of solvent gave essentially pure, solid product. Solvents for recrystallization and physical properties of the individual hydroxybenzaldehydes are described below.

3,4-Dimethoxy-5-hydroxybenzaldehyde (1a) from 4[6] was recrystallized from toluene–hexane: 1 g (55%); mp 64–65 °C (lit. mp 64–65 °C,[6] 60–61 °C,[11] 70–72 °C[12]); IR (Neat) 3480, 1690, 1590 cm^{-1}; NMR ($CDCl_3$) δ 3.83 (s, 3, OMe), 3.89 (s, 3, OMe), 6.98 (d, $J_{2,6}$ = 1.5 Hz, 1, H-6), 7.06 (d, $J_{2,6}$ = 1.5 Hz, 1, H-2), 7.24 (br s, 1, OH), 9.73 (s, 1, CHO).

3,5-Dimethoxy-2-hydroxybenzaldehyde (2a) from 12a[16] was recrystallized from CH_3OH to give pale yellow, silky needles: 1.18 g (65%); mp 129.5–130.5 °C (lit.[14] mp 129 °C); IR (Nujol) 3210, 1660, 1605 cm^{-1}; NMR ($CDCl_3$) δ 3.79 (s, 3, OMe), 3.88 (s, 3, OMe), 6.56 (d, $J_{4,6}$ = 2.9 Hz, 1, H-4), 6.75 (d, $J_{4,6}$ = 2.9 Hz, 1, H-6), 9.90 (s, 1, CHO), 10.62 (s, 1, OH).

3,5-Bis(benzyloxy)-2-hydroxybenzaldehyde (2b) from 12b.[16] To the combined organic layers (see the general procedure above) was added 40 mL of 2 N NaOH, and the resulting mixture was stirred vigorously for 30 min. The precipitated solid (the sodium salt of the phenol **2b**) was collected by filtration and was washed with Et_2O. The solid was then placed in a mixture of 50 mL of CH_2Cl_2 and 40 mL of 4 N HCl, and the resulting mixture was stirred until all the solid dissolved. The organic layer was collected, washed with brine, dried (Na_2SO_4), and then passed directly through a column of silica gel (10 g) in CH_2Cl_2. Further elution with CH_2Cl_2 and evaporation of eluents gave a solid residue which was recrystallized from CH_3OH, affording **2b** as yellow needles: 1.98 g (59%); mp 97–99 °C; IR (Nujol) 1650, 1595 cm^{-1}; NMR ($CDCl_3$) δ 4.92 (s, 2, OCH_2), 5.05 (s, 2, OCH_2), 6.62 (d, $J_{4,6}$ = 2.9 Hz, 1, H-4), 6.81 (d, $J_{4,6}$ = 2.9 Hz, 1, H-6), 7.81 (s, 10, Ph), 9.76 (s, 1, CHO), 10.52 (s, 1, OH). Anal. Calcd for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43. Found: C, 75.60; H, 5.58.

3,4-Dimethoxy-2-hydroxybenzaldehyde (14) from 13[16] was recrystallized from benzene–hexane to give white plates: 1.13 g (62%); mp 70–72 °C (lit.[32] mp 70–72 °C); IR (Nujol) 1640, 1590 cm^{-1}; NMR ($CDCl_3$) δ 3.86 (s, 3, OMe), 3.93 (s, 3, OMe), 6.58 (d, $J_{5,6}$ = 9 Hz, 1, H-5), 7.27 (d, $J_{5,6}$ = 9 Hz, 1, H-6), 9.71 (s, 1, CHO), 11.17 (s, 1, OH).

3-Hydroxy-4,5-(methylenedioxy)benzaldehyde (16) from 15 was recrystallized from toluene to give amorphous solid: 930 mg (56%); mp 133–134 °C (lit.[6] mp 134–134.5 °C); IR (Nujol) 3260, 1650, 1605 cm^{-1}; NMR (acetone-d_6) δ 6.10 (s, 2, OCH_2O), 6.92 (d, $J_{2,6}$ = 1.5 Hz, 1, H-2), 7.12 (d, $J_{2,6}$ = 1.5 Hz, 1, H-6), 8.80 (br s, 1, OH), 9.74 (s, 1, CHO).

4,5-Dimethoxy-2-hydroxybenzaldehyde (18) from 17 (Aldrich) was recrystallized from benzene–hexane to give off-white solid: 1.06 g (58%); mp 104–106 °C (lit.[32] mp 105 °C); IR (Nujol) 1630, 1592 cm^{-1}; NMR ($CDCl_3$) δ 3.84 (s, 3, OMe), 3.90 (s, 3, OMe), 6.44 (s, 1, H-3), 6.89 (s, 1, H-6), 9.68 (s, 1, CHO), 11.38 (s, 1, OH).

