JOC Article

Stereoselective Hydrocoupling of Cinnamic Acid Esters by Electroreduction: Application to Asymmetric Synthesis of Hydrodimers

Naoki Kise,* Shumei Iitaka, Keisuke Iwasaki, and Nasuo Ueda

Department of Biotechnology, Faculty of Engineering, Tottori University, Koyama, Tottori 680-8552, Japan

kise@bio.tottori-u.ac.jp

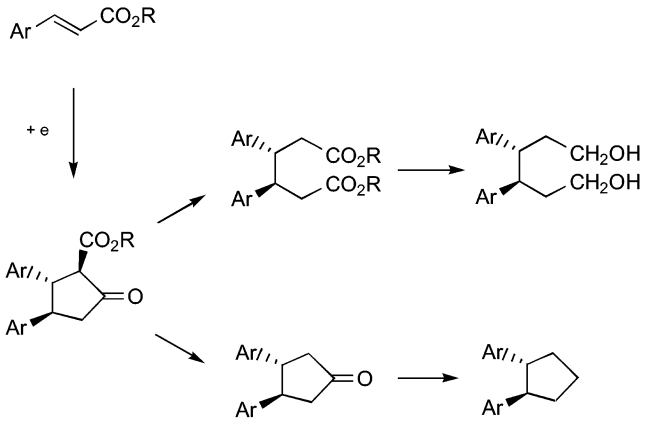
Received July 11, 2002

The electroreduction of Ar-substituted methyl cinnamates in acetonitrile gave all-trans cyclized hydrodimers stereoselectively (58∼90% de). In all cases, small amounts (<10% yield) of meso hydrodimers were also formed. The electrolysis was performed conveniently using an undivided cell at a constant current. The transition states for the hydrocoupling were calculated with semiempirical methods. The all-trans cyclized hydrodimers were transformed to C_2-symmetric *dl*-3,4-diaryladipic acids and *trans*-3,4-diarylcyclopentanones. The chiral auxiliary [(1*R*)-*exo*]-3-*exo*-(diphenylmethyl)borneol, prepared from (1*R*)-(+)-camphor, was highly effective for the stereoselective hydrocoupling of its cinnamates by electroreduction. From the resulting hydrodimers, (3*R*,4*R*)-3,4-diaryladipic acid esters and (3*R*,4*R*)-3,4-diarylhexane-1,6-diols were synthesized in 87−95% ee.

Introduction

Electroreductive hydrodimerization of acrylic acid derivatives is a well-known method for the synthesis of adipic acid derivatives.[1] Although this type of reaction is usually nondiastereoselective, several papers have reported that the electroreduction of cinnamic acid esters in aprotic solvents gave all-trans cyclized hydrodimers stereospecifically.[2] In this paper, we reinvestigated closely the stereoselectivity of the electroreductive hydrocoupling of cinnamates in aprotic solvents and disclosed that small amounts (<10% yield) of meso hydrodimers were also formed. We also examined more practical conditions for the electroreductive hydrocoupling using an undivided cell at a constant current, since the electrolysis was carried out using a divided cell at a constant potential in the previous reports.[2] This improvement of the reaction conditions makes this electroreductive hydrocoupling a more convenient method for the stereoselective synthesis of hydrodimers. We calculated the transition states for the hydrocoupling of methyl cinnamate to explain the high diastereoselectivity. In addition, the obtained all-trans hydrodimers can be easily transformed to *dl*-3,4-diaryladipic acids and *trans*-3,4-diarylcyclopentanones (Scheme 1). Consequently, this reaction provides useful synthetic routes to several C_2-symmetric compounds. We further investigated the stereoselective hydrocoupling of chiral cinnamates for the enantioselective synthesis of hydrodimers. Although we have already reported the electroreductive hydrocoupling of chiral 3-cinnamoyloxazolidinones, the best selectivity for the *dl*-hydrodimer was 70% ee.[3] Therefore, a more effective chiral auxiliary is desirable. We have started the investigation using readily available chiral alcohols such as (−)-menthol, (−)-*endo*-borneol, and (−)-8-phenylmenthol. These chiral auxiliaries, however, gave poor results. We finally found that [(1*R*)]-*exo*]-3-*exo*-(diphenylmethyl)borneol is a highly effective chiral auxiliary for the stereoselective hydrocoupling by electroreduction.[4]

SCHEME 1



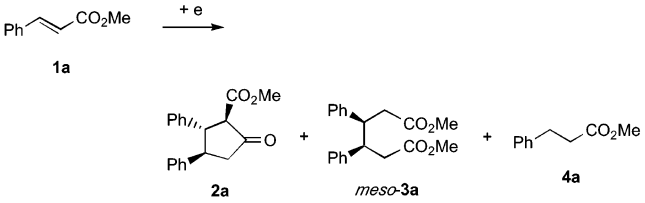
(1) (a) Baizer, M. M. *J. Electrochem. Soc.* **1964**, *111*, 215−222. (b) Baizer, M. M.; Anderson, J. D. *J. Electrochem. Soc.* **1964**, *111*, 223−226. (c) Rifi, M. R. *Technique of Electroorganic Synthesis, Part II*; Weinberg, N. L., Ed.; Wiley: New York, 1975; pp 192−215.

(2) (a) Klemm, L. H.; Olson, D. R. *J. Org. Chem.* **1973**, *58*, 3390−3394. (b) Kanetsuna, H.; Nonaka, T. *Denki Kagaku* **1981**, *49*, 526−531. (c) Smith, C. Z.; Utley, H. P. *J. Chem. Soc., Chem. Commun.* **1981**, 492−494. (d) Nishiguchi, I.; Hirashima, T. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 52−53. (e) Utley, J. H. P.; Güllü, M.; Motevalli, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1961−1970.

(3) (a) Kise, N.; Echigo, M.; Shono, T. *Tetrahedron Lett.* **1994**, *35*, 1897−1900. (b) Kise, N.; Mashiba, S.; Ueda, N. *J. Org. Chem.* **1998**, *63*, 7931−7938.

10.1021/jo026183k CCC: $22.00
Published on Web 10/26/2002

TABLE 1. Constant Current Electrolysis of Methyl Cinnamate[a]



run	cathode	solvent	electrolyte	cell[b]	% yield[c] 2a	% yield[c] *meso*-3a	% yield[c] 4a	dl/meso[d]
1	Pb	CH_3CN	Et_4NOTs	U	68	6	16	92/8
2	Cu	CH_3CN	Et_4NOTs	U	65	7	10	90/10
3	Zn	CH_3CN	Et_4NOTs	U	63	8	9	89/11
4	Sn	CH_3CN	Et_4NOTs	U	62	5	12	92/8
5	Ag	CH_3CN	Et_4NOTs	U	55	7	22	89/11
6	Pb	CH_3CN	Et_4NClO_4	U	48	6	11	89/11
7	Pb	CH_3CN	Bu_4NClO_4	U	45	3	8	94/6
8	Pb	CH_3CN	Et_4NBF_4	U	30	6	10	84/16
9	Pb	DMF	Et_4NOTs	U	56	4	29	93/7
10	Pb	DMF	$LiCl0_4$	U	32	11	30	74/26
11	Pb	THF	Bu_4NClO_4	U	51	9	17	86/16
12	Pb	THF	$LiCl0_4$	U	10	8	4	55/45
13	Pb	CH_3CN	Et_4NOTs	D	70[e]		21	92/8[f]
14	Pb	DMF	Et_4NOTs	D	47[e]		27	93/7[f]

[a] The electroreduction was carried out at 0.1 A in 0.3 M electrolyte/solvent. [b] U: undivided cell. D: divided cell. [c] Isolated yields. [d] The ratios of **2a**/*meso*-**3a** determined by ^1H NMR spectra. [e] Obtained as a mixture of stereoisomers. [f] The ratio of *di*-**3a**/*meso*-**3a** determined by ^1H NMR spectra.

Results and Discussion

Electroreductive Hydrocoupling of Alkyl Cinnamates. (a) Constant Current Electrolysis of Methyl Cinnamate, *tert*-Butyl Cinnamate, and Methyl Crotonate. Since a constant current electrolysis is a much more convenient procedure than a constant potential electrolysis, the reaction conditions for the constant current electrolysis of methyl *trans*-cinnamate (**1a**) were surveyed as summarized in Table 1. The yields of cyclized hydrodimer **2a** and uncyclized hydrodimer **3a** were affected by the choice of cathode material, solvent, and supporting electrolyte. Although Pb, Cu, Zn, Sn, and Ag were effective as a cathode material (runs 1−5), other cathode materials such as Pt, Ni, Al, and graphite carbon gave poor yields of hydrodimers. From the results of runs 1 and 6−12, the combination of acetonitrile and Et_4NOTs (run 1) seemed to be the best choice as an aprotic solvent and a supporting electrolyte. The use of $LiClO_4$ as a supporting electrolyte brought about a decrease in the yield and diastereoselectivity of hydrodimers (runs 10 and 12). It was found that the use of a divided cell was not indispensable (compare run 1 with run 13). Undoubtedly, an undivided cell is more simple and easy than a divided cell. Therefore, the best condition for the constant current electrolysis of **1a** was in Et_4NOTs/acetonitrile using a Pb cathode and an undivided cell (run 1). Figure 1 displays the correlation between yields of **2a** and simply reduced products **4a** and currents. The best yield of **2a** (68%) was given at 0.1 A of current, while the diastereoselectivity (dl/meso = 92/8) was not influenced by currents.

(4) Preliminary report: Kise, N.; Iitaka, S.; Iwasaki, K.; Tokieda, N.; Ueda, N. *Org. Lett.* **2001**, *3*, 3241−3244.

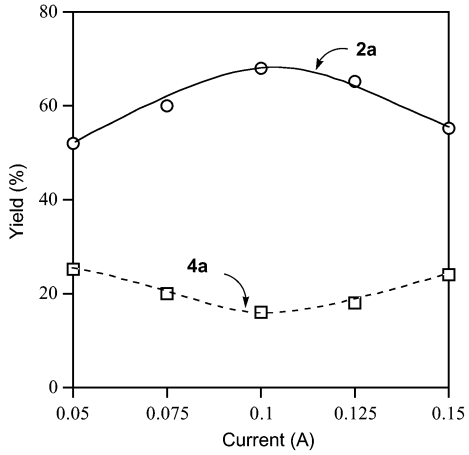
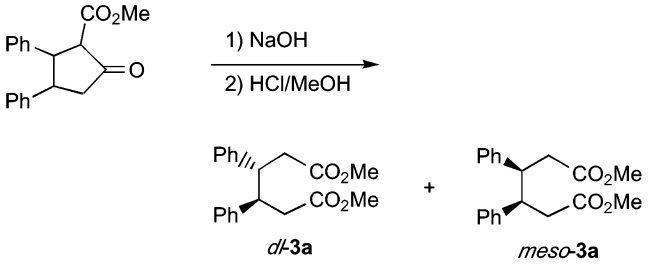
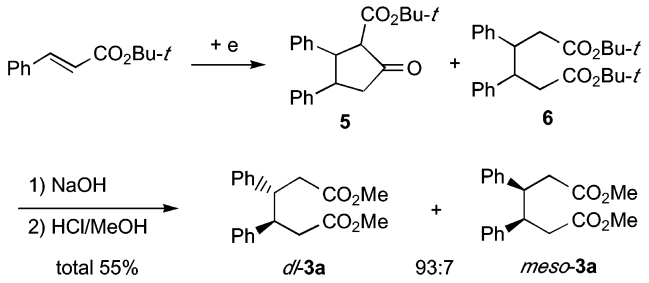


FIGURE 1. Correlation between yields of the products and currents in the electrolysis of **1a** in 0.3 M Et_4NOTs/acetonitrile.

SCHEME 2



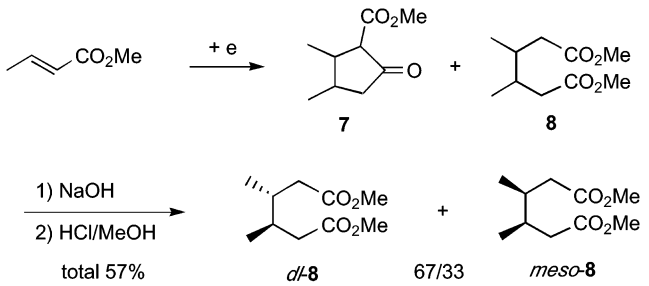
SCHEME 3



Using an undivided cell, all-trans cyclized hydrodimer **2a** was produced with a small amount (<10%) of *meso*-**3a** and these products were separated by column chromatography on alumina. On the other hand, *all-trans*-**2a** was obtained as a mixture with small amounts of its stereoisomers using a divided cell (runs 13 and 14). Because these stereoisomers of **2a** could not be separated, the mixture was converted to dimethyl 3,4-diphenyladipate (**3a**) to determine the dl/meso ratio (Scheme 2). It was thereby found that the diastereoselectivity obtained with a divided cell was virtually the same as that obtained with an undivided cell.

