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Diastereoselective *dl*-Hydrocoupling of Benzalacetones by Electroreduction

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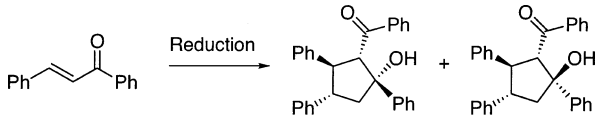
Electroreduction of benzalacetones with an undivided cell in Et_4NOTs/acetonitrile gave cyclized *dl*-hydrodimers as mixtures of two diastereomers. The hydrodimerization proceeded stereoselectively to afford linear *dl*-hydrodimers, and the following cyclization led to two thermodynamically stable diasteromers of cyclopentanols.

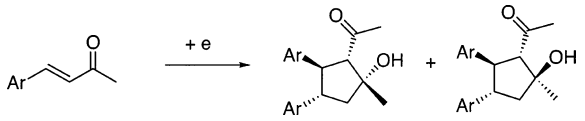
Introduction

The electroreduction of cinnamic acid esters in aprotic media is well-known to give all-trans cyclized hydrodimers stereoselectively.[1] In addition, it has been reported that the reductive coupling of chalcones by chemical[2] and electrochemical methods[3] also produced cyclic *dl*-hydrodimers, cyclopentanols, stereoselectively (Scheme 1). On the other hand, the reductive dimerization of benzalacetones with Yb metal did not give cyclopentanols but cyclohexanones,[2a] and that with $TiCl_4$-Zn led to linear hydrodimers and pinacols.[2c] The reduction of aliphatic α,β-unsaturated ketones with Yb-TMSBr afforded linear hydrodimers albeit nonstereoselectively.[4] To the best of our knowledge, the reductive hydrodimerization of benzalacetones to furnish cyclopentanols stereoselectively has not so far been realized. We report herein that the electroreduction of benzalacetones using an undivided cell gave cyclic hydrodimers with extremely high *dl*-stereoselectivity (Scheme 2). We calculated the transition states for the hydrocoupling of benzalacetones with semiempirical methods to elucidate the high *dl*-selectivity. The product cyclopentanols were formed as mixtures of two diastereomers. Their stereostructures were confirmed by X-ray crystallographic analysis. We furthermore disclosed that the cyclization step from the linear *dl*-hydrodimers to cyclopentanols is governed by thermodynamic control.

SCHEME 1



SCHEME 2



Results and Discussion

The reaction conditions for the constant current electrolysis of benzalacetone **1** at 125 mA were surveyed and the results are summarized in Table 1. The electroreduction of **1** was carried out under the conditions by which the best result was obtained in the hydrocoupling of methyl cinnamate,[1g] that is, in 0.3 M Et_4NOTs/acetonitrile with a Pb cathode and an undivided cell (run 1). In this case also, the best yield of the cyclic hydrodimer **2** (80%) was attained under the same conditions. Of eight possible diastereomers, **2** was obtained as a mixture of two stereoisomers **2a** (major) and **2b** (minor). In addition to **2**, small amounts of saturated ketone (<10%) and linear hydrodimer (<3%) were detected. The electroreductive hydrodimerization of **1** was little affected by currents in the range of 50 to 150 mA (at 50 mA,: 72% yield of **2**; at 75 mA, 75%; at 100mA, 78%; at 150 mA, 70%). As a cathode material, Au, Ag, and Cu afforded comparative results to Pb (runs 2−4). Other cathode materials Zn, Sn, and Pt except for Al produced **2**, although the yields somewhat decreased (runs 5−8). Acetonitrile and Et_4NOTs were the best choice of a solvent and a supporting electrolyte, respectively (compare run 1 with runs 9−16). By employing $LiClO_4$ as a supporting electrolyte, a complex mixture was formed and the hydrodimers were scarcely produced (run 17). It should be noted that the use of an undivided cell was required for the reductive hydrocoupling of **1**. When the

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(2) (a) Takaki, K.; Beppu, F.; Tanaka, S.; Tsubaki, Y.; Jintoku, T.; Fujiwara, Y. *Chem. Commun.* **1990**, 516−517. (b) Takaki, K.; Nagase, K.; Beppu, F.; Fujiwara, Y. *Chem. Lett.* **1991**, 1665−1668. (c) Zhou, L.; Shi, D.; Gao, Y.; Shen, W.; Dai, G.; Chen, W. *Tetrahedron Lett.* **1997**, *38*, 2729−2732.

(3) Utley, J. H. P.; Smith, C. Z.; Motevalli, M. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1053−1057.

(4) Taniguchi, Y.; Nakahashi, M.; Kuno, T.; Tsuno, M.; Makioka, Y.; Takaki, K.; Fujiwara, Y. *Tetrahedron Lett.* **1994**, *35*, 4111−4114.