3-Bromo-4,5-(methylenedioxy)benzaldehyde (15). To a stirred solution 3-bromo-4,5-dihydroxybenzaldehyde[35] (5.43 g, 25 mmol) in 75 mL of dry DMF under an N_2 atmosphere was added anhydrous KF (PCR Inc., anhydrous material freshly dried at 0.01 mm over P_2O_5 for 24 h, 7.25 g, 125 mmol). After 15 min, CH_2Br_2 (4.79 g, 27.5 mol) was added, and the mixture was heated at 105 °C with stirring for 2 h. The mixture was then evaporated in vacuo to dryness, and the residue was extracted exhaustively with Et_2O. The combined Et_2O solutions were washed with water and brine, dried (Na_2SO_4), and then evaporated in vacuo to dryness to give an off-white solid which was recrystallized from benzene–hexane to afford **15**: 4.80 g (85%); mp 125–127 °C (lit.[36] mp 124–126 °C); IR (Nujol) 1685, 1595 cm^{-1}; NMR ($CDCl_3$) δ 6.09 (s, 2, OCH_2O), 7.21 (d, $J_{2,6}$ = 1.6 Hz, 1, H-2), 7.48 (d, $J_{2,6}$ = 1.6 Hz, 1, H-6), 9.72 (s, 1, CHO).

Acknowledgment. The support of this work through a grant (NS15692) from the National Institute of Neurological and Communicative Disorders and Stroke and a postdoctoral fellowship to A.K.S. from the American Heart Association—Kansas Affiliate is gratefully acknowledged.

Registry No. **1a**, 29865-90-5; **2a**, 65162-29-0; **2b**, 85565-92-0; **4**, 6948-30-7; **9**, 120-14-9; **12a**, 85565-93-1; **12a** (debromo derivative), 7311-34-4; **12b**, 85565-94-2; **12b** (debromo derivative), 14615-72-6; **13**, 55171-60-3; **14**, 19283-70-6; **15**, 19522-96-4; **15** (debromo derivative), 120-57-0; **16**, 81805-98-3; **17**, 5392-10-9; **18**, 14382-91-3; 3-bromo-4,5-dihyroxybenzaldehyde, 16414-34-9; dibromomethane, 74-95-3; morpholine, 110-91-8; butyllithium, 109-72-8.

(35) Lange, R. G. *J. Org. Chem.* **1962**, *27*, 2037–2039.
(36) Ishii, H.; Ueda, E.; Nakajima, K.; Ishida, T.; Ishikawa, T.; Harada, K.-I.; Ninomiya, I.; Naito, T.; Kiguchi, T. *Chem. Pharm. Bull.* **1978**, *26*, 864–873.

Electrooxidative Cleavage of Carbon–Carbon Bonds. 2. Double Cleavage of α,β-Epoxyalkanones and Enantiospecific Syntheses of Chiral Methyl *trans*- and *cis*-Chrysanthemates from (+)- and (−)-Carvones

Sigeru Torii,* Tsutomu Inokuchi, and Ryu Oi

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700, Japan

Received August 26, 1982

The stereospecific synthesis of chiral methyl *trans*- and *cis*-chrysanthemates (**1** and **26**) from (+)- and (−)-carvones (**7a,b**) is described. Methyl (3*R*)- and (3*S*)-3-(1-chloro-1-methylethyl)-5-oxohexanoates (**3**) and methyl (3*S*)- and (3*R*)-3-(1-chloro-1-methylethyl)-5,5-dimethoxypentanoates (**4**) are key intermediates in the preparation of **1** and **26** via δ-lactone **2**. Electrochemical cleavage of 5-(1-chloro-1-methylethyl)-2,3-epoxy-2,3-dimethylcyclohexan-1-one (**5**) at the C-1 and C-2 positions in the MeOH–AcOEt (7:1)–0.047 M $LiClO_4$–(Pt) system gave **3** in 86–90% yields. Each enantiomer of **5** was prepared from **7** through four steps in approximately 63% overall yields. Enantiomers **4** were obtained by the electrolysis of 3-hydroxy-2-methoxy- or 2-hydroxy-3-methoxy-5-(1-chloro-1-methylethyl)-2-methylcyclohexan-1-ones (**14** or **15**) in 87% yield. The precursors **14** and **15** were smoothly provided by acid-catalyzed methanolysis of epoxides **6** prepared from **7**. Methylation of **3** with methylmagnesium iodide and geminal dimethylation of **4** with methyllithium followed by oxidation with chromic acid gave the same product **2**. Cyclization of **2** with lithium diisopropylamide gave dihydrochrysanthemolactone (**23**; 80% yield from **3** and 50% yield from **4**, respectively). The conversion of **23** to the desired **1** was achieved by treatment with sodium hydroxide at 230–235 °C in 58–59% yields. The cis isomers **26** were also prepared from **23** by hydrolysis followed by dehydration and subsequent isomerization of the double bond in 80% yield.