Electroreduction of *tert*-butyl cinnamate under the conditions of run 1 in Table 1 afforded a mixture of cyclized hydrodimer **5** and uncyclized hydrodimer **6** (Scheme 3). After the mixture was converted to **3a**, the diastereoselectivity was determined to be dl/meso = 93/7, which was almost the same as that observed in the hydrocoupling of **1a**. Although electroreduction of methyl crotonate also gave a diastereomeric mixture of cyclized and uncyclized hydrodimers **7** and **8**, the stereoselectivity

SCHEME 4



(dl/meso = 67/33) measured after conversion of the mixture to **8** was much lower than that obtained from **1a** (Scheme 4).

(b) Electroreductive Hydrocoupling of Ar-Substituted Methyl Cinnamates. Several aryl-substituted methyl cinnamates **1b**−**i** were electrochemically reduced under the conditions described above (run 1, Table 1). In all cases, all-trans cyclized hydrodimers **2b**−**i** were mainly produced (30−74%) together with small amounts (4−8%) of meso hydrodimers *meso*-**3b**−**i** (Table 2). Para- and meta-substitution did not inhibit the hydrocoupling (runs 2−8), while ortho-substitution decreased the yield and *dl*-selectivity of the hydrodimer (run 1).

Electroreduction of cumarin also gave the hydrodimer **9** in 66% yield (Scheme 5). It is noted that meso hydrodimer was obtained preferentially in this case (50% de). Since electroreductive hydrocoupling of methyl *cis*-cinnamate (*cis*-**1a**) resulted in the same stereoselectivity (dl/meso = 92/8) as obtained from that of methyl *trans*-cinnamate (**1a**), the reversal of the stereoselectivity seems to be attributed to the rigid cyclic structure of cumarin. The stereoconfiguration of each isomer of **9** was confirmed by transformation to the corresponding dimethyl adipate **3b**.

(c) Reaction Mechanism. The reaction mechanism of the hydrocoupling of **1** in aprotic solvents has been discussed in previous reports.[2a,b,5] That is, anion radicals generated by one-electron transfer to **1** couple homolitically and then the resulting hydrodimers cyclize to **2** through a Dieckmann condensation process. Using an undivided cell, the electrolyte is not basic enough for the Dieckmann condensation of *meso*-**3**. The stereospecificity in the formation of **2** has been explained by interaction between anion radicals and the cathode surface[2a,b] or by templating between two anion radicals and water.[5] Though we disclosed in this paper that the hydrocoupling of **1** is not stereospecific, the *dl*-selectivity of the hydrodimers is still high (58∼90% de). We agree that the hydrocoupling of **1** proceeds through homocoupling of the anion radicals,[6] but cannot accept the hypotheses in which the high *dl*-selectivity is elucidated by supposing unusual interactions as above. These hypotheses seem to be proposed necessarily from the common reason that *meso*-hydrodimer is more stable thermodynamically than the corresponding *dl*-hydrodimer. However, is it the case for the transition states, too? The high *dl*-selectivity may be explained without assuming such interactions between anion radicals and the cathode surface or water. We therefore carried out semiempirical calculations[7] of the transition states for the homocoupling of anion radicals derived from **1a**. The geometry optimizations using the PM3 and AM1 methods gave two transition states[8] leading to dianions of *dl*- and *meso*-hydrodimer, respectively (Figure 2). It was found that the transition states leading to *dl*-hydrodimer are more stable than those to *meso*-one. On the contrary, the transition states leading to *meso*-dimer (*meso*-**9**) are more stable than those to *dl*-isomer (*dl*-**9**) in the hydrocoupling of cumarin as shown in Figure 3. These results seem to be consistent with experimental results. Needless to say, these calculations were made by low-level methods[9] and with disregard to the solvent effect. These results nevertheless suggest the possibility that the high *dl*-selectivity in the hydrocoupling of **1** can be interpreted by considering the transition states free from the unusual interactions.

(d) Transformation of 2 to Methyl *dl*-3,4-Diaryladipates and *trans*-3,4-Diarylcyclopentanones. The obtained all-trans cyclized hydrodimers **2** were easily transformed to C_2-symmetric methyl *dl*-3,4-diaryladipates *dl*-**3** and *trans*-3,4-diarylcyclopentanones **10** by alkali hydrolysis with NaOH/H_2O−dioxane followed by esterification with HCl/MeOH and by acid hydrolysis with AcOH, respectively. The results are summarized in Table 3.

Electroreductive Hydrocoupling of Chiral Cinnamates. At first, we employed chiral cinnamates **1j**−**n** prepared from (−)-menthol, (−)-8-phenylmenthol,[10] (−)-*endo*-borneol, (−)-*exo*-borneol, and [(1*R*)-*exo*]-3-*exo*-(phenylmethyl)borneol[11] as the substrates for stereoselective hydrocoupling. As exhibited in Table 4, the electroreduction of these cinnamates gave poor results. We further investigated effective chiral auxiliaries based on a modification of readily available (1*R*)-(+)-camphor and finally found that [(1*R*)-*exo*]-3-*exo*-(diphenylmethyl)borneol (**11**)[12] is a highly effective chiral auxiliary for the electroreductive hydrocoupling of its cinnamates.

(a) Synthesis of Chiral Cinnamates from 11. Unfortunately, all attempts for direct cinnamoylation of **11** failed. Pearson has also reported that ester formation

(5) Fussing, I.; Güllü, M.; Hammerich, O.; Hussain, A.; Nielsen, M. F.; Utley, J. H. P. *J. Chem. Soc., Perkin Trans. 2* **1996**, 649−658.

(6) Hammerich, O.; Nielsen, M. F. *Acta Chem. Scand.* **1998**, *52*, 831−857.

(7) The calculations were carried out using the Gaussian 98W program: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98W*, Revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

(8) The optimized structures had only one imaginary frequency according to the vibration analysis. The imaginary frequency was verified to be consistent with the homo-coupling reaction by displaying the vibrational mode using the Gauss View program.

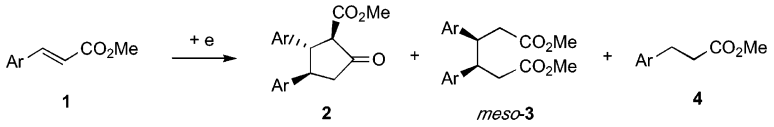
(9) Ab initio and DFT calculations for optimization of the transition states failed.

(10) Oswald, O. *Organic Synthesis*; Wiley: New York, 1993; Vol. VIII, pp 522−528.

(11) Richer, J.-C.; Rossi, A. *Can. J. Chem.* **1972**, *50*, 1376−1385.

(12) (a) Oppolzer, W.; Kurth, M.; Reichlin, D.; Chapuis, C.; Mohnhaupt, M.; Moffatt, F. *Helv. Chim. Acta* **1981**, *64*, 2802−2807. (b) Pearson, A. J.; Gontcharov, A. V. *J. Org. Chem.* **1998**, *63*, 152−162.

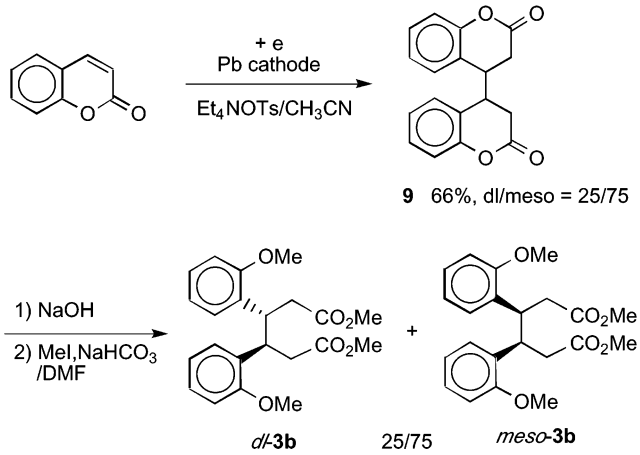
TABLE 2. Electroreductive Coupling of Aryl-Substituted Cinnamates[a]



run	Ar	1	% yield[b] 2	meso-3	4	dl/meso[c]
1	o-$MeOC_6H_4$	**1b**	**2b**, 30	*meso*-**3b** 8	**4b**, 37	79/21
2	*m*-$MeOC_6H_4$	**1c**	**2c**, 67	*meso*-**3c** 6	**4c**, 18	92/8
3	*p*-$MeOC_6H_4$	**1d**	**2d**, 67	*meso*-**3d** 6	**4d**, 16	92/8
4	*p*-FC_6H_4	**1e**	**2e**, 73	*meso*-**3e** 6	**4e**, 13	92/8
5	2-naphthyl	**1f**	**2f**, 62	*meso*-**3f** 8	**4f**, 20	89/11
6	1-furyl	**1g**	**2g**, 67	*meso*-**3g** 4	**4g**, 5	95/5
7	3,4-methylenedioxyphenyl	**1h**	**2h**, 74	*meso*-**3h** 5	**4h**, 14	94/6
8	*p*-$Me_2NC_6H_4$	**1i**	**2i**, 63	*meso*-**3i** 5	**4i**, 22	92/8

[a] The electroreduction was carried out at 0.1 A in 0.3 M Et_4NOTs/acetonitrile using an undivided cell. [b] Isolated yields. [c] The ratios of **2**/*meso*-**3** determined by ^1H NMR spectra.

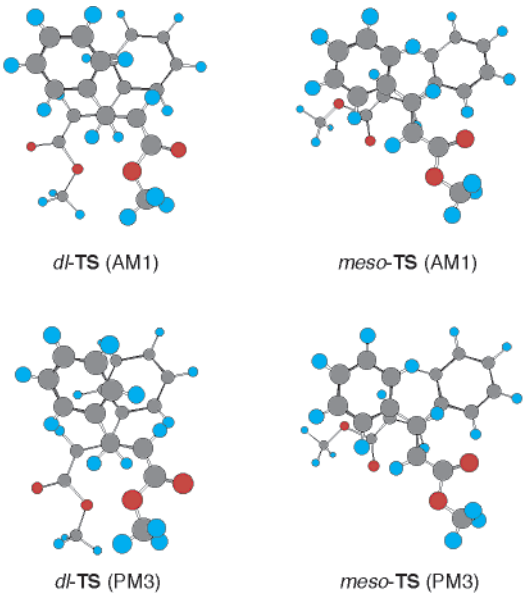
SCHEME 5



and hydrolysis of **11** was very difficult to accomplish due to steric hindrance.[12b] Consequently, the cinnamate of **11** was prepared in three steps (Scheme 6): acetylation of **11**, condensation of the acetate **12** with benzaldehyde, and dehydration of the resulting *β*-hydroxy ester **13a** (Ar = Ph) gave *trans*-cinnamate **14a** in 79% overall yield. Several aryl-substituted *trans*-cinnamates **14b**−**h** were prepared similarly (Table 5).

(b) Electroreductive Hydrocoupling of 14. Electroreduction of **14a** was carried out at a constant current of 75 mA in 0.3 M Et_4NOTs/acetonitrile using an undivided cell and a Pb cathode, according to the method described above. The noncyclized hydrodimer **15a** was obtained in 68% yield along with simply reduced product **16a** (Scheme 7). It is noted that the cyclized hydrodimer could not be detected, since Dieckmann condensation of **15a** is inhibited due to the steric hindrance as mentioned above. The diastereomeric excess (de) of the hydrodimer **15a** seemed to be more than 90%, since the ^1H NMR spectrum of **15a** showed three major (>90%) singlets for three methyl protons at 0.19, 0.67, and 1.20 ppm with three minor (<10%) singlets at 0.11, 0.65, and 1.14 ppm.

To confirm the selectivity and stereochemistry, the dimer **15a** was transformed to known dimethyl ester **3a**[3] (Scheme 8). Hydrolysis of **15a** by usual methods failed owing to the steric hindrance. Alternatively, LAH reduction of **15a** afforded diol **17a** in 88% yield together with

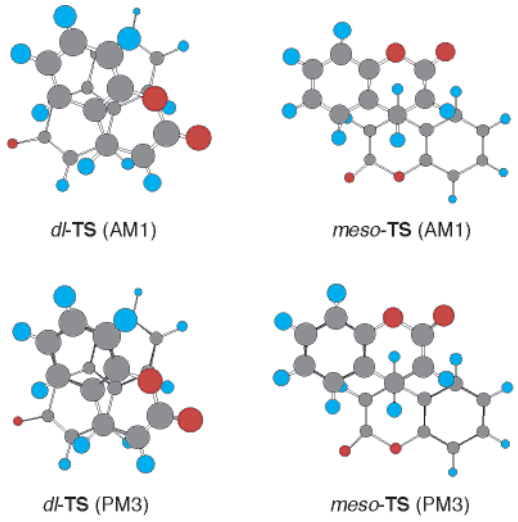


method	energy *dl*-**TS** - *meso*-**TS** (kcal/mol)
UHF/AM1	-2.97
UHF/PM3	-1.75

FIGURE 2. Optimized structures of transition states for the hydrocoupling of anion radicals from **1a**.