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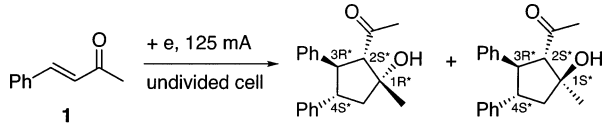
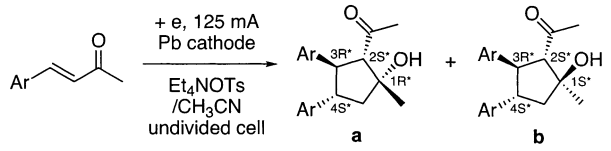
TABLE 1. Electroreduction of Benzalacetone (1)



run	cathode	solvent[a]	% yield of **2**[b] (**2a** + **2b**)
1	Pb	Et_4NOTs/CH_3CN	80 (46 + 34)
2	Au	Et_4NOTs/CH_3CN	72 (42 + 30)
3	Ag	Et_4NOTs/CH_3CN	73 (42 + 31)
4	Cu	Et_4NOTs/CH_3CN	74 (40 + 34)
5	Zn	Et_4NOTs/CH_3CN	58 (34 + 24)
6	Sn	Et_4NOTs/CH_3CN	51 (30 + 21)
7	Pt	Et_4NOTs/CH_3CN	45 (26 + 19)
8	Al	Et_4NOTs/CH_3CN	trace
9	Pb	Et_4NOTs/DMF	39 (20 + 19)
10	Pb	Bu_4NClO_4/DMF	30 (17 + 13)
11	Pb	Bu_4NClO_4/THF	36 (24 + 12)
12	Pb	Et_4NBF_4/CH_3CN	53 (31 + 22)
13	Pb	Et_4NClO_4/CH_3CN	47 (26 + 21)
14	Pb	Bu_4NBF_4/CH_3CN	43 (28 + 15)
15	Pb	Bu_4NClO_4/CH_3CN	42 (25 + 17)
16	Pb	Bu_4NPF_6/CH_3CN	45 (28 + 17)
17	Pb	$LiClO_4/CH_3CN$	trace
18[c]	Pb	Et_4NOTs/CH_3CN	trace
19[d]	Pb	Et_4NOTs/CH_3CN	45 (27 + 18)
20[e]	Pb	Et_4NOTs/CH_3CN	trace

[a] 0.3 M electrolyte in solvent. [b] Isolated yields. [c] With a divided cell. [d] With a Zn anode. [e] With a Mg anode.

TABLE 2. Electroreduction of Benzalacetones



run	Ar	compd no.	% yield[a] (**a** + **b**)
1	*p*-$MeOC_6H_4$	**3**	74 (44 + 30)
2	*p*-FC_6H_4	**4**	80 (48 + 32)
3	3,4-$(MeO)_2C_6H_3$	**5**	47 (27 + 20)
4	α-naphthyl	**6**	64 (38 + 26)
5	*β*-naphthyl	**7**	70 (40 + 30)
6	1-furyl	**8**	74 (41 + 33)

[a] Isolated yields.

reduction of **1** was carried out with a divided cell, a complex mixture was given probably due to the condensation of the starting **1** (run 18). In addition, the use of Zn or Mg as an anode significantly lowered the yield of **2** (runs 19 and 20). In particular, only complex mixture was obtained with a Mg anode.

The hydrodimerization of other benzalacetones was effected by electroreduction under the same conditions as run 1 in Table 1, and the results are depicted in Table 2. In all cases, the corresponding cyclic hydrodimers were obtained in moderate to good yields as mixtures of two diastereomers.

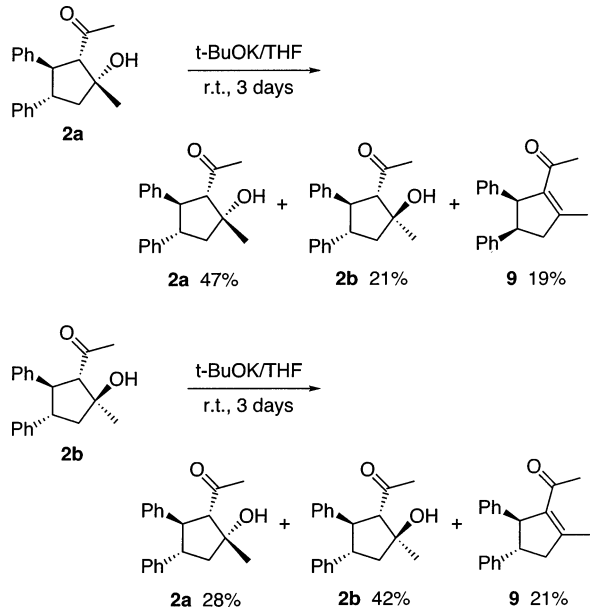
The stereostructure of **2a** (major) was determined to be 1*R**,2*S**,3*R**,4*S** by X-ray crystallography, but **2b** (minor) did not form an analyzable single crystal. Thus, we tried an X-ray crystallographic analysis of the other cyclic hydrodimers shown in Table 2. Fortunately, α-naphthyl derivatives **6a** and **6b** afforded single crystals and their structures were undoubtedly confirmed to be

TABLE 3. ^{1}H NMR Chemical Shifts[a] of 2−8

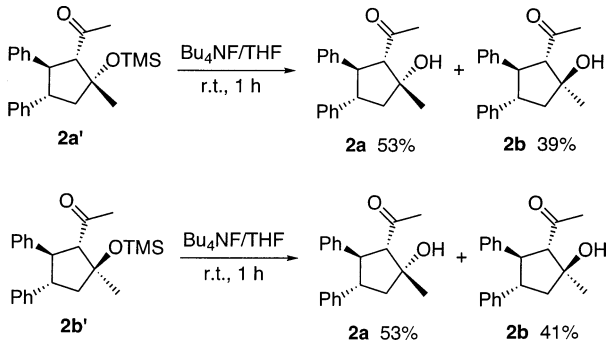
a	1-CH_3	CH_3CO	**b**	1-CH_3	CH_3CO
2a	1.51	1.85	**2b**	1.42	2.15
3a	1.57	1.76	**3b**	1.39	2.14
4a	1.50	1.88	**4b**	1.41	2.16
5a	1.50	1.89	**5b**	1.41	2.17
6a	1.62	1.71	**6b**	1.47	2.12
7a	1.58	1.83	**7b**	1.49	2.17
8a	1.47	2.02	**8b**	1.34	2.24

[a] The chemical shifts (*δ*) of methyl protons (singlet).

