$ (1:1) complex: ^{13}C NMR ($CDCl_3$) δ 166.35 and 168.05 (*tert*-butoxy C=O··Sn and (*trans*-2-phenylcyclohexyl)oxy C=O··Sn), 140.81 (C= of Ph), 135.33 (CH=), 132.55 (CH=), 93.45 (OCH), 84.85 (O—*C*Me$_3$), 48.44 (Ph—*C*H), 27.59 (C(*C*H$_3$)$_3$).

Low-Temperature ^{13}C NMR Spectroscopy of the Maleate 1c–MAD Complex. MAD was prepared and purified by crystallization for the NMR study. Thus, a solution of Me_3Al (15 mL, 30 mmol) was added to a solution of 2,6-di-*tert*-butyl-4-methylphenol (13.22 g, 60 mmol) in degassed hexane (40 mL) at room temperature. A white precipitate appeared immediately. After 1 h, this mixture was heated until the precipitate redissolved in hexane. The resulting solution was allowed to stand for 3 h, yielding colorless crystals which were filtered in an argon box. Since the crystals include some impurities such as 2,6-di-*tert*-butyl-4-methylphenol and inorganic aluminum salts, they were further recrystallized from hexane (45 mL) at -20 °C to give essentially pure MAD (7.83 g, 54% yield): ^1H NMR ($CDCl_3$) δ 7.04 (4H, s, C_6H_2), 2.28 (6H, s, CH_3), 1.53 (36H, s, $C(CH_3)_3$), –0.35 (3H, s, Al—CH_3); ^{13}C NMR ($CDCl_3$) δ 152.02, 138.19, 127.71, 125.94, 34.94, 31.56, 21.40, –9.09 (Al—*C*H_3).

MAD (0.3 mmol) was transferred to the dry flask in an argon box, and $CDCl_3$ (1 mL) was added at room temperature. Then this solution was cooled to –78 °C and the maleate **1c** (0.15 or 0.3 mmol) was added at this temperature. The mixture was transferred by cannula to a 5-mm NMR tube at –78 °C and the 125-MHz ^{13}C NMR spectra were taken at –50 °C. The coordination pattern of the maleate **1c**–MAD complex was measured by low-temperature ^{13}C NMR analysis of carbonyl carbons of the maleate **1c**.

Maleate **1c**–MAD (1:1) complex: ^{13}C NMR ($CDCl_3$) δ 162.44 (*tert*-butoxy C=O··Sn), 176.40 (α-phenethyloxy C=O··Sn).

IR Spectroscopy of Dimethyl Maleate–$SnCl_4$ Complex. The FT-IR spectra of dimethyl maleate and its $SnCl_4$ complex in CH_2Cl_2 show C=O absorptions at 1732 and 1682 cm^{-1}, respectively.

Preparation of Methyl (*S*)-α-Phenethyl Maleate (14c). A solution of maleic anhydride (980 mg, 10 mmol) in MeOH (10 mL) was refluxed for 5 h. The reaction mixture was evaporatively concentrated, and the residue was washed with 4 N HCl and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and concentrated to furnish crude maleic acid monomethyl ester almost quantitatively.

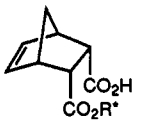
This monomethyl ester in CH_2Cl_2 (10 mL) was treated with (*S*)-α-phenethyl alcohol (0.79 mL, 6.7 mmol), DCC (1.55 g, 7.5 mmol), and catalytic DMAP at room temperature for 5 h. The mixture was filtered through a Celite pad and washed with saturated $NaHCO_3$. The organic layer was extracted with CH_2Cl_2, and the combined organic extracts were dried over concentrated Na_2SO_4. The residue was purified by column chromatography (ether:hexane = 1:4, 1:2 to 1:1) to afford the title compound (753 mg, 48% yield): $[\alpha]_D^{24}$ –72.47° (*c* 1.01, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.20–7.50 (5H, m, Ph—H), 6.25 (2H, s, 2CH=), 6.00 (1H, q, *J* = 7.8 Hz, CH—O), 3.68 (3H, s, OCH_3), 1.60 (3H, d, *J* = 7.8 Hz, CH_3); IR (liquid film) 2994, 2953, 1732, 1648, 1497, 1456, 1437, 1395, 1291, 1250, 1217, 1167, 1063, 700 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.54; H, 6.24.