11 in 95% yield. Oxidation of **17a** followed by esterification in methanol gave dimethyl ester **3a**, which consisted of only the *dl*-isomer; the *meso*-isomer was not detected by ^1H NMR analysis. The absolute stereochemistry and enantiomeric excess of *dl*-**3a** were determined to be 3*R*,4*R* and 92% ee by the ^1H NMR spectrum with Eu(hfc)$_3$ and chiral HPLC analysis.[3b] This result showed that the hydrodimer **15a** was obtained as a mixture of two stereoisomers, *R*,*R*-form (major) and *S*,*S*-form (minor), in 92% de.

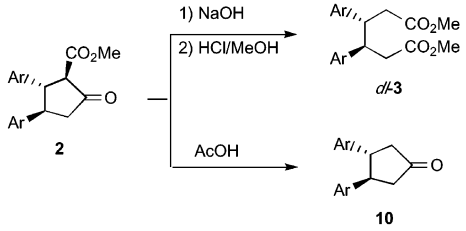
The electroreduction of aryl-substituted cinnamates **14b**−**h** and the subsequent transformation of the hydrodimers **15c**−**h** were carried out by the same procedures as above, and the results are summarized in Table 6. Although ortho-substitution considerably inhibited the electroreductive hydrocoupling (run 2), para- and meta-



method	energy *dl*-**TS** - *meso*-**TS** (kcal/mol)
UHF/AM1	+2.58
UHF/PM3	+1.80

FIGURE 3. Optimized structures of transition states for the hydrocoupling of anion radicals from cumarin.

TABLE 3. Transformation of 2 to *dl*-3 and 10



Ar	% yield[a] *dl*-**3**	**10**
Ph	*dl*-**3a**, 84	**10a**, 88
o-MeOC$_6$H$_4$	*dl*-**3b**, 62	**10b**, 82
m-MeOC$_6$H$_4$	*dl*-**3c**, 88	**10c**, 95
p-MeOC$_6$H$_4$	*dl*-**3d**, 81	**10d**, 87
p-FC$_6$H$_4$	*dl*-**3e**, 78	**10e**, 83
2-naphthyl	*dl*-**3f**, 72	**10f**, 81
1-furyl	*dl*-**3g** 88	**10g**, 95
3,4-methylenedioxyphenyl	*dl*-**3h**, 77	**10h**, 79

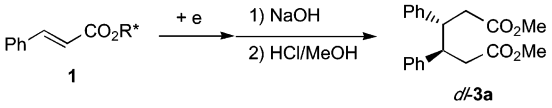
[a] Isolated yields.

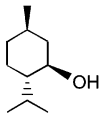
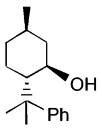
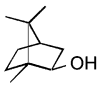
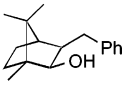
substitution (runs 3−5, 7, and 8) did not hinder it except for the 2-naphthyl group (run 6). The enantioselectivities of diesters *dl*-**3c**−**f** and the diacetates of diols **17g**,**h** were determined to be 87−95% ee by ^{1}H NMR spectra with Eu(hfc)$_3$ (Table 7). The 3*R*,4*R* configuration was confirmed for **3c**−**e** by ^{1}H NMR and chiral HPLC analyses[3b] and was also assumed for **3f** and **17g**,**h** by ^{1}H NMR correlation of **15f**−**h** with **15a**.

In addition, the enantiomer of **11** (*ent*-**11**) was prepared from readily available (−)-*endo*-borneol. Therefore, *3S*,*4S*-**3a** was also easily accessible from *ent*-**11** by the same method as above (Scheme 9).

(c) Reaction Mechanism. The reaction mechanism of the hydrocoupling of **14** can be speculated to be similar

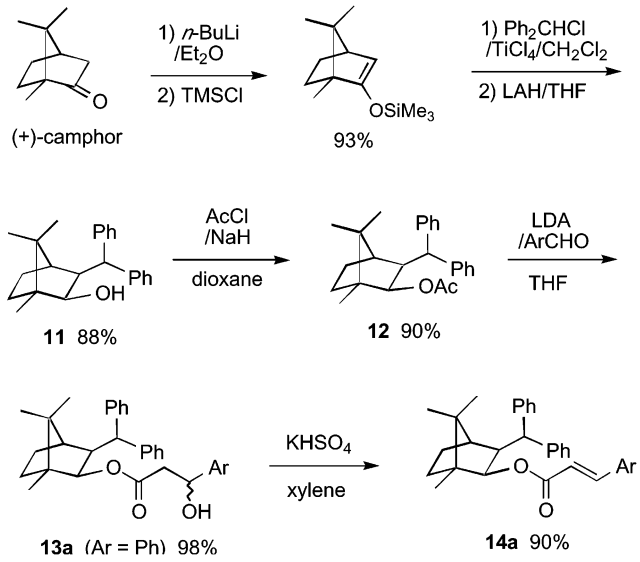
TABLE 4. Electroreductive Coupling of Chiral Cinnamate[a]



R*OH in **1**		% yield of *dl*-**3a**[b]	ee of *dl*-**3a** (config)[c]
	**1j**	68	11 (RR)
	**1k**	65	15 (SS)
	**1l**	63	5 (SS)
	**1m**	60	8 (SS)
	**1n**	55	37 (SS)

[a] The electroreduction was carried out at 0.1 A in 0.3 M Et$_4$NOTs/acetonitrile using an undivided cell. [b] Isolated yields. [c] Determined by ^{1}H NMR spectra with Eu(hfc)$_3$.

SCHEME 6



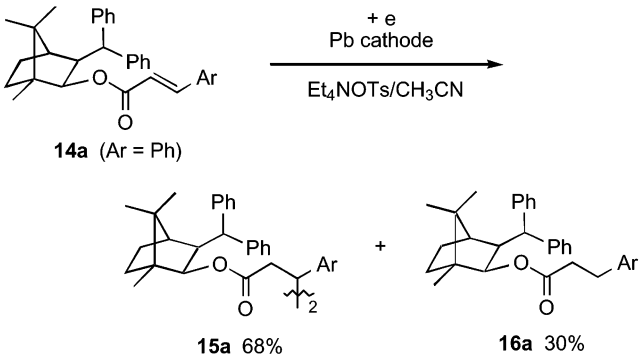
to that described above for cinnamic acid esters. An anion radical is produced by one-electron transfer to **14** and couples with another anion radical. Semiempirical (UHF/AM1) and DFT (UB3LYP 3-21G* and 6-31G*) calculations[7] of the anion radical of **14a** gave two optimized structures **A** and **B** (Figure 4).[13] From the results described above, it seems that the coupling occurs from the more stable **A** at the less hindered *Si* face (*β*-side) and gives the *R*,*R*-dimer selectively (Scheme 10).

TABLE 5. Synthesis of *trans*-Cinnamates 14 from 11

Ar	% yield of **13**[a]	% yield of **14**[a]
Ph	**13a**, 98	**14a**, 90
o-$MeOC_6H_4$	**13b**, 81	**14b**, 86
m-$MeOC_6H_4$	**13c**, 82	**14c**, 85
p-$MeOC_6H_4$	**13d**, 98	**14d**, 79
p-FC_6H_4	**13e**, 95	**14e**, 86
2-naphthyl	**13f**, 83	**14f**, 75
1-furyl	**13g**, 98	**14g**, 64
3,4-methylenedioxyphenyl	**13h**, 87	**14h**, 85

[a] Isolated yields.

SCHEME 7



SCHEME 8

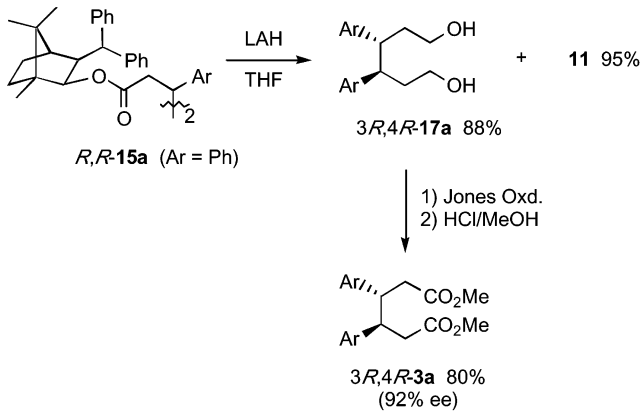


TABLE 6. Electroreduction of *trans*-Cinnamates 14

run	Ar	% yield of **15**[a]	% yield of **16**[a]
1	Ph	**15a**, 68	**16a**, 30
2	*o*-$MeOC_6H_4$	**15b**, 3	**16b**, 77
3	*m*-$MeOC_6H_4$	**15c**, 54	**16c**, 28
4	*p*-$MeOC_6H_4$	**15d**, 54	**16d**, 35
5	*p*-FC_6H_4	**15e**, 62	**16e**, 24
6	2-naphthyl	**15f**, 18	**16f**, 57
7	1-furyl	**15g**, 52	**16g**, 31
8	3,4-methylenedioxyphenyl	**15h**, 64	**16h**, 22

[a] Isolated yields.

Conclusion

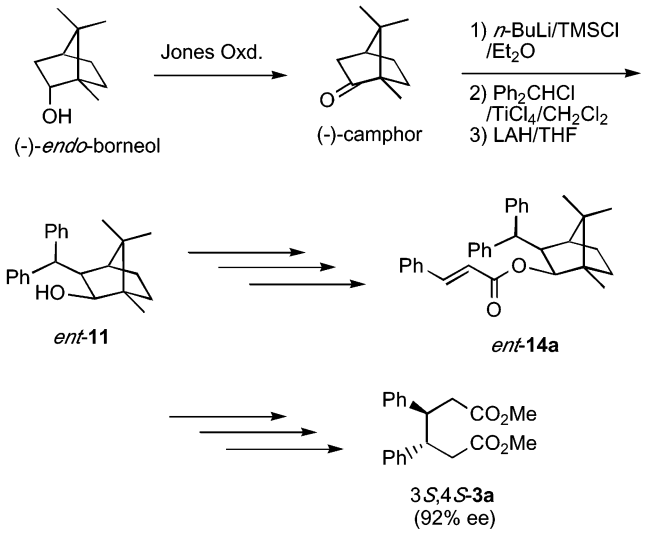
The electroreductive hydrodimerization of methyl cinnamates in aprotic solvents gave all-trans cyclized hydrodimers as the major products. However, it was found by detailed investigation that small amounts (<10% yield) of meso hydrodimers were also formed. None the less, the *dl*-selectivity in the electroreductive hydrocoupling is still high (58−90% de). The electroysis could be conveniently carried out using an undivided cell under a constant current. Several aryl-substituted methyl cinnamates were electrochemically reduced to the corresponding all-trans cyclized hydrodimers in satisfactory yields and high diastereoselectivities. The diastereoselectivity in the hydrocoupling of cinnamates was in agreement with the semiempirical calculations of the transition states for the hydrocoupling. The obtained all-trans hydrodimers were easily transformed to C_2-symmetric methyl *dl*-3,4-diaryladipates and *trans*-3,4-diarylcyclopentanones. Highly enantioselective synthesis of *R,R*-hydrodimers (87−95% ee) was accomplished using [(1*R*)-*exo*]-3-*exo*-(diphenylmethyl)borneol as a chiral auxiliary for the electroreductive hydrocoupling of chiral cinnamates.

TABLE 7. Transformation of 15 to 17 and *dl*-3

Ar	% yield of **17**[a]	% yield of *dl*-**3**[a] (% ee)[b]
Ph	**17a**, 88	*dl*-**3a**, 80 (92)
m-$MeOC_6H_4$	**17c**, 84	*dl*-**3c**, 75 (92)
p-$MeOC_6H_4$	**17d**, 90	*dl*-**3d**, 78 (92)
p-FC_6H_4	**17e**, 90	*dl*-**3e**, 80 (87)
2-naphthyl	**17f**, 68	*dl*-**3f**, 52 (95)
1-furyl	**17g**, 56 (87)[c]	
3,4-methylenedioxyphenyl	**17h**, 70 (89)[c]	

[a] Isolated yields. [b] Determined by ^1H NMR analysis with Eu(hfc)$_3$. [c] Determined from the corresponding diacetate by ^1H NMR analysis with Eu(hfc)$_3$.