SCHEME 3



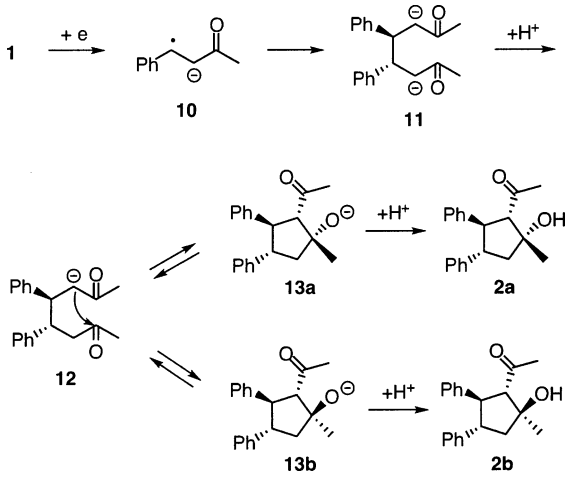
SCHEME 4



1*R**,2*S**,3*R**,4*S** and 1*S**,2*S**,3*R**,4*S**, respectively. The same stereostructures for the other cyclic hydrodimers were assumed by ^{1}H NMR correlation with **6** (Table 3). These results disclose that both isomers of the cyclic hydrodimers come from linear *dl*-hydrodimers, namely, the *dl*-hydrodimers were formed predominantly.

Interestingly, each isomer of **2** isomerized slowly by treatment with *t*-BuOK in THF at room temperature to give a mixture of **2a** and **2b** together with dehydrated product **9** after 3 days (Scheme 3). Moreover, treatment of trimethylsilyl ether of each isomer of **2** (**2a′** and **2b′**) with Bu_4NF in THF at room temperature reached equilibrium within 1 h (Scheme 4). These observations imply that the cyclization from linear *dl*-hydrodimer to the cyclic hydrodimers is subject to thermodynamic control.

SCHEME 5



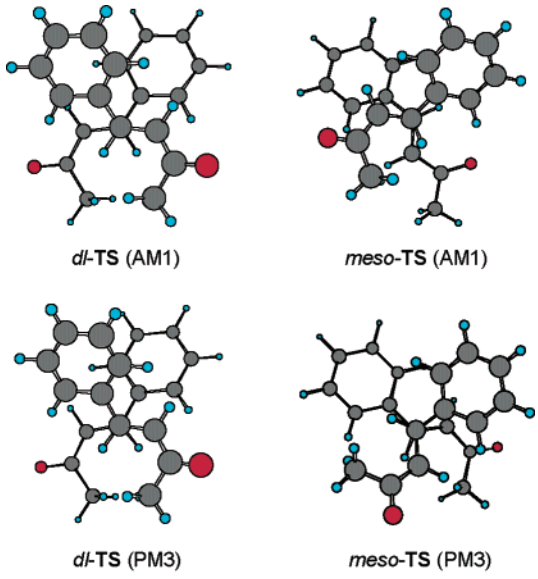
Reaction Mechanism. The reaction mechanism of the electroreductive hydrocoupling of **1** can be presumed to be as illustrated in Scheme 5. Anion radicals **10** generated from **1** by one-electron transfer couple each other to give a dianion of linear *dl*-hydrodimer (**11**). Since it is likely that the high *dl*-selectivity is determined kinetically,[1e,g,3] we calculated the transition states for the homocoupling of **10** by semiempirical methods (Figure 1).[5,6] The results of calculations suggest that the transition states leading to *dl*-hydrodimer are more stable than those to *meso*-hydrodimer and, therefore, well explain the high *dl*-selectivity despite low-level methods.[7] Next, the dienolate anion **11** was protonated to monoenolate anion **12** and then the enolate anion **12** immediately cyclized to *O*-anion **13** via an intramolecular aldol condensation process. From the experimental results as shown in Schemes 3 and 4, the formation of the stereoisomers of **2** seems to be determined by equilibrium between stereoisomers of the *O*-anion **13** in the cyclization step from **12**. Thus, preliminary calculations for the four possible stereoisomers of **13** were performed by the RHF/AM1 method to evaluate their thermodynamic stability (Figure 2).[5,8] These computational results are in accordance with the experimental observations. Thus, **13a** is slightly more stable than **13b**, and these isomers **13a** and **13b** are much more stable than the other isomers **13c** and **13d**.

(5) The calculations were carried out with use of 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.

(6) It was confirmed that the optimized structures had only one imaginary frequency according to the vibration analysis. The imaginary frequency was verified to be consistent with the intermolecular homocoupling by displaying the vibrational mode with the Gauss View program.