The use of chiral synthons derived from biomass for the synthesis of chiral, bioactive compounds has been of current interest.[1] The preparation of chiral *trans*- and *cis*-chrysanthemic acids (**1** and **26**; R = H) is of key importance

0022-3263/83/1948-1944$01.50/0

Table I. Conditions and Results of Regioselective Electrochemical Cleavage of 5, 11, 12, 14, and 15[a]

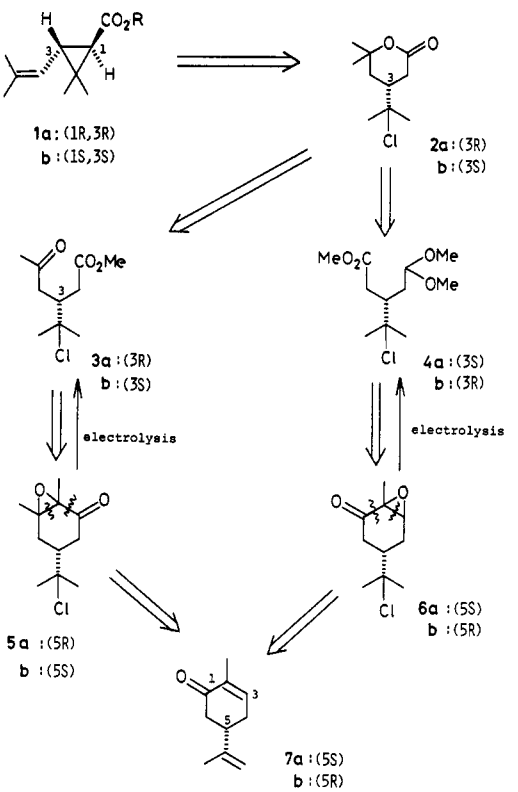
entry	substrate	solvent[b]	electrolyte	current, mA/cm²	electricity,[c] F/mol	product (yield,[d] %)
1	5a	A	$LiClO_4$	27–30	45	3a (90)
2	5a	B	$LiClO_4$	30	12	3a (87)
3	5b	A	$LiClO_4$	30	12	3b (52) + 5b (32)
4	5b	B	$LiClO_4$	30	12	3b (86)
5	5a	B	$LiBF_4$	30	28	3a (85)
6	5b	B	CF_3COOLi	30	27	3b (16) + 5b (68) + others (13)
7	5b	A	Et_4NOTs	6–7	23	5b (28) + 11b (46) + 12b (15)[e]
8	11b	A	$LiClO_4$	30	8	3b (94)
9	12b	A	$LiClO_4$	30	6	3b (96)
10	14a	A	$LiClO_4$	20	10	4a (87)
11	15a	A	$LiClO_4$	20	10	4a (87)
12	15b	A	H_2SO_4	8	5	4b (20) + 18b (44)[f]

[a] Unless otherwise noted electrolyses were carried out under an applied voltage of 6.5–11.5 V (entries 1–6) or at 3.0–6.0 V (entries 8–12) with Pt (3 cm²) electrodes in an undivided cell. [b] Solvents: A, MeOH; B, MeOH–AcOEt (7:1). [c] Faradays/mole during preparative run. [d] Based on isolated products in complete conversion of 0.5–3.5 mmol of the substrates. [e] Carried out in a divided cell under a constant applied voltage of 20 V. [f] Carried out with carbon electrodes.