SCHEME 9

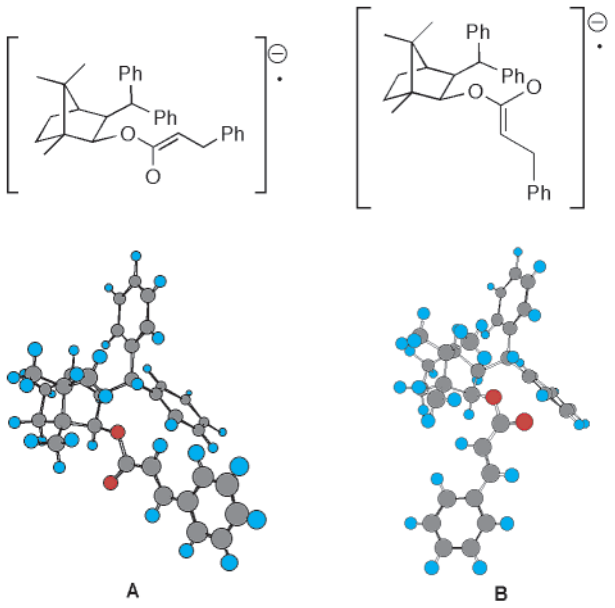


Experimental Section

General Methods. Column chromatography was performed on silica gel 60 or neutral alumina. Acetonitrile and DMF were distilled from CaH_2. THF was distilled from benzophenone ketyl. Aryl-substituted methyl cinnamates **1b**−**i** were synthesized by Knoevenagel condensation[14] and following esterification with HCl/MeOH. Chiral cinnamates **1j**−**n** were prepared from cinnamoyl chloride and chiral alcohols by the

(13) The optimized structures given by AM1 method were local minima according to the vibration analysis.

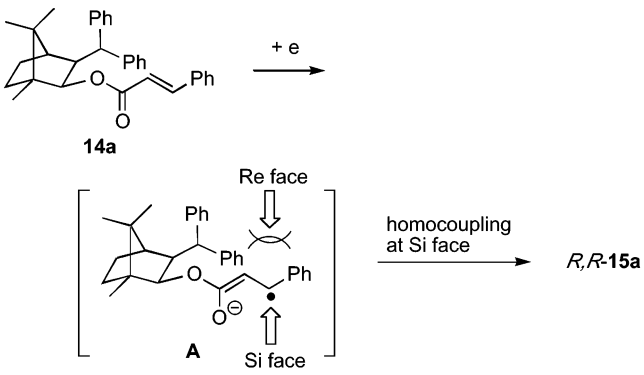
(14) Rajagopalan, S.; Raman, P. V. A. *Organic Synthesis*; Wiley: New York, 1955; Vol. III, pp 425−427.



method	energy **A**-**B** (kcal/mol)
UHF/AM1	-3.12
UB3LYP/3-21G*	-5.48
UB3LYP/6-31G*	-5.99

FIGURE 4. Optimized structures of the anion radical of **14a**.

SCHEME 10



usual methods.[2e] Authentic samples of **4b**−**i** were obtained by hydrogenation of **1b**−**i**.

Typical Procedure for Constant Current Electrolysis. A solution of methyl cinnamate (**1a**: 1.0 mmol) and Et_4NOTs (1.5 g, 5.0 mmol) in dry acetonitrile (16.5 mL) was put into a 40-mL beaker (3-cm diameter, 6-cm height) equipped with a lead cathode (5 × 5 cm^2) and a platinum anode (2 × 2 cm^2). Electricity was passed at a constant current of 100 mA at room temperature until almost all of **1a** was consumed (150 C). The mixture was poured into water (50 mL) and extracted with Et_2O. The hydrodimers (a mixture of **2a** and *meso*-**3a**) and methyl phenylpropionate (**4a**) were isolated by column chromatography on silica gel. From the mixture, *all-trans*-**2a** and *meso*-**3a** were separated by column chromatography on neutral alumina (activity III).

2a:[2d] R_f 0.4 (hexanes−ethyl acetate, 5:1). Mp 122−124 °C (lit.[2d] mp 126−127 °C). IR (KBr) 1755, 1724, 1601, 1493, 762, 748, 696 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.72 (dd, 1 H, J = 12.2, 18.9 Hz), 2.98 (dd, 1 H, J = 7.6, 18.9 Hz), 3.50 (dt, 1 H, J = 7.6, 12.2 Hz), 3.61 (d, 1 H, J = 12.2 Hz), 3.72 (s, 3 H), 3.92 (t, 1 H, J = 12.2 Hz), 7.10−7.28 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 46.86 (t), 47.48 (d), 52.56 (q), 53.37 (d), 63.64 (d), 126.99 (d), 127.21 (d), 128.48 (d), 128.53 (d), 138.58 (s), 139.46 (s), 168.40 (s), 207.84 (s).

2b: R_f 0.27 (hexanes−ethyl acetate, 5:1). Mp 154−156 °C. IR (KBr) 1751, 1726, 1603, 1585, 1495, 754 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.67 (dd, 1 H, J = 11.3, 18.4 Hz), 2.94 (ddd, 1 H, J = 1.1, 1.8, 18.4 Hz), 3.70 (s, 3 H), 3.71 (s, 3 H), 3.78 (s, 3 H), 3.86 (dd, 1 H, J = 1.1, 11.3 Hz), 4.05−4.18 (m, 1 H), 4.30 (t, 1 H, J = 11.3 Hz), 6.75−6.87 (m, 4 H), 7.06−7.22 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 39.30 (d), 45.46 (t), 47.73 (d), 52.20 (q), 55.13 (q), 55.17 (q), 61.20 (d), 110.52 (d), 110.72 (d), 120.43 (d), 127.43 (s), 127.53 (d), 127.95 (d), 128.92 (s), 129.25 (d), 157.41 (s), 157.56 (s), 169.18 (s), 209.82 (s). Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.07; H, 6.33.

2c: R_f 0.22 (hexanes−ethyl acetate, 5:1). Mp 104−106 °C. IR (KBr) 1751, 1728, 1601, 1585, 1493, 789, 745, 698 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.70 (dd, 1 H, J = 12.2, 18.9 Hz), 2.96 (dd, 1 H, J = 7.6, 12.2 Hz), 3.39−3.53 (m, 1 H), 3.59 (d, 1 H, J = 12.2 Hz), 3.70 (s, 3 H), 3.720 (s, 3 H), 3.724 (s, 3 H), 3.89 (t, 1 H, J = 12.2 Hz), 6.64−6.80 (m, 6 H), 7.13−7.21 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 46.67 (t), 47.13 (d), 52.42 (q), 53.00 (d), 54.92 (q), 63.51 (d), 112.05 (d), 112.26 (d), 113.20 (d), 113.27 (d), 119.27 (d), 119.37 (d), 129.39 (d), 129.43 (d), 140.21 (s), 141.13 (s), 159.39 (s), 159.42 (s), 168.30 (s), 207.62 (s). Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.26; H, 6.31.

2d:[2d] R_f 0.19 (hexanes−ethyl acetate, 5:1). Mp 115−117 °C (lit.[2d] mp 121−123 °C). IR (KBr) 1753, 1722, 1612, 1583, 1514, 837, 804 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.66 (dd, 1 H, J = 12.2, 18.6 Hz), 2.93 (dd, 1 H, J = 7.6, 12.2 Hz), 3.33−3.47 (m, 1 H), 3.54 (d, 1 H, J = 12.2 Hz), 3.71 (s, 3 H), 3.74 (s, 3 H), 3.75 (s, 3 H), 3.80 (t, 1 H, J = 12.2 Hz), 6.72−6.81 (m, 4 H), 7.00−7.09 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 46.76 (d), 46.83 (t), 52.39 (q), 52.84 (d), 55.00 (q), 55.04 (q), 63.72 (d), 113.79 (d), 113.84 (d), 128.08 (d), 128.12 (d), 130.59 (s), 131.47 (s), 158.26 (s), 158.40 (s), 168.50 (s), 208.06 (s).

2e: R_f 0.26 (hexanes−ethyl acetate, 5:1). Mp 145−147 °C. IR (KBr) 1757, 1726, 1603, 1510, 841, 814, 795 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.67 (dd, 1 H, J = 12.2, 18.6 Hz), 2.96 (dd, 1 H, J = 7.8 Hz, 18.6 Hz), 3.36−3.49 (m, 1 H), 3.55 (d, 1 H, J = 12.2 Hz), 3.72 (s, 3 H), 3.83 (t, 1 H, J = 12.2 Hz), 6.89−6.98 (m, 4 H), 7.05−7.13 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 45.71 (t), 46.65 (d), 52.64 (q), 52.98 (d), 63.51 (d), 115.48 (d, J_{CCF} = 21.2 Hz), 115.57 (d, J_{CCF} = 21.2 Hz), 128.62 (d, J_{CCCF} = 7.8 Hz), 128.69 (d, J_{CCCF} = 7.8 Hz), 134.03 (s, J_{CCCCF} = 3.3 Hz), 134.87 (s, J_{CCCCF} = 3.4 Hz), 161.65 (s, J_{CF} = 243.8 Hz), 161.79 (s, J_{CF} = 243.8 Hz), 168.17 (s), 207.09 (s). Anal. Calcd for $C_{19}H_{16}F_2O_3$: C, 69.08; H, 4.88. Found: C, 69.01; H, 4.96.

2f: R_f 0.28 (hexanes−ethyl acetate, 5:1). Mp 163 °C. IR (KBr) 1753, 1720, 1634, 1601, 1508, 856, 820, 745 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.88 (dd, 1 H, J = 12.2, 18.9 Hz), 3.09 (dd, 1 H, J = 7.6, 18.9 Hz), 3.71 (s, 3 H), 3.75−3.87 (m, 1 H), 3.77 (d, 1 H, J = 12.2 Hz), 4.23 (t, 1 H, J = 12.2 Hz), 7.27−7.50 (m, 6 H), 7.60−7.63 (m, 2 H), 7.65−7.88 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 46.90 (t), 47.47 (d), 52.55 (q), 53.40 (d), 63.70 (q), 124.81 (d), 124.96 (d), 125.58 (d), 125.65 (d), 125.98 (d), 126.10 (d), 126.40 (d), 127.36 (d), 127.41 (d), 127.53 (d), 128.29 (d), 128.37 (d), 132.34 (s), 132.47 (s), 133.10 (s), 135.98 (s), 136.85 (s), 168.40 (s), 207.65 (s). Anal. Calcd for $C_{27}H_{22}O_3$: C, 82.21; H, 5.62. Found: C, 82.25; H, 5.60.

2g: R_f 0.43 (hexanes−ethyl acetate, 5:1). Mp 91−92 °C. IR (KBr) 1759, 1722, 1603, 1508, 808, 733 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.76 (dd, 1 H, J = 11.6, 18.9 Hz), 2.90 (dd, 1 H, J = 7.8, 18.9 Hz), 3.61−3.74 (m, 2 H), 3.76 (s, 3 H), 4.09 (t, 1 H, J = 11.6 Hz), 6.04−6.09 (m, 2 H), 6.25−6.29 (m, 2 H), 7.32−7.35 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 38.56 (d), 43.73 (t), 44.44 (d), 52.73 (q), 60.68 (d), 106.41 (d), 107.15 (d), 110.17 (d), 110.22 (d), 141.71 (d), 141.90 (d), 151.80 (s), 152.73 (s), 167.86 (s), 206.63 (s). Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.67; H, 5.11.

2h: R_f 0.23 (hexanes−ethyl acetate, 5:1). Mp 153−155 °C. IR (KBr) 1751, 1720, 1610, 1506, 1492, 816 cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.60 (dd, 1 H, J = 12.2, 18.9 Hz), 2.92 (dd, 1 H, J = 7.6, 18.9 Hz), 3.29−3.43 (m, 1 H), 3.48 (d, 1 H, J = 12.2 Hz),

3.72 (s, 3 H), 3.76 (t, 1 H, J = 12.1 Hz), 5.905 (s, 2 H), 5.910 (s, 2 H), 6.57−6.62 (m, 2 H), 6.63−6.70 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 46.97 (t), 47.22 (d), 51.30 (q), 52.52 (q), 53.17 (d), 63.84 (d), 100.89 (t), 107.17 (d), 108.14 (d), 108.24 (d), 120.53 (d), 120.67 (d), 132.27 (d), 133.19 (d), 146.36 (s), 146.54 (s), 147.68 (s), 168.29 (s), 207.56 (s). Anal. Calcd for $C_{21}H_{18}O_7$: C, 65.96; H, 4.74. Found: C, 65.88; H, 4.62.