Methyl (1*R*,2*S*)-2-Phenylcyclohexyl Maleate (14d): $[\alpha]_D^{23}$ –39.41° (*c* 0.81, THF); ^1H NMR ($CDCl_3$) δ 7.10–7.33 (5H, m, Ph—H), 6.08 (1H, d, *J* = 12 Hz, CH=), 5.95 (1H, d, *J* = 12 Hz, CH=), 5.08 (1H, td, *J* = 4.6, 10.4 Hz, CH—O), 3.71 (3H, s, OCH_3), 2.70 (1H, td, *J* = 3.4, 10.4 Hz, Ar—CH), 2.20–2.40 (1H, m, CH), 1.22–2.05 (7H, m, CH and $3CH_2$); IR (liquid film) 3031, 2938, 2861, 1730, 1646, 1495, 1449, 1437, 1395, 1291, 1252, 1215, 1165, 1013, 756, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.82; H, 6.99. Found: C, 70.97; H, 7.13.

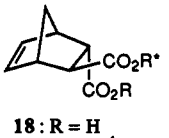
Diels–Alder Adduct 15c: $[\alpha]_D^{23}$ –69.96° (*c* 0.94, THF); ^1H NMR ($CDCl_3$) δ 7.20–7.43 (5H, m, Ph—H), 6.26 and 6.36 (1H, dd, *J* = 3.2, 5.6 Hz, diastereomeric CH=), 6.05 and 6.20 (1H, dd, *J* = 3.2, 5.6 Hz, diastereomeric CH=), 5.80 (1H, q, *J* = 6.6 Hz, CH—O), 3.58 (3H, s, OCH_3), 3.08–3.69 (4H, m, 2CH—C= and 2CH—C=O), 1.21–1.60 (2H, m, CH_2), 1.48 (3H, d, *J* = 6.6 Hz, CH_3); IR (liquid film) 2980, 2950, 2872, 1744, 1455, 1435, 1372, 1341, 1254, 1196, 1167, 1069, 762, 720, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.00; H, 6.70. The isomeric ratio was determined by capillary GLC analysis: t_R(**16c**) = 79.5 min, t_R(**15c**) = 86.2 min at the (column temperature of 180 °C).

Diels–Alder Adduct 16d: $[\alpha]_D^{23}$ +10.16° (*c* 1.30, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.13–7.37 (5H, m, Ph—H), 6.22 (1H, dd, *J* = 2.6, 5.6 Hz, CH=), 5.11 (1H, dd, *J* = 3, 5.6 Hz, CH=), 4.90 (1H, dt, *J* = 4.4, 11.4 Hz, CH—O), 3.58 (3H, s, OCH_3), 2.91–3.13 (3H, m, 3CH), 2.63 (1H, dt, *J* = 4.4, 11.5 Hz, Ph—CH), 2.52 (1H, br s, CH), 2.00–2.16 (1H, m, CH), 1.07–2.00 (9H, m, CH and CH_2); IR (liquid film) 3031, 2940, 2861, 1736, 1341, 1254, 1198, 1173, 1076, 1022, 722 cm^{-1}. Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.60; H, 7.45. The isomeric ratio was determined by HPLC analysis (ether:hexane = 1:15, flow rate = 1 mL/min): t_R(**16d**) = 25.4 min, t_R(**15d**) = 28.4 min.

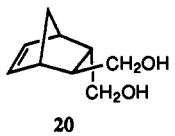
Determination of the Absolute Configuration of the Cycloadduct 2c. The absolute configuration of **2c** was assigned by correlation to the known (5*S*,6*S*)-5,6-bis(hydroxymethyl)-2-norbornene (**20**).[12]



17



18: R = H
19: R = Bu^t



20

A solution of **2c** (800 mg, 2.3 mmol) in CH_2Cl_2 (8 mL) was treated with CF_3CO_2H (0.36 mL, 4.7 mmol) at room temperature for 24 h. The reaction was quenched with diluted $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and chromatographed (ether:hexane = 5:2 to 5:1) to furnish a monoacid **17** (599 mg, 91% yield).