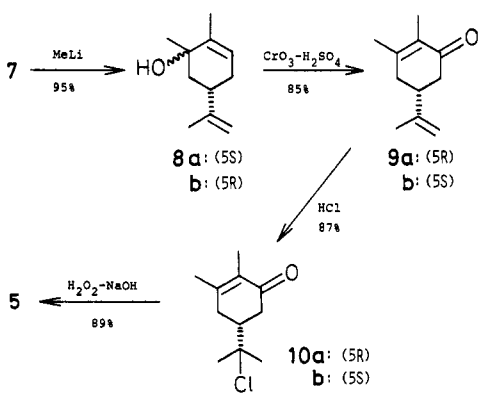
in pesticide chemistry.[2] Several attempted enantiospecific syntheses of 1 (R = H) have been tried by (i) asymmetric synthesis of the cyclopropane ring by using chiral copper chelate complexes,[3] (ii) optical resolution of racemic acids 1 with chiral amines,[4] and (iii) use of (+)-Δ^3-carene.[5] The methods based on the last concept are considered to be the most attractive strategy in terms of producing the acids 1 (R = H) with high optical purity.[6] However, the methods dealing with the conversion of (+)-Δ^3-carene to 1 are disadvantageous due to many reaction steps and lower overall yields. We now report an efficient enantiospecific synthesis of methyl *trans*-(3*R*)-chrysanthemate (**1a**, R = Me) and *cis*-(3*R*)-chrysanthemate (**26a**, R = Me) via a new electrolytic double-cleavage reaction of the α,β-epoxycyclohexanone moiety of **5a** and **6a** derived from (+)-carvone (**7a**). Similarly, *trans*-(3*S*)-chrysanthemate (**1b**, R = Me) and *cis*-(3*S*)-chrysanthemate (**26b**, R = Me) can be prepared from (−)-carvone (**7b**). The structural formulas shown in the following schemes are depicted as enantiomers starting from (5*S*)-**7a**.

Our retrosynthetic design for the target molecule (3*R*)-**1a** from (+)-**7a** is outlined in Scheme I wherein the 5*S* carbon of (+)-carvone is incorporated into the requisite C-3 position of **1a**. The key intermediate (3*R*)-**2a** may be obtained by two different routes from **7a** via **3a** or **4a** followed by either methylation at the terminal acetyl group of **3a** or geminal methylation of the ester group of **4a**. The merit of the approaches depends upon the ease of electrooxi-

Scheme I



Scheme II



(1) For recent reviews on the synthesis of natural products from the "chiral pool" note: (a) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159. (b) Seebach, D.; Hungerbühler, E. In "Modern Synthetic Methods, 1980"; Sheffold, R., Ed.; Salle (Frankfurt) Sauerlander (Aarau): 1980, pp 91–171. (c) Fraser-Reid, B.; Anderson, R. C. *Fortschr. Chem. Org. Naturst.* **1980**, *39*, 1. (d) Kovaly, K. A. *CHEMTECH* **1982**, 486.

(2) (a) Casida, J. E., Ed. "Pyrethrum—The Natural Insecticide"; Academic Press: New York, 1973. (b) Elliot, M.; Janes, N. F. *Chem. Soc. Rev.* **1978**, *7*, 473. (c) Arlt, D.; Jautelat, M.; Lantzsch, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 703 and references cited therein.

(3) (a) Hirai, H.; Matsui, M. *Agric. Biol. Chem.* **1976**, *40*, 169. (b) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707. (c) *Ibid.* **1977**, 2599.

(4) (a) Campbell, I. G. M.; Harper, S. H. *J. Sci. Food. Agric.* **1952**, *4*, 189. (b) Goffinet, B.; Locatelli, A. Fr. Pat. 1536458, 1967; *Chem. Abstr.* **1969**, *71*, 90923.

(5) (a) Matsui, M.; Yoshioka, H.; Yamada, Y.; Sakamoto, H.; Kitahara, T. *Agric. Biol. Chem.* **1965**, *29*, 784. (b) *Ibid.* **1967**, *31*, 33. (c) Sobti, R.; Dev, S. *Tetrahedron* **1974**, *30*, 2927. (d) Gopichand, Y.; Khanra, A. S.; Mitra, R. B.; Chakravarti, K. K. *Indian J. Chem.* **1975**, *13*, 433. (e) Cocker, W.; Lauder, H. S. J. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 332. (f) Khanra, A. S.; Mitra, R. B. *Indian J. Chem., Sect. B* **1976** *14B*, 716. (g) Ho, T. -L.; Din, Z. U. *Synth. Commun.* **1980**, *10*, 921. (h) Mane, B. M.; Gore, K. G.; Kulkarni, G. H. *Indian J. Chem. Sect. B* **1980**, *19B*, 605. (i) Bhat, N. G.; Mane, B. M.; Kulkarni, G. H.; Mitra, R. B. *Ibid.* **1981**, *20B*, 204.