2i: R_f 0.17 (hexanes−ethyl acetate, 5:1). Mp 139−141 °C. IR (KBr) 1753, 1722, 1616, 1524, 819, 806 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.64 (dd, 1 H, J = 12.2, 18.9 Hz), 2.84−2.95 (m, 1 H), 2.879 (s, 6 H), 2.882 (s, 6 H), 3.31−3.44 (m, 1 H), 3.52 (d, 1 H, J = 12.2 Hz), 3.70 (s, 3 H), 3.79 (t, 1 H, J = 12.2 Hz), 6.56−6.65 (m, 4 H), 6.97−7.06 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 40.43 (q), 40.51 (q), 46.44 (d), 47.20 (t), 52.34 (q), 52.55 (d), 64.01 (d), 112.44 (d), 112.52 (d), 126.66 (s), 127.57 (s), 127.82 (d), 149.28 (s), 149.33 (s), 168.82 (s), 209.00 (s). Anal. Calcd for $C_{23}H_{28}N_2O_3$: C, 72.60; H, 7.42; N, 7.36. Found: C, 72.40; H, 7.53; N, 7.12.

5: R_f 0.34 (hexanes−ethyl acetate, 10:1). Mp 145−146 °C. IR (KBr) 1751, 1713, 762, 752, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 9 H), 2.69 (dd, 1 H, J = 12.2, 18.9 Hz), 2.95 (dd, 1 H, J = 8.1, 18.9 Hz), 3.41−3.56 (m, 2 H), 3.86 (t, 1 H, J = 12.2 Hz), 7.10−7.28 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 28.03 (q), 47.02 (t), 47.10 (d), 53.48 (d), 64.82 (d), 82.09 (s), 126.91 (d), 127.03 (d), 127.23 (d), 128.43 (d), 128.47 (d), 138.91 (s), 139.77 (s), 167.31 (s). Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.50; H, 7.21.

***dl*-6**: R_f 0.41 (hexanes−ethyl acetate, 10:1). Mp 109−110 °C. IR (KBr) 1719, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 18 H), 2.52 (dd, 2 H, J = 9.2, 14.9 Hz), 2.67 (dd, 2 H, J = 5.9, 14.9 Hz), 3.33−3.45 (m, 2 H), 6.84−6.91 (m, 4 H), 7.11−7.18 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 27.82 (q), 39.33 (t), 47.05 (d), 80.26 (s), 126.35 (d), 127.49 (d), 128.88 (d), 140.18 (s), 171.17 (s). Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.35. Found: C, 75.98; H, 8.34.

8 (dl/meso = 67/33): R_f 0.4 (hexanes−ethyl acetate, 5:1). ^{1}H NMR ($CDCl_3$) δ 0.88 (d, 4 H, J = 6.8 Hz), 0.92 (d, 2 H, J = 6.5 Hz), 1.95−2.20 (m, 4 H), 2.29−2.40 (m, 2 H), 3.67 (s, 6 H). ^{13}C NMR ($CDCl_3$) δ 14.90 (q), 16.65 (q), 34.08 (d), 34.59 (d), 38.11 (t), 39.25 (t), 51.44 (q), 173.18 (s), 173.33 (s).

***dl*-9**: R_f 0.34 (methylene chloride). Mp 262−264 °C. IR (KBr) 1773, 1763, 1613, 1590, 1487, 770, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.86−2.95 (m, 2 H), 3.05−3.13 (m, 4 H), 6.45 (dd, 2 H, J = 1.6, 7.6 Hz), 6.89 (dt, 2 H, J = 1.1, 7.6 Hz), 7.07 (dd, 2 H, J = 1.1, 8.1 Hz), 7.26 (ddd, 2 H, J = 1.6, 7.6, 8.1 Hz). ^{13}C NMR ($CDCl_3$) δ 32.97 (t), 38.68 (d), 117.85 (d), 123.39 (s), 124.86 (d), 129.55 (d), 129.71 (d), 151.25 (s), 167.79 (s). Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.45; H, 4.83.

***meso*-9**: R_f 0.57 (methylene chloride). Mp 289−291 °C. IR (KBr) 1771, 1760, 1611, 1588, 1487, 766, 752 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.67−2.76 (m, 2 H), 2.81−2.89 (m, 2 H), 2.89−2.93 (m, 2 H), 7.14 (dd, 2 H, J = 1.4, 8.1 Hz), 7.21 (dt, 2 H, J = 1.4, 7.3 Hz), 7.29 (dd, 2 H, J = 1.9, 7.3 Hz), 7.37 (ddd, 2 H, J = 1.9, 7.3, 8.1 Hz).. ^{13}C NMR ($CDCl_3$) δ 32.56 (t), 38.93 (d), 117.02 (d), 122.88 (s), 123.98 (d), 129.15 (d), 151.32 (s), 166.80 (s). Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.41; H, 4.80.

Synthesis of (*S*,*S*)-8. An authentic sample of (*S*,*S*)-**8** was synthesized from (2*R*,3*R*)-dimethylsuccinic acid according to our method[3b] for the synthesis of (*S*,*S*)-**3a**. (2*R*,3*R*)-Dimethylsuccinic acid was prepared by oxidative coupling of (4*S*)-3-propanoyl-4-isopropyl-2-oxazolidinone and subsequent hydrolysis.[15] **(*S*,*S*)-8**: R_f 0.4 (hexanes−ethyl acetate, 5:1). $[\alpha]^{25}_D$ −4.4 (*c* 2.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 0.88 (d, 6 H, J = 6.8 Hz), 1.96−2.12 (m, 2 H), 2.14 (dd, 2 H, J = 8.6, 14.6 Hz), 2.34 (dd, 2 H, J = 4.9, 14.6 Hz), 3.68 (s, 6 H). ^{13}C NMR ($CDCl_3$) δ 14.86 (q), 34.04 (d), 39.22 (t), 51.43 (q), 173.16 (s).

Typical Procedure for Transformation of 2 to 3. A mixture of **2a** (88 mg, 0.3 mmol) and NaOH (1.0 g) in dioxane (5 mL) and water (5 mL) was refluxed for 6 h. After cooling, the mixture was acidified to pH 2 with 3 M HCl and extracted with CH_2Cl_2. The crude diacid was dissolved in methanol (5 mL) containing chlorotrimethylsilane (0.7 mL). The solution was stirred for 12 h at room temperature. After removal of the solvent, dimethyl diester *dl*-**3a** was isolated by column chromatography on silica gel (78 mg, 84%).

Transformation of 9 to 3b. A mixture of **9** (88 mg, 0.3 mmol) and NaOH (1.0 g) in dioxane (5 mL) and water (5 mL) was refluxed for 6 h. After cooling, the mixture was acidified to pH 2 with 3 M HCl and extracted with CH_2Cl_2. The crude diacid was dissolved in DMF (3 mL) containing MeI (0.6 mL) and $NaHCO_3$ (0.18 g). The suspension was stirred for 6 h at room temperature, diluted with water (20 mL), and extracted with Et_2O. After removal of the solvent, dimethyl diester **3b** (93 mg, 80%) was isolated by column chromatography on silica gel.

Typical Procedure for Transformation of 2 to 10. A solution of **2a** (88 mg, 0.3 mmol) in AcOH (5 mL) was refluxed for 12 h. After removal of the solvent, the product **10a** (62 mg, 88%) was isolated by column chromatography on silica gel.

Synthesis of [(1*R*)-*exo*]-3-*exo*-(Diphenylmethyl)borneol (11). To a solution of trimethyl silyl enol ether of (+)-camphor (4.5 g, 20 mmol) and chlorodiphenylmethane (4.05 g, 20 mmol) in dry CH_2Cl_2 (50 mL) was added $TiCl_4$ (2.2 mL, 20 mmol) at −50 °C. After being stirred for 1 h, the mixture was diluted with 1 M HCl (100 mL) and extracted with CH_2Cl_2. The obtained crude ketone (6.8 g) was subjected to subsequent LAH reduction without further purification. Recrystallization of the crude product from hexane/ethyl acetate (5/1) gave a pure sample of (1*R*)-3-*exo*-(diphenylmethyl)camphor: Mp 110 °C. $[\alpha]^{25}_D$ 93.9 (*c* 1.37, $CHCl_3$). IR (KBr) 1730, 1480, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.87 (s, 6 H), 1.04 (s, 3 H), 1.42−1.69 (m, 3 H), 1.86 (d, 1 H, J = 4.1 Hz), 1.93−2.04 (m, 1 H), 2.91 (d, 1 H, J = 12.1 Hz), 4.09 (d, 1 H, J = 12.1 Hz), 7.11−7.32 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 9.21 (q), 20.13 (q), 21.64 (q), 29.12 (t), 29.33 (t), 45.69 (s), 46.82 (d), 53.87 (d), 57.15 (d), 57.96 (s), 125.85 (d), 126.01 (d), 127.57 (d), 127.68 (d), 127.84 (d), 128.38 (d), 143.66 (s), 143.98 (s). Anal. Calcd for $C_{23}H_{26}O$: C, 86.75; H, 8.23. Found: C, 86.71; H, 8.25.

To a solution of crude ketone (6.8 g) in dry THF (50 mL) was added LAH (0.76 g, 20 mmol) at 0 °C. After being stirred for 6 h at room temperature, the mixture was quenched with H_2O (1.5 mL) and 3 M NaOH (1.6 mL) and extracted with CH_2Cl_2. Recrystallization of the crude product from hexane/ethyl acetate (10/1) gave **11** (5.6 g, 88%).

11: Mp 127−128 °C. $[\alpha]^{25}_D$ −95.6 (*c* 1.49, $CHCl_3$). IR (KBr) 3580, 1480, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.75 (s, 3 H), 0.90 (s, 3 H), 0.98−1.07 (m, 1 H), 1.10−1.20 (m, 1H), 1.23 (d, 1 H, J = 3.2 Hz), 1.34 (s, 3 H), 1.40 (d, 1 H, J = 3.8 Hz), 1.45−1.54 (m, 1 H), 1.57−1.70 (m, 1 H), 2.70 (dd, 1 H, J = 7.5, 13.0 Hz), 3.83 (dd, 1 H, J = 3.2, 7.5 Hz), 4.35 (d, 1 H, J = 13.0 Hz), 7.09−7.17 (m, 2 H), 7.21−7.30 (m, 6 H), 740−7.45 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 11.83 (q), 21.77 (q), 22.21 (q), 30.39 (t), 33.67 (t), 47.13 (s), 48.11 (d), 50.02 (s), 52.13 (d), 55.02 (d), 81.31 (d), 125.86 (d), 126.21 (d), 127.43 (d), 128.17 (d), 128.46 (d), 128.81 (d), 145.65 (s). Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 86.15; H, 8.78.

***ent*-11**: Mp 126−127 °C. $[\alpha]^{25}_D$ 94.0 (*c* 1.05, $CHCl_3$).

Acetylation of 11. A 1.0-g (25 mmol) sample of NaH (60% in oil) was washed with dry hexane three times and suspended with dry dioxane (10 mL). To the suspension was added **11** (3.2 g, 10 mmol) and freshly distilled acetyl chloride (0.90 mL, 12.5 mmol). After the usual workup, recrystallization of the crude product from hexane/ethyl acetate (20/1) gave **12** (3.26 g, 90%).

12: R_f 0.50 (hexanes−ethyl acetate, 10:1). Mp 111−112 °C. $[\alpha]^{25}_D$ −115 (*c* 1.0, $CHCl_3$). IR (KBr) 1740, 1597, 1495, 746, 704, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.76 (s, 6 H), 0.99−1.11 (m, 1 H), 1.31 (s, 3 H), 1.32−1.41 (m, 1 H), 1.44 (d, 1 H, J = 3.8 Hz), 1.45 (s, 3 H), 1.48−1.72 (m, 2 H), 2.81 (dd, 1 H, J = 8.4, 13.0 Hz), 4.28 (d, 1 H, J = 13.0 Hz), 5.15 (d, 1 H, J = 8.4 Hz),

(15) Kise, N.; Ueda, T.; Kumada, K.; Terao, Y.; Ueda, N. *J. Org. Chem.* **2000**, *65*, 464−468.

7.05−7.30 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 11.49 (q), 20.26 (q), 21.55 (q), 22.00 (q), 29.74 (t), 30.22 (t), 32.93 (t), 47.50 (s), 47.80 (d), 50.31 (s), 52.24 (d), 53.05 (d), 80.40 (d), 125.71 (d), 125.87 (d), 126.98 (d), 127.97 (d), 128.32 (d), 128.43 (d), 144.48 (s), 145.42 (s), 169.64 (s). Anal. Calcd for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.57; H, 8.34.