The acid **17** in THF (2 mL) was added to a solution of excess LDA (6 mmol) in THF (18 mL) at –78 °C. After 30 min at –78 °C and the usual workup (flash chromatography, ether:hexane = 2:1), a mixture of *trans*-monoacid **18** and **17** was obtained (401 mg, 67% yield).

This mixture was converted to their *tert*-butyl esters, **19** and **2c** with isobutylene and catalytic H_2SO_4 in CH_2Cl_2 as described in the preparation of *tert*-butyl maleate **1**, and the desired *trans*-ester **19** was separated from **2c** by column chromatography (ether:hexane = 1:15) in 55% yield (263 mg).

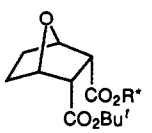
The ester **19** was reduced with $LiAlH_4$ (38 mg, 1 mmol) in ether (3 mL) at 0 °C for 30 min to afford, after purification by column chromatography (ether:hexane = 1:2 to ether), (5*S*,6*S*)-5,6-bis(hydroxymethyl)-2-norbornene (**20**) (113 mg, 95% yield): $[\alpha]_D^{22}$ –7.26° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 6.24 (1H, dd, *J* = 3.2, 5.6 Hz, CH=), 5.98 (1H, dd, *J* = 2.8, 5.6 Hz, CH=), 3.77 (1H, dd, *J* = 5.6, 9.6 Hz, CH—O), 3.65 (1H, dd, *J* = 5.2, 9.6 Hz, CH—O), 3.41 (1H, t, *J* = 10 Hz, CH—O), 3.02 (1H, t, *J* = 10 Hz, CH—O), 2.82 (1H, s, CH), 2.59 (1H, s, CH), 1.87–2.00 (1H, m, CH), 1.45 (2H, br s, CH_2), 1.18–1.42 (1H, m, CH).

Since the optical rotation value of the authentic, optically pure (5*S*,6*S*)-5,6-bis(hydroxymethyl)-2-norbornene is reported to be $[\alpha]_D$ –21° ($CHCl_3$),[12] the absolute structure of the Diels–Alder adduct should be **2c**.

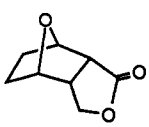
Determination of the Absolute Configuration of the Cycloadduct 16d. The absolute configuration of **16d** was assigned by correlation to the cycloadduct **3d**. Thus, **3d** (397 mg, 1 mmol) in CH_2Cl_2 (5 mL) was treated with CF_3CO_2H (0.23 mL, 3 mmol) at room temperature for 40 h. The reaction was quenched with diluted $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and chromatographed (ether:hexane = 2:1 to ether as the eluant) to furnish a monoacid **7** (293 mg, 86% yield).

A solution of the monoacid **7** in ether (3 mL) was reacted with diazomethane (~2 equiv) in ether at 0 °C for 30 min. Then excess diazomethane was decomposed with acetic acid. The reaction was quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and chromatographed (ether:hexane = 1:2) to give the methyl ester (268 mg, 88% yield; $[\alpha]_D^{22}$ +9.92° (*c* 1.03, $CHCl_3$)) with the same optical rotation sign as that of **16d**.

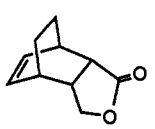
Determination of the Absolute Configuration of the Cycloadduct 4d. The absolute configuration of **4d** was assigned by correlation to the known optically active lactone **22**.[13] Thus, **4d** (481 mg, 1.2 mmol) in EtOAc (5 mL) was hydrogenated over 5% Pd/C under a H_2 atmosphere at room temperature for 2 h. The reaction mixture was filtered and washed with EtOAc. The combined filtrates were concentrated and chromatographed (ether:hexane = 1:4) to furnish a hydrogenated diester **21** (458 mg, 95% yield).