(7) Ab initio and DFT calculations for optimization of the transition states have not been successful so far.

(8) It was confirmed that the optimized structures had no imaginary frequency according to the vibration analysis. The relative free energies shown in Figure 4 were based on the values after thermal correction.



method	energy *dl*-**TS** - *meso*-**TS** (kcal/mol)
UHF/AM1	-4.08
UHF/PM3	-3.73

FIGURE 1. Optimized structures of transition states for the hydrocoupling of anion radicals **10** to **11**.

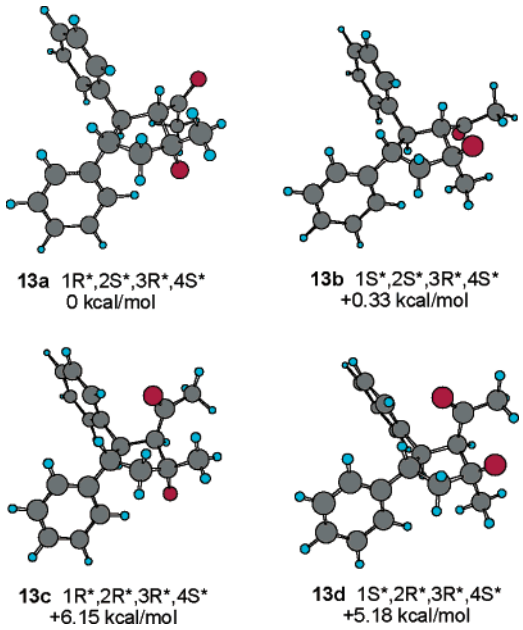


FIGURE 2. Optimized structures and relative free energies of four isomers of **13** by the RHF/AM1 method.

Conclusion

This paper describes that the reductive hydrodimerization of benzalacetones was efficiently accomplished by electroreduction, using an undivided cell in Et_4NOTs/acetonitrile to give cyclized hydrodimers as mixtures of two diastereomers. The electroreductive hydrodimerization of benzalacetones gave linear *dl*-hydrodimers stereoselectively according to kinetic control, and subse-

quent cyclization of the linear *dl*-hydrodimers produced mixtures of two cyclopentanols under thermodynamic control.

Experimental Section

Starting Materials. Benzalacetone (**1**) is commercially available. Other benzalacetones in Table 2 were prepared by reaction of aromatic aldehydes with acetone according to the reported method.[9]

Typical Procedure for Constant Current Electrolysis. A solution of benzalacetone (**1**) (146 mg, 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 125 mA at room temperature until almost all of **1** was consumed (150 C). The mixture was poured into water (50 mL) and extracted with Et_2O. The cyclic hydrodimers **2a** (46%) and **2b** (34%) were isolated by column chromatography on silica gel (hexanes−ethyl acetate). Small amounts of saturated ketone (4-phenylbutane-2-one, <10%) and linear hydrodimer (probably meso, <3%) were also detected.

2a: R_f 0.6 (hexanes−ethyl acetate, 2:1). White solid. Mp 113−114 °C. IR (KBr) 3449, 1711, 1493, 762, 743, 696 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.51 (s, 3 H), 1.85 (s, 3 H), 2.18 (dd, 1 H, J = 7.3, 13.8 Hz), 2.40 (dd, 1 H, J = 10.8, 13.8 Hz), 3.17 (d, 1 H, J = 11.6 Hz), 3.29 (dt, 1 H, J = 7.3, 10.8 Hz), 3.65 (dd, 1 H, J = 10.8, 11.6 Hz), 3.88 (br s, 1 H), 7.08−7.30 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 28.4 (q), 33.1 (q), 49.4 (t), 51.7 (d), 58.0 (d), 67.9 (d), 79.7 (s), 126.1 (d), 126.8 (d), 127.4 (d), 127.6 (d), 128.1 (d), 128.5 (d), 140.8 (s), 143.2 (s), 212.9 (s). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.58; H, 7.54.

2b: R_f 0.43 (hexanes−ethyl acetate, 2:1). White solid. Mp 127−128 °C. IR (KBr) 3477, 1688, 1601, 1493, 764, 745, 698 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H), 1.83 (s, 1 H), 2.15 (s, 3 H), 2.11−2.33 (m, 2 H), 3.40−3.60 (m, 3 H), 7.08−7.23 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 26.6 (q), 33.0 (q), 50.5 (d), 50.9 (t), 55.5 (d), 71.2 (d), 79.7 (s), 126.2 (d), 126.4 (d), 127.3 (d), 127.6 (d), 128.1 (d), 128.3 (d), 141.7 (s), 209.6 (s). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.53; H, 7.55.

Linear *meso*-hydrodimer of 1: R_f 0.55 (hexanes−ethyl acetate, 2:1). White solid. Mp 138−140 °C. IR (KBr) 1711, 1601, 1495, 768, 706 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.74 (s, 6 H), 2.31−2.42 (m, 2 H), 2.59−2.72 (m, 2 H), 3.30−3.43 (m, 2 H), 7.17−7.36 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 30.7 (q), 46.8 (d), 48.8 (t), 126.8 (d), 128.2 (d), 128.6 (d), 142.4 (s), 207.1 (s). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.49; H, 7.47.