***ent*-12**: Mp 109−111 °C. $[\alpha]^{25}_D$ 113 (*c* 1.15, $CHCl_3$).

Typical Procedure for Condensation of 12 with Aryl Aldehydes. To a solution of LDA (10 mmol) in THF−hexane (15 mL) was added a solution of **12** (3.26 g, 9.0 mmol) in THF (5 mL) at −70 °C. After the mixture was stirred for 15 min, benzaldehyde (1.05 mL, 10 mmol) was added. The mixture was stirred for 1 h at −70 °C, diluted with 1 M HCl (30 mL), and then extracted with Et_2O. The product **13a** was isolated as a 1:1 mixture of two diastereomers by column chromatography on silica gel (4.13 g, 98%).

Typical Procedure for Dehydration of 13. A solution of **13a** (4.13 g, 8.8 mmol) and $KHSO_4$ (0.1 g) in xylene (20 mL) was refluxed for 1.5 h. The mixture was diluted with water and extracted with Et_2O. The product **14a** was isolated by column chromatography on silica gel (3.57 g, 90%).

14a: R_f 0.70 (hexanes−ethyl acetate, 5:1). Mp 54−56 °C. $[\alpha]^{25}_D$ 12.7 (*c* 1.2, $CHCl_3$). IR (KBr) 1713, 1640, 1599, 1578, 1495, 766, 743, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.80 (s, 3 H), 1.07−1.16 (m, 1 H), 1.36−1.46 (m, 1 H), 1.39 (s, 3 H), 1.51 (d, 1 H, J = 4.1 Hz), 1.53−1.76 (m, 2 H), 2.88 (dd, 1 H, J = 8.1, 13.0 Hz), 4.34 (d, 1 H, J = 13.0 Hz), 5.28 (d, 1 H, J = 8.1 Hz), 5.96 (d, 1 H, J = 15.9 Hz), 6.91−6.98 (m, 1 H), 7.06−7.17 (m, 3 H), 7.22−7.32 (m, 7 H), 7.34−7.45 (m, 5 H). ^{13}C NMR ($CDCl_3$) δ 11.50 (q), 21.62 (q), 21.92 (q), 30.13 (t), 32.84 (t), 47.44 (s), 47.78 (d), 50.48 (s), 52.39 (d), 53.30 (d), 80.36 (d), 118.01 (d), 125.58 (d), 125.76 (d), 126.91 (d), 127.58 (d), 127.85 (d), 128.07 (d), 128.32 (d), 128.48 (d), 129.62 (d), 134.34 (s), 143.13 (d), 144.11 (s), 145.29 (s), 165.25 (s). Anal. Calcd for $C_{32}H_{34}O_2$: C, 85.29; H, 7.61. Found: C, 85.16; H, 7.64.

***ent*-14a**: Mp 54−56 °C. $[\alpha]^{25}_D$ −12.5 (*c* 0.95, $CHCl_3$).

14b: R_f 0.51 (hexanes−ethyl acetate, 5:1). Mp 52−53 °C. $[\alpha]^{20}_D$ 25.8 (*c* 1.05, $CHCl_3$). IR (KBr) 1709, 1489, 745, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.80 (s, 3 H), 1.06−1.16 (m, 1 H), 1.40 (s, 3 H), 1.35−1.46 (m, 1 H), 1.50 (d, 1 H, J = 3.5 Hz), 1.54−1.75 (m, 2 H), 2.88 (dd, 1 H, J = 8.1, 13.2 Hz), 3.85 (s, 3 H), 4.36 (d, 1 H, J = 13.2 Hz), 5.26 (d, 1 H, J = 8.1 Hz), 6.02 (d, 1 H, J = 16.2 Hz), 6.85−6.98 (m, 3 H), 7.07−7.15 (m, 3H), 7.20−7.42 (m, 8 H), 7.68 (d, 1 H, J = 16.2 Hz). ^{13}C NMR ($CDCl_3$) δ 11.55 (q), 21.57 (q), 21.96 (q), 30.18 (t), 32.82 (t), 47.46 (s), 47.82 (d), 50.54 (s), 52.44 (d), 53.39 (d), 55.33 (q), 80.13 (d), 110.91 (d), 118.27 (d), 120.38 (d), 123.42 (s), 125.61 (d), 125.75 (d), 126.99 (d), 127.88 (d), 127.98(d), 128.07 (d), 128.33 (d), 130.90 (d), 138.49 (d), 144.14 (s), 145.40 (s), 157.75 (s), 165.69 (s). Anal. Calcd for $C_{33}H_{36}O_3$: C, 82.46; H, 7.55. Found: C, 82.42; H, 7.60.

14c: R_f 0.57 (hexanes−ethyl acetate, 5:1). Mp 39−41 °C. $[\alpha]^{20}_D$ 9.4 (*c* 1.15, $CHCl_3$). IR (KBr) 1711, 1493, 745, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.80 (s, 3 H), 1.05−1.15 (m, 1 H), 1.40 (s, 3 H), 1.34−1.46 (m, 1 H), 1.51 (d, 1 H, J = 3.8 Hz), 1.54−1.75 (m, 2 H), 2.88 (dd, 1 H, J = 8.4, 13.0 Hz), 3.80 (s, 3 H), 4.34 (d, 1 H, J = 13.0 Hz), 5.28 (d, 1 H, J = 8.4 Hz), 5.63 (d, 1 H, J = 15.9 Hz), 6.86−7.03 (m, 4 H), 7.06−7.15 (m, 3 H), 7.19−7.30 (m, 8 H). ^{13}C NMR ($CDCl_3$) δ 11.49 (q), 21.63 (q), 21.90 (q), 30.12 (t), 32.85 (t), 47.45 (s), 47.80 (d), 50.50 (s), 52.40 (d), 53.30 (d), 55.06 (q), 80.42 (d), 112.77 (d), 115.35 (d), 118.31 (d), 120.28 (d), 125.59 (d), 125.77 (d), 126.92 (d), 127.85 (d), 128.09 (d), 128.33 (d), 129.49 (d), 135.74 (s), 143.06 (d), 144.14 (s), 145.30 (s), 159.54 (s), 165.23 (s). Anal. Calcd for $C_{33}H_{36}O_3$: C, 82.46; H, 7.55. Found: C, 82.35; H, 7.63.

14d: R_f 0.50 (hexanes−ethyl acetate, 5:1). Mp 66−68 °C. $[\alpha]^{22}_D$ 33.0 (*c* 0.97, $CHCl_3$). IR (KBr) 1709, 1605, 1512, 1493, 764, 745, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.80 (s, 3 H), 1.06−1.16 (m, 1 H), 1.39 (s, 3 H), 1.35−1.46 (m, 1 H), 1.50 (d, 1 H, J = 4.1 Hz), 1.57−1.74 (m, 3 H), 2.88 (dd, 1 H, J = 8.1, 13.0 Hz), 3.84 (s, 3 H), 4.34 (d, 1 H, J = 13.0 Hz), 5.27 (d, 1 H, J = 8.1 Hz), 5.84 (d, 1 H, J = 15.7 Hz), 6.86−6.98 (m, 3 H), 7.07−7.18 (m, 3 H), 7.20−7.30 (m, 6 H), 7.35−7.41 (m, 3 H). ^{13}C NMR ($CDCl_3$) δ 11.41 (q), 21.56 (q), 21.86 (q), 30.10 (t), 32.79 (t), 47.43 (s), 47.79 (d), 50.49 (s), 52.39 (d), 53.33 (d), 55.16 (q), 80.24 (d), 114.09 (d), 115.68 (d), 125.69 (d), 125.87 (d), 127.06 (d), 127.23 (s), 128.00 (d), 128.18 (d), 128.45 (d), 129.34 (d), 142.97 (d), 144.32 (s), 145.53 (s), 160.99 (s), 165.87 (s). Anal. Calcd for $C_{33}H_{36}O_3$: C, 82.46; H, 7.55. Found: C, 82.32; H, 7.51.

14e: R_f 0.7 (hexanes−ethyl acetate, 5:1). Mp 59−61 °C. $[\alpha]^{22}_D$ 4.23 (*c* 0.96, $CHCl_3$). IR (KBr) 1713, 1508, 1493, 745, 702 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.80 (s, 3 H), 1.06−1.16 (m, 1 H), 1.39 (s, 3 H), 1.35−1.47 (m, 1 H), 1.51 (d, 1 H, J = 3.5 Hz), 1.55−1.76 (m, 2 H), 2.88 (dd, 1 H, J = 8.1, 13.0 Hz), 4.34 (d, 1 H, J = 13.0 Hz), 5.28 (d, 1 H, J = 8.1 Hz), 5.88 (d, 1 H, J = 16.2 Hz), 6.91−6.98 (m, 1 H), 7.01−7.20 (m, 6 H), 7.22−7.30 (m, 6 H), 7.36−7.44 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 11.45 (q), 21.59 (q), 21.88 (q), 30.13 (t), 32.84 (t), 47.51 (s), 47.82 (d), 50.50 (s), 52.44 (d), 53.34 (d), 80.59 (d), 115.82 (d, J_{CCF} = 21.7 Hz), 117.90 (d), 125.76 (d), 125.97 (d), 127.08 (d), 128.04 (d), 128.25 (d), 128.53 (d), 129.62 (d, J_{CCCF} = 8.4 Hz), 130.79 (s, J_{CCCCF} = 3.4 Hz), 142.03 (s), 144.36 (d), 145.50 (s), 163.61 (s, J_{CF} = 249.2 Hz), 165.50 (s). Anal. Calcd for $C_{32}H_{33}FO_2$: C, 82.02; H, 7.10. Found: C, 82.07; H, 7.12.

14f: R_f 0.60 (hexanes−ethyl acetate, 5:1). Mp 52−54 °C. $[\alpha]^{20}_D$ 25.1 (*c* 1.09, $CHCl_3$). IR (KBr) 1711, 1493, 745, 702 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.80 (s, 3 H), 0.83 (s, 3 H), 1.07−1.17 (m, 1 H), 1.43 (s, 3 H), 1.36−1.48 (m, 1 H), 1.53 (d, 1 H, J = 3.5 Hz), 1.56−1.76 (m, 2 H), 2.90 (dd, 1 H, J = 8.1, 13.0 Hz), 4.38 (d, 1 H, J = 13.0 Hz), 5.31 (d, 1 H, J = 8.1 Hz), 6.07 (d, 1 H, J = 16.2 Hz), 6.88−6.94 (m, 1 H), 7.06−7.18 (m, 3 H), 7.22−7.30 (m, 6 H), 7.39−7.58 (m, 4 H), 7.78−7.88 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 11.56 (q), 21.71 (q), 21.94 (q), 30.16 (t), 32.90 (t), 47.50 (s), 47.85 (d), 50.55 (s), 52.46 (d), 53.37 (d), 80.46 (d), 118.20 (d), 123.32 (d), 125.63 (d), 125.80 (d), 126.37 (d), 126.79 (d), 126.97 (d), 127.49 (d), 127.90 (d), 128.08 (d), 128.13 (d), 128.28 (d), 128.37 (d), 129.18 (d), 131.88 (s), 133.04 (d), 133.81 (d), 143.19 (d), 144.19 (d), 145.36 (s), 165.39 (s). Anal. Calcd for $C_{36}H_{36}O_2$: C, 86.36; H, 7.25. Found: C, 86.20; H, 7.38.

14g: R_f 0.63 (hexanes−ethyl acetate, 5:1). Mp 45−47 °C. $[\alpha]^{23}_D$ 21.0 (*c* 0.96, $CHCl_3$). IR (KBr) 1707, 1639, 1479, 745, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.78 (s, 6 H), 1.06−1.16 (m, 1 H), 1.37 (s, 3H), 1.33−1.44 (m, 1 H), 1.49 (d, 1 H, J = 3.8 Hz), 1.54−1.76 (m, 1 H), 2.87 (dd, 1 H, J = 8.1, 13.0 Hz), 4.32 (d, 1 H, J = 13.0 Hz), 5.24 (d, 1 H, J = 8.1 Hz), 5.90 (d, 1 H, J = 15.9 Hz), 6.43 (dd, 1 H, J = 1.6. 3.2 Hz), 6.51 (d, 1 H, J = 3.2 Hz), 6.93−7.18 (m, 5 H), 7.22−7.29 (m, 6 H), 7.44 (d, 1 H, J = 1.6 Hz). ^{13}C NMR ($CDCl_3$) d 11.53 (q), 21.65 (q), 21.97 (q), 30.22 (t), 32.86 (t), 47.51 (s), 47.84 (d), 50.57 (s), 52.41 (d), 53.36 (d), 80.37 (d), 111.98 (d), 113.87 (d), 115.80 (d), 125.65 (d), 125.81 (d), 127.01 (d), 127.91 (d), 128.17 (d), 128.39 (d), 129.75 (d), 144.15 (d), 145.36 (s), 150.78 (s), 165.41 (s). Anal. Calcd for $C_{30}H_{32}O_3$: C, 81.78; H, 7.32. Found: C, 81.87; H, 7.35.