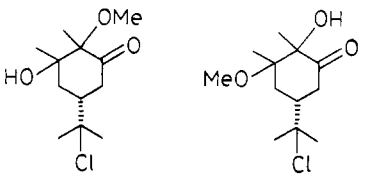
(6) Several approaches from another chiral pools have been investigated. (−)-β-pinene: (a) Mitra, R. B.; Khanra, A. S. *Synth. Commun.* **1977**, *7*, 245. Pantolactone: (b) Matsuo, T.; Mori, K.; Matsui, M. *Tetrahedron Lett.* **1976**, 1979. (−)-Carvone: (c) Ho, T.-L.; Din, Z. U. *Synth. Commun.* **1982**, *12*, 257. *cis*-Caronic acid half-ester: (d) De Vos, J.-J.; Krief, A. *J. Am. Chem. Soc.* **1982**, *104*, 4282.

dative carbon–carbon bond cleavage of α,β-epoxy ketones **5a** or **6a**.[7]

Both enantiomers of α,β-epoxy ketones **5** were independently prepared from **7a** and **7b**. Carvone **7** was alkylated with methyllithium, leading to alcohols **8**, followed by oxidation with chromic acid[8] to give products **9**. The desired **5** was obtained in 63–64% overall yields (from **7**) by epoxidation of the chloro enone **10** prepared from **9** by hydrochlorination (Scheme II). The epoxy ketones **6** were smoothly obtained by hydrochlorination of **7**[9] followed by epoxidation[10] in ca. 75% yield.

The electrochemical cleavage of the carbon–carbon bonds, marked with wavy lines, of **5** was carried out in a MeOH or MeOH–AcOEt (7:1)–0.047 M $LiClO_4$–(Pt) system at a constant current of 30 mA/cm^2 under an applied voltage of 6.0–7.0 V (anode potential 2.10–2.23 V vs. Ag/0.1 M AgCl) at 2–5 °C in an undivided cell. As shown in entry 1 of Table I, the passage of 45 F/mol of electricity yielded the desired **3a** in 90% yield. The employment of a cosolvent system of MeOH–AcOEt (7:1 v/v) can improve the current efficiency strikingly (entry 2). The significant improvement of the current efficiency in the cosolvent system may be the result of increased solubility of **5** in the solution. The results from the electrolyses of **5b** utilizing equal amounts of electricity (entries 3 and 4) demonstrate that the cosolvent system is favorable for producing **3b**.

Particularly noteworthy is the effect of the supporting electrolyte. In the preceding paper,[11] we discussed the role of strong electrolytes, i.e., $LiClO_4$, $LiBF_4$, and CF_3COOLi, in methanol in the electrooxidative cleavage reaction of carbon–carbon linkages of 2-oxocycloalkan-1-ols and cycloalkanone enol acetates. A similar effect of strong electrolytes was observed in the cleavage reaction of the α,β-epoxycycloalkanone system. As shown in entries 1, 2, 4, and 5, use of $LiClO_4$ or $LiBF_4$ as a supporting electrolyte facilitated the formation of **3**. Lithium trifluoroacetate was less effective in producing **3b** (entry 6). In contrast, the electrolysis of **5b** with Et_4NOTs produced the epoxy ring-opened products **11b** (46%) and **12b** (15%) together

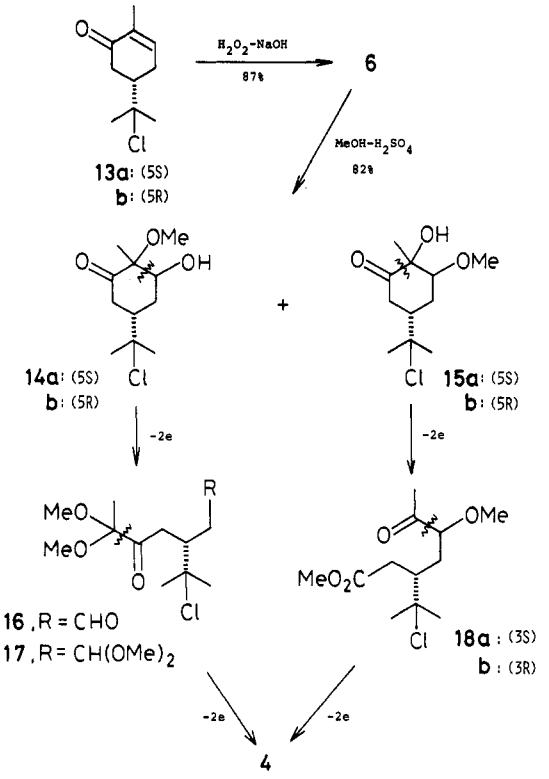


11a: (5R) **12a**: (5R)
b: (5S) **b**: (5S)

with the starting material **5b** (28%, entry 7). However, the electrolysis of **11b** and **12b** in the same way with $LiClO_4$ afforded **3b** in 94–96% yields (entries 8 and 9).