3a: R_f 0.33 (hexanes−ethyl acetate, 2:1). Colorless oil. IR (neat) 3474, 1701, 1612, 1583, 1514, 1464, 831 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.57 (s, 3 H), 1.76 (s, 3 H), 2.13 (dd, 1 H, J = 7.3, 13.8 Hz), 2.36 (dd, 1 H, J = 10.3, 13.8 Hz), 3.09 (d, 1 H, J = 11.9 Hz), 3.19 (dt, 1 H, J = 7.3, 10.3 Hz), 3.53 (dd, 1 H, J = 10.3, 11.9 Hz), 3.74 (s, 3 H), 3.76 (s, 3 H), 3.93 (s, 1 H), 6.70−6.81 (m, 4 H), 6.99−7.05 (m, 2 H), 7.07−7.13 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 28.4 (q), 32.7 (q), 49.4 (t), 50.6 (d), 54.8 (d), 56.7 (d), 67.9 (d), 79.1 (s), 113.3 (d), 113.6 (d), 128.1 (d), 128.2 (d), 132.6 (s), 135.0 (s), 157.6 (s), 157.9 (s), 212.2 (s). Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.38; H, 7.35.

3b: R_f 0.23 (hexanes−ethyl acetate, 2:1). Colorless oil. IR (neat) 3449, 1701, 1612, 1583, 1514, 1464, 831, 731 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.39 (s, 3 H), 1.86 (br s, 1 H), 2.04−2.16 (m, 1 H), 2.14 (s, 3 H), 2.18−2.28 (m, 1 H), 3.32−3.47 (m, 3 H), 3.729 (s, 3 H), 3.732 (s, 3 H), 6.70−6.77 (m, 4 H), 7.00−7.08 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 26.5 (q), 32.9 (q), 49.6 (q), 50,9 (t), 54.7 (d), 55.0 (q), 71.3 (d), 79.2 (s), 113.5 (d), 113.6 (d), 128.1 (d), 128.4 (d), 133.7 (s), 133.8 (s), 157.8 (s), 210.0 (s). Anal. Calcd for $C_{22}H_{20}O_4$: C, 74.55; H, 7.39. Found: C, 74.45; H, 7.43.

(9) Drakes, N. L.; Allen, P., Jr. *Organic Synthesis*; Wiley: New York, 1941; Vol. I, pp 77−78.

4a: R_f 0.35 (hexanes−ethyl acetate, 2:1). Colorless oil. IR (neat) 3460, 1699, 1605, 1510, 835, 820, 733 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.50 (s, 3 H), 1.88 (s, 3 H), 2.11 (dd, 1 H, J = 7.0, 14.3 Hz), 2.39 (dd, 1 H, J = 10.5, 14.3 Hz), 3.*12* (d, 1 H, J = 1*1*.9 Hz), 3.20 (dt, 1 H, J = 7.0, 10.5 Hz), 3.57 (dd, 1 H, J = 10.5, 11.9 Hz), 3.83 (br s, 1 H), 6.83−6.99 (m, 4 H), 7.02−7.18 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 28.3 (q), 33.1 (q), 49.2 (t), 51,2 (d), 57.3 (d), 67.8 (d), 79.6 (s), 114.9 (d, J_{CCF} = 21.1 Hz), 115.5 (d, J_{CCF} = 21.1 Hz), 128.8 (d, J_{CCCF} = 7.8 Hz), 128.9 (d, J_{CCCF} = 7.8 Hz), 136.2 (s, J_{CCCCF} = 2.8 Hz), 138.7 (s, J_{CCCCF} = 3.3 Hz), 161.3 (s, J_{CF} = 242.1 Hz), 161.6 (s, J_{CF} = 243.3 Hz), 212.2 (s). Anal. Calcd for $C_{20}H_{20}O_2F_2$: C, 72.71; H, 6.10. Found: C, 72.84; H, 6.18.

4b: R_f 0.3 (hexanes−ethyl acetate, 2:1). Colorless oil. IR (neat) 3435, 1699, 1605, 1512, 835, 793, 735 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 1.78 (br s, 1 H), 2.06−2.27 (m, 2 H), 2.16 (s, 3 H), 3.33−3.50 (m, 3 H), 6.84−6.93 (m, 4 H), 7.02−7.14 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 26.6 (q), 33.1 (q), 50.1 (d), 50.8 (t), 55.1 (d), 71.1 (d), 79.6 (s), 115.0 (d, J_{CCF} = 20.6 Hz), 115.2 (d, J_{CCF} = 20.6 Hz), 128.6 (d, J_{CCCF} = 7.8 Hz), 129.0 (d, J_{CCCF} = 7.8 Hz), 137.1 (s, J_{CCCCF} = 2.8 Hz), 137.3 (s, J_{CCCCF} = 3.4 Hz), 161.3 (s, J_{CF} = 242.2 Hz), 161.4 (s, J_{CF} = 242.1 Hz), 209.5 (s). Anal. Calcd for $C_{20}H_{20}O_2F_2$: C, 72.71; H, 6.10. Found: C, 72.96; H, 6.21.