14h: R_f 0.67 (hexanes−ethyl acetate, 5:1). Mp 55−56 °C. $[\alpha]^{21}_D$ 32.0 (*c* 1.02, $CHCl_3$). IR (KBr) 1709, 1491, 745, 702, 617 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.80 (s, 3 H), 1.06−1.16 (m, 1 H), 1.38 (s, 3 H), 1.34−1.46 (m, 1 H), 1.50 (d, 1 H, J = 3.5 Hz), 1.54−1.75 (m, 2 H), 2.87 (dd, 1 H, J = 8.1, 13.0 Hz), 4.33 (d, 1 H, J = 13.0 Hz), 5.26 (d, 1 H, J = 8.1 Hz), 5.79 (d, 1 H, J = 15.9 Hz), 5.98 (s, 2 H), 6.78 (d, 1 H, J = 7.8 Hz), 6.87−6.98 (m, 3 H), 7.06−7.22 (m, 4 H), 7.22−7.28 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 11.45 (q), 21.58 (q), 21.87 (q), 30.08 (t), 32.79 (t), 47.40 (s), 47.74 (d), 50.43 (s), 52.33 (d), 53.26 (d), 80.20 (d), 101.19 (t), 106.09 (d), 108.14 (d), 115.93 (d), 123.72 (d), 125.50 (d), 125.71 (d), 126.87 (d), 127.81 (d), 128.00 (d), 128.27 (d), 128.73 (s), 142.81 (d), 144.12 (s), 145.30 (s), 147.93 (s), 148.97 (s), 165.41 (s). Anal. Calcd for $C_{33}H_{34}O_4$: C, 80.13; H, 6.93. Found: C, 80.11; H, 6.94.

Typical Procedure for Electroreduction of 14. A solution of **14a** (0.45 g, 1.0 mmol) and Et_4NOTs (1.5 g, 5.0 mmol) in dry acetonitrile (16.5 mL) was put into a 40-mL beaker (3-cm diameter, 6-cm height) equipped with a lead cathode (5 ×

5 cm^2) and a platinum anode (2 × 2 cm^2). Electricity was passed at a constant current of 75 mA at room temperature (300 C). The mixture was poured into water (50 mL) and extracted with Et_2O. The products **15a** (68%) and **16a** (30%) were isolated by column chromatography on silica gel.

15a: R_f 0.50 (hexanes−ethyl acetate, 5:1). $[\alpha]^{25}_D$ −64.1 (*c* 0.94, $CHCl_3$). IR (KBr) 1734, 1599, 1495, 764, 745, 700, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.67 (s, 12 H), 0.92−1.04 (m, 2 H), 1.20 (s, 6 H), 1.36 (d, 2 H, J = 3.8 Hz), 1.38−1.47 (m, 2 H), 1.50−1.68 (m, 6 H), 1.88 (dd, 2 H, J = 10.3, 15.4 Hz), 2.71 (dd, 2 H, J = 8.4, 13.0 Hz), 3.19−3.30 (m, 2 H), 4.08 (d, 2 H, J = 13.0 Hz), 5.03 (d, 2 H, J = 8.4 Hz), 6.83−6.88 (m, 4 H), 6.94−7.16 (m, 16 H), 7.16−7.30 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 10.79 (q), 21.72 (q), 21.85 (q), 30.13 (t), 33.02 (t), 34.44 (t), 45.87 (d), 47.35 (s), 47.67 (d), 50.24 (s), 52.14 (d), 52.98 (d), 80.49 (d), 125.50 (d), 125.78 (d), 126.62 (d), 126.78 (d), 127.78 (d), 127.84 (d), 128.28 (d), 128.35 (d), 128.58 (d), 139.91 (s), 144.25 (s), 145.36 (s), 170.56 (s). Anal. Calcd for $C_{64}H_{70}O_4$: C, 85.10; H, 7.81. Found: C, 85.23; H, 7.80.

***ent*-15a**: $[\alpha]^{25}_D$ 63.7 (*c* 1.22, $CHCl_3$).

15c: R_f 0.32 (hexanes−ethyl acetate, 5:1). Mp 88−90 °C. $[\alpha]^{20}_D$ −74.7 (*c* 1.05, $CHCl_3$). IR (KBr) 1734, 1493, 746, 702, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.18 (s, 6 H), 0.67 (s, 6 H), 0.92−1.04 (m, 2 H), 1.20 (s, 6 H), 1.25−1.30 (m, 2 H), 1.30−1.48 (m, 4 H), 1.50−1.67 (m, 4 H), 1.90 (dd, 2 H, J = 10.5, 15.4 Hz), 2.71 (dd, 2 H, J = 8.1, 12.7 Hz), 3.24−3.34 (m, 2 H), 3.76 (s, 6 H), 4.05 (d, 2 H, J = 12.7 Hz), 5.02 (d, 2 H, J = 8.1 Hz), 6.47−6.50 (m, 2 H), 6.58 (d, 2 H, J = 8.1 Hz), 6.79 (dd, 2 H, J = 1.9, 8.1 Hz), 6.89−6.94 (m, 4 H), 6.97−7.05 (m, 6 H), 7.06−7.30 (m, 12 H). ^{13}C NMR ($CDCl_3$) δ 10.62 (q), 21.60 (q), 21.80 (q), 30.05 (t), 32.91 (t), 33.80 (t), 46.10 (d), 47.27 (s), 47.53 (d), 50.12 (s), 52.05 (d), 52.88 (d), 54.96 (q), 80.25 (d), 112.07 (d), 114.21 (d), 120.83 (d), 125.45 (d), 125.70 (d), 126.66 (d), 127.73 (d), 128.17 (d), 128.27 (d), 128.81 (d), 141.74 (s), 144.06 (s), 145.24 (s), 159.18 (s), 170.38 (s). Anal. Calcd for $C_{66}H_{74}O_6$: C, 82.29; H, 7.74. Found: C, 82.15; H, 7.78.

15d: R_f 0.40 (hexanes−ethyl acetate, 5:1). Mp 106−108 °C. $[\alpha]^{20}_D$ −45.6 (*c* 0.97, $CHCl_3$). IR (KBr) 1734, 1512, 1495, 745, 702, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.28 (s, 6 H), 0.69 (s, 6 H), 0.94−1.05 (m, 2 H), 1.23 (s, 6 H), 1.18−1.32 (m, 1 H), 1.38 (d, 2 H, J = 3.5 Hz), 1.40−1.85 (m, 8 H), 2.73 (dd, 2 H, J = 8.1, 13.0 Hz), 3.07−3.18 (m, 2 H), 3.75 (s, 6 H), 4.13 (d, 4 H, J = 13.0 Hz), 5.06 (d, 2 H, J = 8.1 Hz), 6.70 (d, 4 H, J = 8.7 Hz), 6.78 (d, 4 H, J = 8.7 Hz), 6.98−7.26 (m, 20 H). ^{13}C NMR ($CDCl_3$) δ 10.93 (q), 21.78 (q), 21.88 (q), 30.14 (t), 32.99 (t), 35.13 (t), 44.92 (d), 47.35 (s), 47.64 (d), 50.24 (s), 52.13 (d), 52.92 (d), 55.18 (q), 80.44 (d), 113.10 (d), 125.51 (d), 125.78 (d), 126.79 (d), 127.85 (d), 128.27 (d), 128.36 (d), 129.57 (d), 131.73 (s), 144.36 (s), 145.36 (s), 158.20 (s), 170.76 (s). Anal. Calcd for $C_{66}H_{74}O_6$: C, 82.29; H, 7.74. Found: C, 82.22; H, 7.83.

15e: R_f 0.60 (hexanes−ethyl acetate, 5:1). Mp 108−110 °C. $[\alpha]^{21}_D$ −31.9 (*c* 1.25, $CHCl_3$). IR (KBr) 1734, 1510, 1495, 745, 702 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.35 (s, 6 H), 0.72 (s, 6 H), 0.95−1.16 (m, 2 H), 1.22 (s, 6 H), 1.23−1.35 (m, 2 H), 1.40 (d, 2 H, J = 3.5 Hz), 1.45−1.76 (m, 8 H), 2.74 (dd, 2 H, J = 8.4, 13.0 Hz), 2.98−3.08 (m, 2 H), 4.19 (d, 2 H, J = 13.0 Hz), 5.10 (d, 2 H, J = 8.4 Hz), 6.56−6.63 (m, 4 H), 6.85−6.92 (m, 4 H), 7.07−7.27 (m, 20 H). ^{13}C NMR ($CDCl_3$) δ 11.03 (q), 21.78 (q), 21.80 (q), 30.04 (t), 32.97 (t), 35.95 (t), 44.39 (d), 47.32 (s), 47.61 (d), 50.24 (s), 52.09 (d), 52.84 (d), 80.80 (d), 114.39 (d, J_{CCF} = 21.1 Hz), 125.47 (d), 125.82 (d), 126.78 (d), 127.84 (d), 128.27 (d), 128.37 (d), 130.10 (d, J_{CCCF} = 7.8 Hz), 134.82 (s, J_{CCCCF} = 2.8 Hz), 144.48 (s), 145.24 (s), 161.47 (s, J_{CF} = 243.3 Hz), 170.31 (s). Anal. Calcd for $C_{64}H_{68}F_2O_4$: C, 81.84; H, 7.30. Found: C, 81.92; H, 7.34.

15f: R_f 0.53 (hexanes−ethyl acetate, 5:1). Mp 120−122 °C. $[\alpha]^{20}_D$ −41.0 (*c* 0.92, $CHCl_3$). IR (KBr) 1734, 1494, 743, 702, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.08 (s, 6 H), 0.62 (s, 6 H), 0.84−1.02 (m, 2 H), 1.21 (s, 6 H), 1.10−1.63 (m, 8 H), 1.70 (dd, 2 H, J = 4.6, 15.4 Hz), 2.01 (dd, 2 H, J = 10.3, 15.4 Hz), 2.66 (dd, 2 H, J = 8.1, 13.0 Hz), 3.51−3.61 (m, 2 H), 3.93 (d, 2 H, J = 13.0 Hz), 5.01 (d, 2H, J = 8.1 Hz), 6.72−6.90 (m, 8 H), 6.98−7.22 (m, 14 H), 7.39 (br s, 2 H), 7.40−7.52 (m, 4 H), 7.74−7.86 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 10.77 (q), 21.79 (q), 21.84 (q), 30.10 (t), 32.91 (t), 33.79 (t), 46.16 (d), 47.33 (s), 47.60 (d), 50.19 (s), 51.96 (d), 52.82 (d), 80.41 (d), 125.41 (d), 125.63 (d), 125.74 (d), 125.99 (d), 126.56 (d), 126.94 (d), 127.12 (d), 127.35 (d), 127.53 (d), 127.61 (d), 127.80 (d), 128.08 (d), 128.31 (d), 132.38 (s), 133.10 (s), 137.61 (s), 143.98 (s), 145.30 (s), 170.59 (s). Anal. Calcd for $C_{72}H_{74}O_4$: C, 86.19; H, 7.43. Found: C, 86.03; H, 7.40.

15g: R_f 0.67 (hexanes−ethyl acetate, 5:1). $[\alpha]^{20}_D$ −72.7 (*c* 1.05, $CHCl_3$). IR (KBr) 1734, 1495, 743, 702, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.45 (s, 6 H), 0.72 (s, 6 H), 0.97−1.08 (m, 2 H), 1.21 (s, 6 H), 1.23−1.73 (m, 10 H), 1.80 (dd, 2 H, J = 9.5, 15.9 Hz), 2.76 (dd, 2 H, J = 8.1, 13.0 Hz), 3.40−3.50 (m, 2 H), 4.16 (d, 2 H, J = 13.0 Hz), 5.11 (d, 2 H, J = 8.1 Hz), 5.81 (d, 2 H, J = 3.2 Hz), 6.29 (dd, 2 H, J = 1.9, 3.2 Hz), 7.00−7.32 (m, 20 H), 7.37 (*d*, 2 H, J = 1.9 Hz). ^{13}C NMR ($CDCl_3$) δ 11.09 (q), 21.51 (q), 21.89 (q), 30.14 (t), 32.97 (t), 33.88 (t), 38.10 (d), 47.36 (s), 47.64 (d), 50.30 (s), 52.15 (d), 53.01 (d), 80.59 (d), 106.75 (d), 110.09 (d), 125.63 (d), 125.81 (d), 126.79 (d), 127.86 (d), 128.27 (d), 128.37 (d), 141.05 (d), 144.27 (s), 145.27 (s), 153.99 (s), 170.60 (s). Anal. Calcd for $C_{60}H_{66}O_6$: C, 81.60; H, 7.53. Found: C, 81.45; H, 7.38.