Cleavage of the carbon–carbon bond of the compounds **11b** and **12b** in the MeOH–$LiClO_4$–(Pt) system occurs with less electricity than electrolysis of **5b**, suggesting that the electrolysis reaction can easily proceed after the opening

Scheme III



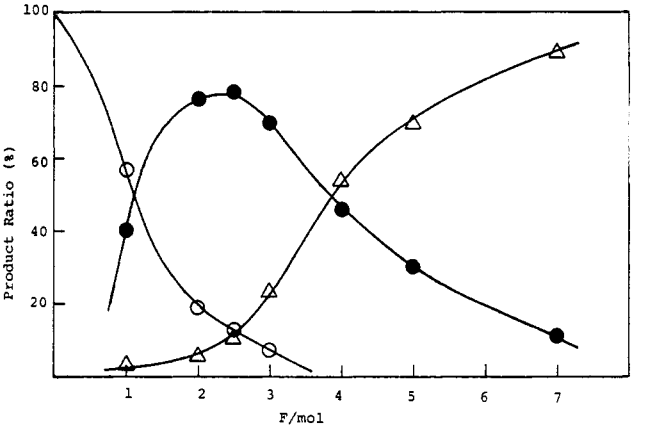


Figure 1. Plots of the product ratio of the electrooxidation of **14b** (○) against passed electricity (F/mol) at a current of 20 mA/cm^2: two-electron oxidation product (●), **16b**; four-electron oxidation product (△), **4b**.

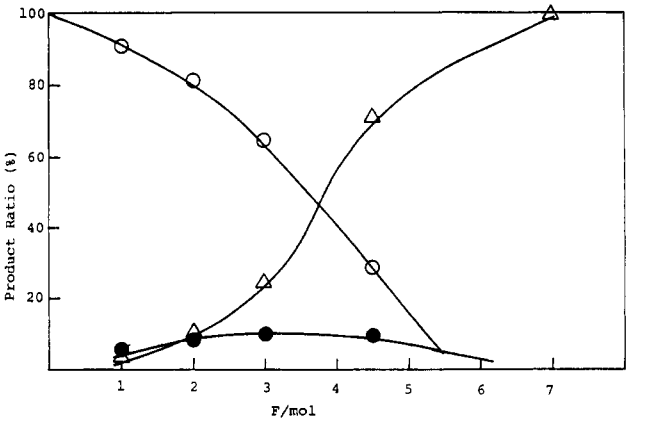


Figure 2. Plots of the product ratio of the electrooxidation of **15b** (○) against passed electricity (F/mol) at a current of 4 mA/cm^2: two-electron oxidation product (●), **18b**; four-electron oxidation product (△), **4b**.

(7) The conversion of the enones to the oxo esters has been achieved by the oxidation with osmium tetraoxide followed by treatment with lead tetraacetate or by direct ozonolysis, leading to δ-lactones: (a) Pappo, R.; Jung, C. J. *Tetrahedron Lett.* **1962**, 365. (b) Danishefsky, S.; Schuda, P.; Kato, K. *J. Org. Chem.* **1976**, *41*, 1081. (c) Chavdarian, C. G.; Heathcock, C. H. *Ibid.* **1975**, *40*, 2970. (d) Roelofs, W.; Gieselmann, M.; Cardé, A.; Tashiro, H.; Moreno, D. S.; Henrick, C. A.; Anderson, R. J. *J. Chem. Ecol.* **1978**, *4*, 211.

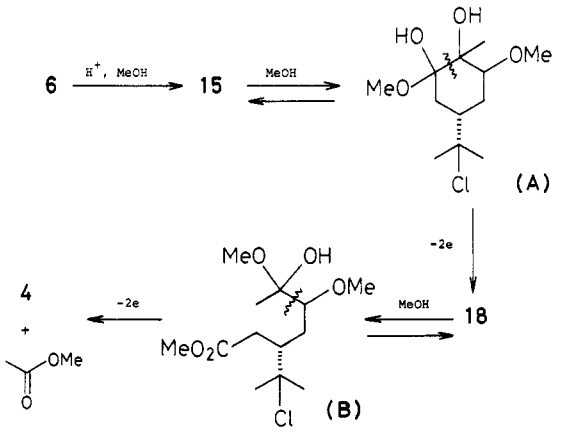
(8) Büchi, G.; Egger, B. *J. Org. Chem.* **1971**, *36*, 2021.

(9) Mestres, R.; Polo, M. C.; Valero, M. J. *An. Quim.* **1979**, *75*, 970; *Chem. Abstr.* **1980**, *93*, 114713.

(10) Burns, W. D. P.; Carson, M. S.; Cocker, W.; Shannon, P. V. R. *J. Chem. Soc. C* **1968**, 3073.

(11) Torii, S.; Inokuchi, T.; Oi, R. *J. Org. Chem.* **1982**, *47*, 47.