5a: R_f 0.59 (hexanes−ethyl acetate, 1:2). Pale yellow oil. IR (neat) 3497, 1701, 1591, 1518, 1464, 914, 808, 764, 733 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.50 (s, 3 H), 1.89 (s, 3 H), 2.15 (dd, 1 H, J = 7.0, 14.3 Hz), 2.37 (dd, 1 H, J = 10.3, 14.3 Hz), 3.12 (d, 1 H, J = 11.9 Hz), 3.18 (dt, 1 H, J = 10.3, 14.3 Hz), 3.52 (dd, 1 H, J = 7.0, 10.3 Hz), 3.79 (s, 3 H), 3.80 (s, 3 H), 3.81 (s, 3 H), 3.84 (s, 3 H), 3.97 (br s, 1 H), 6.53−6.88 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 28.1 (q), 32.9 (q), 48.8 (t), 51.1 (d), 55.6 (q), 57.6 (d), 67.4 (d), 79.3 (s), 110.6 (d), 111.1 (d), 119.1 (d), 119.4 (d), 133.2 (s), 135.9 (s), 147.1 (s), 147.5 (s), 148.5 (s), 212.7 (s). Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.47; H, 7.28.

5b: R_f 0.53 (hexanes−ethyl acetate, 1:2). Pale yellow oil. IR (neat) 3508, 1705, 1591, 1514, 1464, 914, 810, 764, 731 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.41 (s, 3 H), 2.05−2.28 (m, 2 H), 2.17 (s, 3 H), 3.37−3.47 (m, 3 H), 3.77 (s, 3 H), 3.78 (s, 3 H), 3.81 (s, 6 H), 6.60−6.75 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 26.4 (q), 32.9 (q), 49.9 (q), 50.3 (t), 55.1 (d), 55.6 (q), 70.8 (d), 79.2 (s), 110.6 (d), 110.9 (d), 119.0 (d), 119.3 (d), 134.4 (s), 134.5 (s), 147.2 (s), 148.3 (s), 209.7 (s). Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30. Found: C, 69.40; H, 7.22.

6a: R_f 0.45 (hexanes−ethyl acetate, 2:1). White solid. Mp 191−193 °C. IR (KBr) 3464, 1697, 1597, 1508, 795, 775 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.62 (s, 3 H), 1.71 (s, 3 H), 2.28 (dd, 1 H, J = 7.6, 14.0 Hz), 2.72 (dd, 1 H, J = 10.8, 14.0 Hz), 3.45 (d, 1 H, J = 10.8 Hz), 4.14 (s, 1 H), 4.41−4.54 (m, 1 H), 5.02 (t, 1 H, J = 10.8 Hz), 7.17−7.47 (m, 6 H), 7.53−7.95 (m, 8 H). ^{13}C NMR ($CDCl_3$) δ 28.6 (q), 33.3 (q), 46.0 (d), 50.0 (d and t), 68.6 (d), 79.9 (s), 122.8 (d), 122.9 (d), 123.4 (d), 124.1 (d), 124.9 (d), 125.2 (d), 125.4 (d), 125.7 (d), 125.9 (d), 126.6 (d), 127.3 (d), 128.5 (d), 131.9 (s), 132.2 (s), 133.5 (s), 133.7 (s), 137.5 (s), 139.5 (s), 213.3 (s). Anal. Calcd for $C_{28}H_{26}O_2$: C, 85.25; H, 6.64. Found: C, 85.20; H, 6.65.

6b: R_f 0.3 (hexanes−ethyl acetate, 2:1). White solid. Mp 194−196 °C. IR (KBr) 3435, 1701, 1597, 1508, 800, 793, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.47 (s, 3 H), 2.12 (s, 3 H), 2.21 (dd, 1 H, J = 11.3, 13.2 Hz), 2.47−2.56 (m, 1 H), 3.62 (d, 1 H, J = 8.4 Hz), 4.75−4.97 (m, 2 H), 7.23−7.43 (m, 6 H), 7.55 (d, 1 H, J = 7.6 Hz), 7.58 (d, 1 H, J = 7.6 Hz), 7.65−7.71 (m, 3 H), 7.79 (d, 1 H, J = 7.3 Hz), 7.97−8.05 (m, 1 H), 8.18 (d, 1 H, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ 26.3 (q), 33.3 (q), 45.1 (d), 47.9 (d), 51.6 (t), 72.0 (d), 80.1 (s), 122.9 (d), 122.99 (d), 123.30 (d), 124.1 (d), 124.9 (d), 125.1 (d), 125.3 (d), 125.38 (d), 125.41 (d), 125.6 (d), 126.5 (d), 126.8 (d), 128.4 (d), 131.9 (s), 132.1 (s), 133.5 (s), 133.6 (s), 137.9 (s), 138.9 (s), 210.5 (s). Anal. Calcd for $C_{28}H_{26}O_2$: C, 85.25; H, 6.64. Found: C, 85.17; H, 6.60.