15h: R_f 0.40 (hexanes−ethyl acetate, 5:1). Mp 88−90 °C. $[\alpha]^{22}_D$ −58.7 (*c* 1.03, $CHCl_3$). IR (KBr) 1732, 1489, 745, 704, 617 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.33 (s, 6 H), 0.70 (s, 6 H), 0.92−1.06 (m, 2 H), 1.23 (s, 6 H), 1.25−1.80 (m, 12 H), 2.73 (dd, 2 H, J = 8.4, 13.2 Hz), 3.03−3.12 (m, 2 H), 4.12 (d, 2 H, J = 13.2 Hz), 5.07 (d, 2 H, J = 8.4 Hz), 5.90 (dd, 4 H, J = 1.4, 7.8 Hz), 6.26−6.34 (m, 4 H), 6.70 (d, 2 H, J = 8.1 Hz), 7.00−7.30 (m, 20 H). ^{13}C NMR ($CDCl_3$) δ 10.97 (q), 21.72 (q), 21.88 (q), 30.13 (t), 32.97 (t), 34.94 (t), 45.60 (d), 47.36 (s), 47.62 (d), 50.26 (s), 52.12 (d), 52.93 (d), 80.55 (d), 100.73 (t), 107.61 (d), 108.99 (d), 121.65 (d), 125.61 (d), 125.82 (d), 126.76 (d), 127.86 (d), 128.14 (d), 128.38 (d), 133.64 (s), 144.33 (s), 145.34 (s), 146.09 (s), 147.11 (s), 170.60 (s). Anal. Calcd for $C_{66}H_{70}O_8$: C, 79.97; H, 7.12. Found: C, 80.11; H, 7.17.

Typical Procedure for LAH Reduction of 15. To a solution of **15a** (0.31 g, 0.34 mmol) in dry THF (5 mL) was added LAH (53 mg, 1.4 mmol) at 0 °C. After being stirred for 12 h at room temperature, the mixture was quenched with H_2O (0.1 mL) and 3 M NaOH (0.1 mL), and extracted with CH_2Cl_2. The products **17a** (81 mg, 88%) and **11** (95% recovered) were isolated by column chromatography on silica gel.

17a: R_f 0.20 (hexanes−ethyl acetate, 1:1). Mp 96−97 °C. $[\alpha]^{25}_D$ 7.0 (*c* 0.91, $CHCl_3$). IR (KBr) 3298, 1495, 756, 698, 611 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.43 (br s, 2 H), 1.80−1.93 (m, 2 H), 2.12−2.24 (m, 2 H), 2.98−3.07 (m, 2 H), 3.34−3.46 (m, 2 H), 3.48−3.59 (m, 2 H), 6.87−6.92 (m, 4 H), 7.05−7.17 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 35.94 (t), 47.63 (d), 60.86 (t), 125.94 (d), 127.58 (d), 128.75 (d), 147.76 (s). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.90; H, 8.22.

***ent*-17a**: Mp 95−97 °C. $[\alpha]^{25}_D$ −6.8 (*c* 1.0, $CHCl_3$).

17c: R_f 0.16 (hexanes−ethyl acetate, 1:2). $[\alpha]^{20}_D$ −11.1 (*c* 3.7, $CHCl_3$). IR (KBr) 3288, 1593, 785, 704 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.59 (br s, 2 H), 1.75−1.90 (m, 2 H), 2.06−2.20 (m, 2 H), 2.92−3.04 (m, 2 H), 3.32−3.45 (m, 2 H), 3.47−3.57 (m, 2 H), 3.67 (s, 6 H), 6.41−6.44 (m, 2 H), 6.52−6.56 (m, 2 H), 6.61−6.66 (m, 2 H), 7.06 (t, 2 H, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ 35.90 (t), 47.78 (d), 55.04 (q), 61.04 (t), 114.45 (d), 114.60 (d), 121.35 (d), 128.55 (d), 143.40 (s), 158.89 (s). Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.72; H, 7.96.

17d: R_f 0.38 (hexanes−ethyl acetate, 1:2). Mp 58−59 °C. $[\alpha]^{24}_D$ 33.8 (*c* 2.9, $CHCl_3$). IR (KBr) 3331, 1612, 1512, 799, 603 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.60−1.87 (m, 4 H), 2.00−2.13 (m, 2 H), 2.88−3.00 (m, 2 H), 3.30−3.44 (m, 2 H), 3.44−3.55 (m, 2 H), 3.73 (s, 6 H), 6.66−6.72 (m, 4 H), 6.75−6.81 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 36.10 (t), 46.76 (d), 55.08 (q), 61.03 (t), 113.10 (d), 129.87 (d), 133.64 (s), 157.81 (s). Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.67; H, 7.98.

17e: R_f 0.13 (hexanes−ethyl acetate, 1:2). Mp 75−77 °C. $[\alpha]^{20}_D$ 9.2 (*c* 3.4, $CHCl_3$). IR (KBr) 3265, 1509, 725, 700, 600 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.27 (br s, 2 H), 1.72−1.87 (m, 2 H), 2.10−2.23 (m, 2 H), 2.96−3.06 (m, 2 H), 3.32−3.43 (m, 2 H), 3.48−3.59 (m, 2 H), 6.79−6.88 (m, 8 H). ^{13}C NMR ($CDCl_3$) δ 36.22 (t), 46.94 (d), 60.70 (t), 114.56 (d, J_{CCF} = 20.6 Hz), 129.99 (d, J_{CCCF} = 7.8 Hz), 137.14 (s, J_{CCCCF} = 3.3 Hz), 161.12 (s, J_{CF} = 242.2 Hz). Anal. Calcd for $C_{18}H_{20}F_2O_2$: C, 70.57; H, 6.58. Found: C, 70.67; H, 6.65.

17f: R_f 0.30 (hexanes−ethyl acetate, 1:2). $[\alpha]^{20}_D$ 102 (*c* 1.1, $CHCl_3$). IR (KBr) 3362, 1506, 738, 623 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.50 (br s, 2 H), 1.88−2.05 (m, 2 H), 2.18−2.32 (m, 2 H), 3.25−3.43 (m, 4 H), 3.45−3.57 (m, 2 H), 7.04 (dd, 2 H, *J* = 1.9, 8.4 Hz), 7.33−7.41 (m, 6 H), 7.56−7.73 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 36.00 (t), 47.73 (d), 61.02 (t), 125.18 (d), 125.63 (d), 127.05 (d), 127.24 (d), 127.35 (d), 127.44 (d), 127.67 (d), 132.12 (s), 132.98 (s), 139.09 (s). Anal. Calcd for $C_{26}H_{26}O_2$: C, 84.29; H, 7.07. Found: C, 84.20; H, 7.01.

17g: R_f 0.30 (hexanes−ethyl acetate, 1:2). $[\alpha]^{20}_D$ 9.2 (*c* 1.3, $CHCl_3$). IR (KBr) 3354, 1504, 731, 600 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.83−2.00 (m, 6 H), 3.19−3.29 (m, 2 H), 3.35−3.53 (m, 2 H), 3.55−3.70 (m, 2 H), 5.90 (d, 2 H, *J* = 3.2 Hz), 6.20−6.25 (m, 2 H), 7.27 (d, 2 H, *J* = 1.6 Hz). ^{13}C NMR ($CDCl_3$) δ 33.92 (t), 39.31 (d), 60.64 (t), 106.39 (d), 109.81 (d), 140.82 (d), 155.72 (s). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.01; H, 7.13.

Diacetate of 17g (87% ee): R_f 0.25 (hexanes−ethyl acetate, 5:1). $[\alpha]^{20}_D$ 21.7 (*c* 2.0, $CHCl_3$). IR (KBr) 1738, 1589, 1506, 737 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.93−2.06 (m, 4 H), 2.00 (s, 6 H), 3.12−3.22 (m, 2 H), 2.77−2.88 (m, 2 H), 3.72−3.84 (m, 2 H), 3.86−3.97 (m, 2 H), 5.87−5.91 (m, 4 H), 6.33 (dd, 2 H, *J* = 1.6, 8.1 Hz), 6.39 (d, 2 H, *J* = 1.6 Hz), 6.60 (d, 2 H, *J* = 8.1 Hz). ^{13}C NMR ($CDCl_3$) δ 20.97 (q), 32.42 (t), 47.90 (d), 62.94 (t), 100.70 (t), 107.66 (d), 108.64 (d), 121.93 (d), 134.52 (s), 145.80 (s), 147.14 (s), 170.74 (s). Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.58; H, 6.56.

17h: R_f 0.20 (hexanes−ethyl acetate, 1:2). $[\alpha]^{22}_D$ −25.8 (*c* 1.3, $CHCl_3$). IR (KBr) 3362, 1609, 1504, 756, 667 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.48 (br s, 2 H), 1.65−1.85 (m, 2 H), 2.02−2.20 (m, 2 H), 2.82−2.95 (m, 2 H), 3.32−3.45 (m, 2 H), 3.45−3.58 (m, 2 H), 5.87 (dd, 2 H, *J* = 1.6, 3.5 Hz), 6.37 (dd, 2 H, *J* = 1.6, 7.8 Hz), 6.43 (d, 1 H, *J* = 1.6 Hz), 6.60 (d, 2 H, *J* = 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ 36.25 (t), 47.35 (d), 60.69 (t), 100.53 (t), 107.46 (d), 108.64 (d), 121.82 (d), 135.70, (s), 145.38 (s), 146.89 (s). Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 66.97; H, 6.22.

Diacetate of 17h (89% ee): R_f 0.42 (hexanes−ethyl acetate, 2:1). $[\alpha]^{20}_D$ 14.9 (*c* 1.4, $CHCl_3$). IR (KBr) 1738, 1603, 1495, 768, 702 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.73−1.90 (m, 2 H), 2.01 (s, 6 H), 2.08−2.21 (m, 2 H), 2.77−2.88 (m, 2 H), 3.72−3.84 (m, 2 H), 3.86−3.97 (m, 2 H), 5.87−5.91 (m, 4 H), 6.33 (dd, 2 H, *J* = 1.6, 8.1 Hz), 6.39 (d, 2 H, *J* = 1.6 Hz), 6.60 (d, 2 H, *J* = 8.1 Hz). ^{13}C NMR ($CDCl_3$) δ 20.97 (q), 32.42 (t), 47.90 (d), 62.94 (t), 100.70 (t), 107.66 (d), 108.64 (d), 121.93 (d), 134.52 (s), 145.80 (s), 147.14 (s), 170.74 (s). Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92. Found: C, 65.18; H, 5.92.

Typical Procedure for Transformation of 17 to 3. To a solution of **17a** (81 mg, 0.30 mmol) in acetone (2 mL) was added Jones reagent (2.5 M, 0.4 mL) at 0 °C. After being stirred for 30 min at this temperature, the mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2. The crude diacid was dissolved in saturated HCl−MeOH (5 mL), and the solution was stirred for 12 h at room temperature. After removal of the solvent, the product (3*R*,4*R*)-**3a** (78 mg, 80%) was isolated by column chromatography on silica gel. The enantiomeric excess of (3*R*,4*R*)-**3a** was measured by ^1H NMR analysis with Eu(hfc)$_3$ (92% ee), chiral HPLC analysis (92% ee), or its specific rotation (93% ee).

(3*R*,4*R*)-**3a** (92% ee): R_f 0.63 (hexanes−ethyl acetate, 2:1). $[\alpha]^{20}_D$ 16.5 (*c* 2.85, $CHCl_3$) (lit.[3] $[\alpha]^{20}_D$ 17.4 (*c* 2.85, $CHCl_3$)) for (3*R*,4*R*)-**3a** (98% ee).

(3*S*,4*S*)-**3a** (92% ee): $[\alpha]^{20}_D$ −16.2 (*c* 1.25, $CHCl_3$).

(3*R*,4*R*)-**3c** (92% ee): R_f 0.56 (hexanes−ethyl acetate, 2:1). $[\alpha]^{20}_D$ 2.0 (*c* 1.6, $CHCl_3$).

(3*R*,4*R*)-**3d** (92% ee): R_f 0.58 (hexanes−ethyl acetate, 2:1). $[\alpha]^{24}_D$ 49.0 (*c* 2.1, $CHCl_3$).

(3*R*,4*R*)-**3e** (87% ee): R_f 0.61 (hexanes−ethyl acetate, 2:1). $[\alpha]^{20}_D$ 10.4 (*c* 2.1, $CHCl_3$).

(3*R*,4*R*)-**3f** (95% ee): R_f 0.37 (hexanes−ethyl acetate, 2:1). $[\alpha]^{20}_D$ 90.2 (*c* 1.0, $CHCl_3$).

Acknowledgment. One of the authors (N.K.) is grateful to the Electric Technology Research Foundation of Chugoku for financial support.

Supporting Information Available: Characterization data for **1k**, **1m**, **1n**, *meso*-**3**, *dl*-**3**, **10**, **13**, and **16** and the results of calculations shown in Figures 2−4. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026183K