21



22



23

(12) Horton, D.; Machinami, T. *J. Chem. Soc., Chem. Commun.* **1981**, 88.
(13) Jones, J. B.; Francis, C. J. *Can. J. Chem.* **1984**, *62*, 2578. See also ref 2f.

The diester **21** was converted to the known optically active lactone **22** in a manner similar to that described in the chemoselective transformation of **3d** to the lactone **9**.

Lactone **22**: $[\alpha]_D^{20}$ +147.6° (*c* 0.96, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.82–4.88 (1H, m, CH—O), 4.66–4.72 (1H, m, CH—O), 4.35 (1H, dd, *J* = 8, 10.4 Hz, C*H*H—O), 4.21 (1H, dd, *J* = 2.4, 10.4 Hz, CH*H*—O), 3.35 (1H, dd, *J* = 6.6, 11.1 Hz, CH—C═O), 3.13–3.24 (1H, m, CH), 1.72–1.87 (4H, m, $2CH_2$); IR ($CHCl_3$) 3021, 1767, 1379, 1218, 1177, 1011, 949, 833, 735, 669 cm^{-1}.

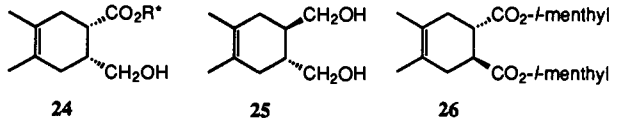
Since the optical rotation value of the authentic, optically pure lactone **22** is reported to be $[\alpha]_D^{20}$ +132° (*c* 1, $CHCl_3$),[2f,13] the absolute structure of the Diels–Alder adduct should be **4d**.

Determination of the Absolute Configuration of the Cycloadduct 5d. The absolute configuration of **5d** was assigned by correlation to the known optically active lactone **23**.[13] Thus, the adduct **5d** was converted to the lactone **23** in a manner similar to that described in the chemoselective transformation of **3d** to the lactone **9**.

Lactone **23**: $[\alpha]_D^{20}$ +96.3° (*c* 1.87, $CHCl_3$); ^1H NMR δ 6.23–6.39 (2H, m, 2CH═), 4.35 (1H, dd, *J* = 8.5, 9 Hz, C*H*H—O), 3.85 (1H, dd, *J* = 3.8, 9 Hz, CH*H*—O), 3.03–3.12 (1H, m, CH—C═), 2.63–2.82 (3H, m, CH—C═, CH—C═O, and CH), 1.21–1.67 (4H, m, $2CH_2$); IR ($CHCl_3$) 2946, 1755, 1248, 1211, 1186, 1051, 1013, 783, 772, 752, 745, 733, 708, 669 cm^{-1}.

Since the optical rotation value of the authentic, optically pure lactone **23** is reported to be $[\alpha]_D^{25}$ +92° (*c* 3.9, $CHCl_3$),[13] the absolute structure of the Diels–Alder adduct should be **5d**.

Determination of the Absolute Configuration of the Cycloadduct 6d. The absolute configuration of **6d** was assigned by correlation to the known *l*-menthyl diester **26**.[14] Thus, **6d** was transformed to hydroxy ester **24**



24 **25** **26**

according to the procedures of chemoselective transformation of **3d** to the hydroxy ester **8**. The hydroxy ester **24**, thus obtained, was isomerized with LDA in THF to a *trans*-hydroxy ester which was reduced with $LiAlH_4$ in ether, in a manner similar to that described in the determination of the absolute configuration of **2c**, to furnish *trans*-diol **25**: $[\alpha]_D$ −76.9° (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$) δ 3.56–3.82 (4H, m, $2CH_2$—O), 1.89–2.15 (6H, m, 2CH and $2CH_2$), 1.57 (6H, s, $2CH_3$).

Since the optical rotation value of the enantiomer of *trans*-diol **25**, which was derived by the reduction of *l*-menthyl diester **26**[14] with $LiAlH_4$ in ether, is found to be $[\alpha]_D$ +73.0° (*c* 1.16, MeOH), the absolute structure of the Diels–Alder adduct should be **6d**.

(14) Furuta, K.; Iwanaga, K.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 4507.