7a: R_f 0.41 (hexanes−ethyl acetate, 2:1). White solid. Mp 137−139 °C. IR (KBr) 3462, 1682, 1632, 1599, 1508, 862, 835, 819, 746 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.58 (s, 3 H), 1.83 (s, 3 H),

2.32 (dd, 1 H, J = 7.0, 14.3 Hz), 2.52 (dd, 1 H, J = 10.5, 14.3 Hz), 3.35 (d, 1 H, J = 11.9 Hz), 3.60 (dt, 1 H, J = 7.0, 10.5 Hz), 3.94 (dd, 1 H, J = 10.5, 11.9 Hz), 4.08 (s, 1 H), 7.32−7.44 (m, 5 H), 7.48−7.56 (m, 3 H), 7.60−7.81 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 28.3 (q), 33.2 (q), 49.4 (t), 51.9 (d), 58.1 (d), 67.8 (d), 79.90 (s), 125.1 (d), 125.5 (d), 125.6 (d), 125.95 (d), 126.02 (d), 126.1 (d), 126.5 (d), 127.3 (d), 127.4 (d), 127.49 (d), 127.53 (d), 128.0 (d), 128.4 (d), 132.1 (s), 132.4 (s), 133.17 (s), 133.24 (s), 138.1 (s), 140.7 (s), 212.8 (s). Anal. Calcd for $C_{28}H_{26}O_2$: C, 85.25; H, 6.64. Found: C, 85.12; H, 6.54.

7b: R_f 0.28 (hexanes−ethyl acetate, 2:1). White solid. Mp 176−178 °C. IR (KBr) 3506, 1688, 1634, 1601, 1508, 853, 822, 746 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.49 (s, 3 H), 1.89 (s, 1 H), 2.17 (s, 3 H), 2.27−2.41 (m, 2 H), 3.52−3.63 (m, 1 H), 3.77−3.92 (m, 2 H), 7.30−7.45 (m, 6 H), 7.54−7.60 (m, 2 H), 7.62−7.76 (m, 6 H). ^{13}C NMR ($CDCl_3$) δ 26.6 (q), 33.2 (q), 50.8 (d), 51.0 (t), 55.8 (d), 71.2 (d), 79.9 (s), 125.2 (d), 125.3 (d), 125.68 (d), 125.72 (d), 125.77 (d), 125.84 (d), 126.4 (d), 127.3 (d), 127.4 (d), 127.5 (d), 127.9 (d), 128.1 (d), 132.20 (s), 132.24 (s), 133.2 (s), 139.2 (s), 139.3 (s), 209.7 (s). Anal. Calcd for $C_{28}H_{26}O_2$: C, 85.25; H, 6.64. Found: C, 85.15; H, 6.61.

8a: R_f 0.67 (hexanes−ethyl acetate, 1:1). Pale yellow oil. IR (neat) 3462, 1701, 1595, 1506, 926, 804, 735 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 3 H), 2.02 (s, 3 H), 2.16 (dd, 1 H, J = 7.3, 13.8 Hz), 2.24−2.34 (m, 1 H), 3.19 (d, 1 H, J = 11.6 Hz), 3.44−3.56 (m, 1 H), 3.54 (br s, 1 H), 3.87 (dd, 1 H, J = 9.7, 11.3 Hz), 6.02−6.05 (m, 2 H), 6.23−6.28 (m, 2 H), 7.28−7.30 (m, 1 H), 7.34−7.36 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 28.0 (q), 32.1 (q), 41.0 (d), 46.2 (t), 47.0 (d), 65.0 (d), 79.2 (s), 104.8 (d), 106.4(d), 109.9 (d), 110.2 (d), 141.0 (d), 141.4 (d), 153.9 (s), 156.0 (s), 211.1 (s). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.89; H, 6.53.

8b: R_f 0.42 (hexanes−ethyl acetate, 1:1). Pale yellow oil. IR (neat) 3437, 1705, 1597, 1508, 924, 806, 735 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3 H), 2.14 (dd, 1 H, J = 9.5, 13.5 Hz), 2.24 (s, 3 H), 2.28 (dd, 1 H, J = 8.1, 13.5 Hz), 3.43 (d, 1 H, J = 9.5 Hz), 3.58−3.80 (m, 2 H), 5.98−6.02 (m, 2 H), 6.21−6.26 (m, 2 H), 6.28−6.30 (m, 2 H). ^{13}C NMR ($CDCl_3$) δ 25.9 (q), 32.3 (q), 40.4 (d), 45.3 (d), 47.5 (t), 67.6 (d), 79.4 (s), 105.0 (d), 105.7 (d), 109.9 (d), 110.1 (d), 141.1 (d), 141.2 (d), 154.6 (s), 155.6 (s), 208.7 (s). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 68.82; H, 6.48.

Isomerization of 2. A mixture of **2a** or **2b** (100 mg, 0.34 mmol) and *t*-BuOK (11 mg, 0.034 mmol) in dry THF (5 mL) was stirred at room temperature for 3 days. The mixture was diluted with 1 M HCl (10 mL) and extracted with Et_2O. The products **2** and **9** were isolated by column chromatography on silica gel (hexanes−ethyl acetate).

9: R_f 0.8 (hexanes−ethyl acetate, 2:1). Pale yellow oil. IR (neat) 1678, 1616, 1601, 1495, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.91 (s, 3 H), 2.21−2.24 (m, 3 H), 2.63−2.75 (m, 1 H), 2.99−3.13 (m, 1 H), 3.14−3.24 (m, 1 H), 4.18−4.25 (m, 1 H), 7.02−7.07 (m, 2 H), 7.11−7.33 (m, 8 H). ^{13}C NMR ($CDCl_3$) δ 16.7 (q), 30.1 (q), 47.4 (t), 53.1 (d), 62.2 (d), 126.4 (d), 126.5 (d), 126.9 (d), 127.0 (d), 128.5 (d), 128.7 (d), 137.7 (s), 144.2 (s), 144.8 (s), 153.1 (s), 198.8 (s).