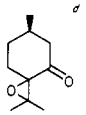
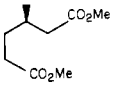
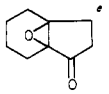
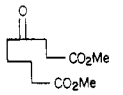
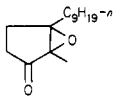
Scheme IV



of the oxirane ring of **5** by an acid-catalyzed methanolysis near the surface of the anode.[12] The electrooxidative carbon–carbon bond cleavage of **6**, which lacks the C-3 methyl of **5** did not proceed under the same electrolysis conditions used for **5**. However, the electrolysis of **14a** and **15a**, prepared by an acid-catalyzed hydrolysis of **6** in methanol, in the MeOH–$LiClO_4$–(Pt) system gave the desired **4a** in 87% yield (Scheme III). The profiles of the product ratios in relation to passed electricity in the electrolysis of **14b** and **15b** are shown in Figures 1 and 2. Figure 1 reveals that the yield of **16b**[13] (2.25–2.35 V vs. Ag/0.1 M AgCl) reached a maximum when ca. 2.5 F/mol of electricity was passed in the oxidation of **14b** at 2.00–2.15 V, showing 0.20–0.25 V of potential gap between **14b** and **16b**, which can facilitate the accumulation of the intermediate **16b** in the initial electrolysis stage. In contrast, cleavage of carbon–carbon bonds of **15b** and **18b** suppresses the accumulation of **18b** in the media due to the proximity of their oxidation potentials (**15b**, 2.00–2.10 V; **18b**, 2.00–2.15 V) as shown in Figure 2. Electrolysis of **15b** with sulfuric acid in methanol afforded **18b** as a major product (44%) along with **4b** (20%) (entry 12). These results reveal that the cleavage of the carbon–carbon bond of the α-hydroxy carbonyl moiety of **15b** occurs more easily than at the α-methoxy carbonyl moiety of **14b**. These results can be interpreted by assuming that the cleavage reaction of **15b** would proceed by anodic electrolysis of the 1,2-diol A derived from the formation of the corresponding hemiacetal, which may be produced by acid-catalyzed equilibration near the anode in the MeOH–$LiClO_4$–(Pt) system, giving **18**.[11] The acid-catalyzed hemiacetalization of **18** that follows may produce the hemiacetal B, which would undergo a two-electron discharge to give the cleavage product **4** (Scheme IV). Similarly, electrolysis of a variety of α,β-epoxycycloalkanones afforded the corresponding double cleavage products in good yields (Table II).

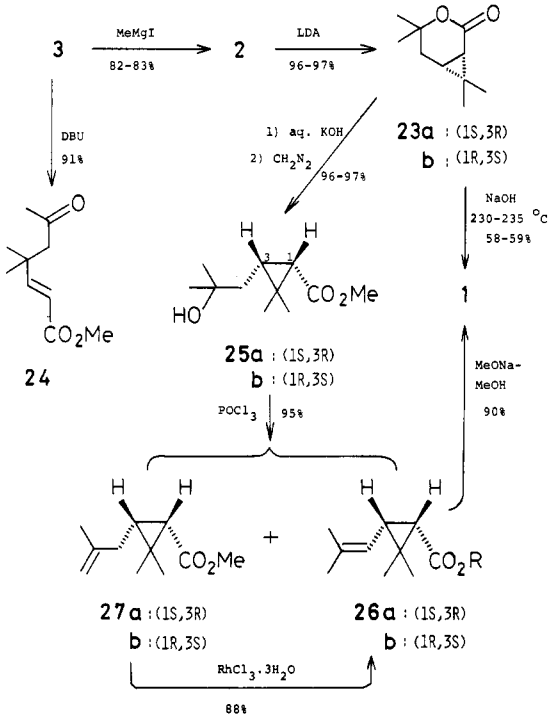
The last stages of the synthesis were accomplished in a manner as described in Scheme V. Treatment of enantiomers (3*R*)-**3a** and (3*S*)-**3b** with methylmagnesium iodide at −20 °C afforded an 82% yield of (3*R*)-δ-lactone **2a** and an 83% yield of (3*S*)-δ-lactone **2b**, respectively. However, the reaction of **3** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in toluene afforded the enone **24**, exclusively. The latter reaction proceeds by initial cyclopropane ring formation with DBU followed by ring opening with the same base.[14] Cyclization of δ-lactone **2** with lithium diisopropylamide yielded 97% of (1*S*,3*R*)-**23a** and 96% of (1*R*,3*S*)-**23b**. The direct conversion of the lactones **23** into the desired trans isomers **1** (R = Me) was carried out according to the reported procedure.[5c] Heating of **23** with sodium hydroxide at 230–235 °C in diethylene glycol and esterification of the reaction products with diazo-