Silylation of 2. A solution of **2a** (100 mg, 0.34 mmol), chlorotrimethylsilane (0.13 mL, 1 mmol), and triethylamine (0.14 mL, 1 mmol) in dry THF (2.5 mL) was stirred for 20 h. After the solvent was removed in vacuo, dry Et_2O (10 mL) was added to the residue. Insoluble solid was filtered off and the filtrate was evaporated. The crude mixture was purified by column chromatography on silica gel (hexanes−ethyl acetate) to give **2a′** in 90% yield.

2a′: R_f 0.6 (hexanes−ethyl acetate, 5:1). Colorless oil. IR (neat) 1715, 1701, 1603, 1497, 841, 762, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9 H), 1.69 (s, 3 H), 2.11 (s, 3 H), 2.22 (dd, 1 H, J = 10.8, 13.0 Hz), 2.35 (d, 1 H, J = 8.1, 13.0 Hz), 3.00 (d, 1 H, J = 10.8 Hz), 3.11 (dt, 1 H, J = 8.1, 10.8 Hz), 3.96 (t, 1 H, J = 10.8 Hz), 7.00−7.24 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ −2.3 (q), 30.6 (q), 31.3 (q), 51.0 (d), 51.2 (t), 53.5 (d), 70.8 (d), 81.9 (s), 126.19 (d), 126.21 (d), 127.3 (d), 127.4 (d), 128.1 (d), 128.2 (d), 141.4 (s), 142.2 (s), 207.1 (s).

2b′: R_f 0.4 (hexanes−ethyl acetate, 5:1). Colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.24 (s, 9 H), 1.40 (s, 3 H), 2.04−2.11 (m, 1 H), 2.15 (s, 3 H), 2.36−2.42 (m, 1 H), 3.44−3.53 (m, 1 H), 7.09−7.22 (m, 10 H). ^{13}C NMR ($CDCl_3$) δ 2.3 (q), 26.4 (q), 32.8 (q), 50.4 (t), 50.7 (d), 54.5 (d), 72.5 (d), 82.3 (s), 126.1 (d), 126.2 (d), 127.3 (d), 127.6 (d), 128.1 (d), 142.3 (s), 209.3 (s).

Desilylation of 2a′. To a solution of **2a′** (110 mg, 0.3 mmol) in dry THF (2.5 mL) was added a 1 M solution of Bu_4NF in THF (0.33 mL, 0.33 mmol). After being stirred for 1 h at room temperature, the mixture was quenched with AcOH (0.02 mL, 0.33 mmol) and evaporated. The residue was column chromatographed on silica gel (hexanes−ethyl acetate) to give **2a** (50%) and **2b** (43%).

X-ray Crystallographic Analysis. All measurements were made on a Rigaku RAXIS imaging plate area detector with graphite monochromated Mo Kα radiation. The structure was solved by direct methods with SIR92 and expanded by using Fourier techniques with DIRDIF99. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. All calculations were performed with the CrystalStructure crystallographic software package.

Crystal Data for 2a. $C_{20}H_{22}O_2$, FW 294.39, triclinic, $P\bar{1}$ (no. 2), colorless block, a = 5.726(1) Å, b = 9.535(2) Å, c = 16.038(3) Å, α = 82.246(3)°, β = 89.04(1)°, γ = 76.988(7)°, V = 845.1(3) Å^3, T = 298 K, Z = 2, D_{calcd} = 1.157 g/cm^3, μ = 0.73 cm^{-1}, GOF = 1.002. The final cycle of full-matrix least-squares refinement on F^2 was based on 3663 observed reflections and 222 variable parameters and converged with unweighted and weighted agreement factors of R_1 = 0.096 and wR_2 = 0.100.

Crystal Data for 6a. $C_{28}H_{26}O_2$, FW 394.51, monoclinic, $P2_1/c$ (no. 14), colorless block, a = 14.908(2) Å, b = 8.2274(9) Å, c = 18.524(2) Å, β = 109.164(3)°, V = 2146.1(4) Å^3, T = 298 K, Z = 4, D_{calcd} = 1.221 g/cm^3, μ = 0.75 cm^{-1}, GOF = 1.001. The final cycle of full-matrix least-squares refinement on F^2 was based on 2364 observed reflections and 297 variable parameters and converged with unweighted and weighted agreement factors of R_1 = 0.038 and wR_2 = 0.034.

Crystal Data for 6b. $C_{28}H_{26}O_2$, FW 394.51, orthorombic, *Pbca* (no. 61), colorless block, a = 13.392(2) Å, b = 10.953(1) Å, c = 28.412(2) Å, V = 4167.2(8) Å^3, T = 298 K, Z = 8, D_{calcd} = 1.258 g/cm^3, μ = 0.77 cm^{-1}, GOF = 0.982. The final cycle of full-matrix least-squares refinement on F^2 was based on 4757 observed reflections and 298 variable parameters and converged with unweighted and weighted agreement factors of R_1 = 0.041 and wR_2 = 0.041.

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Supporting Information Available: Crystallographic CIF files for **2a**, **6a**, and **6b**; a PDF file of ^{1}H and ^{13}C NMR spectra of **2a**, **2b**, **6a**, and **6b**, X-ray crystallographic structures (ortep) of **2a**, **6a**, and **6b**, and the results of calculations shown in Figures 1 and 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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