Table II. Electrooxidative Double Cleavage of α,β-Epoxycycloalkanones[a]

entry	substrate	electricity,[b] F/mol	product	yield,[c] %
1	 [d]	12		83
2	 [e]	16		71
3		28	n-$C_9H_{19}C(O)$-$CH_2CH_2CO_2Me$	74

[a] All electrolyses were carried out in MeOH (7 mL)–AcOEt (1 mL)–0.047 M $LiClO_4$ under a constant current of 30 mA/cm² (applied voltage 6.5–7.5 V) with Pt (3 cm²) electrodes at 2–5 °C in an undivided cell. [b] Faradays/mole during the preparative run. [c] Based on the isolated product in complete conversion of 0.5–0.8 mmol of the substrate. [d] Reusch, W.; Anderson, D. F.; Johnson, C. K. *J. Am. Chem. Soc.* **1968**, *90*, 4988. [e] Felix, D.; Müller, R. K.; Horn, U.; Joos, R.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1972**, *55*, 1276.

Scheme V

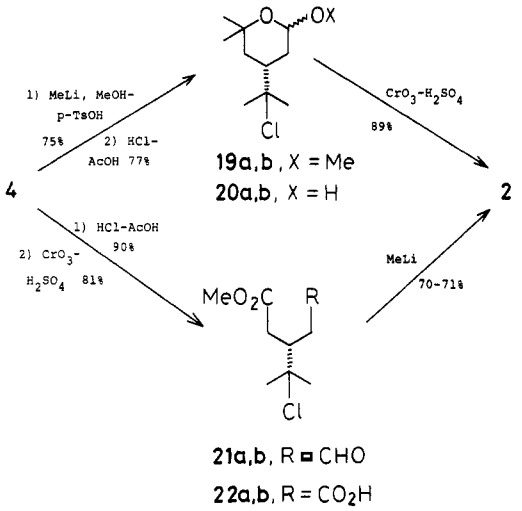


(12) The acid-catalyzed epoxy ring opening of **5** and **6** in MeOH–$LiClO_4$ was encountered when the solution was stirred in the anode compartment after passing electricity through it for a while. Similar phenomena may be expected to occur in the course of electrolysis of **5** with $LiClO_4$ in an undivided cell. See the following references in relation to such action as an acid–catalyst in electrolysis: (a) Mayeda, E. A.; Miller, L. L.; Wolf, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 6812. (b) Gassman, P. G.; Yamaguchi, R. *Ibid.* **1979**, *101*, 1308. (c) Imagawa, T., Nakashima, Y.; Kawanishi, M. *Chem. Lett.* **1980**, 1609. (d) Delaunay, J.; Lebouc, A.; Tallec, A.; Simonet, J. *J. Chem. Soc., Chem. Commun.* **1982**, 387. (e) Torii, S.; Tanaka, H.; Nakane, S. *Bull. Chem. Soc. Jpn* **1982**, *55*, 1673.

(13) Characterized by the conversion to acetal **17b** by treatment with methyl orthoformate and *p*-TsOH in methanol.

(14) Tomažič. A.; Ghera, E. *Tetrahedron Lett.* **1981**, *22*, 4349.

Scheme VI



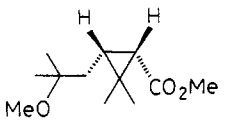
21a,b, R = CHO

22a,b, R = CO_2H

methane gave a 58% yield of (1*R*,3*R*)-**1a** (R = Me) and a 59% yield of (1*S*,3*S*)-**1b** (R = Me) together with a small amount of **26** (R = Me, 8%) and **27** (7%).

An alternative route to the δ-lactone **2** from the acetal ester **4** was examined (Scheme VI) in the hope that the overall yield might be improved. Methylation of enantiomers (3*S*)-**4a** and (3*R*)-**4b** with methyllithium at −60 to −35 °C followed by an acidic workup in methanol gave the pyranyl ether **19** which could be converted to (3*R*)-**2a** and (3*S*)-**2b** by hydrolysis followed by oxidation of lactol **20** with chromic acid (51% overall yield from **4a** and **4b**, respectively). A second route involves hydrolysis of (3*S*)-**4a** and (3*R*)-**4b** to give the somewhat unstable aldehyde **21** which was oxidized with chromic acid. The carboxylic acid **22** was reacted with methyllithium, affording 51% overall yields of **4a** and **4b**, respectively.

As shown in Scheme V, methyl (+)- and (−)-*cis*-chrysanthemates (**26**, R = Me) were also prepared by hydrolysis of either (1*R*,3*S*)- or (1*S*,3*R*)-**23** with potassium hydroxide in methanol and subsequent esterification with diazomethane, affording **25**, which in turn dehydrated on treatment with phosphorus oxychloride in HMPA at 50–100 °C[15] to give a 1:2 mixture of **26** (R = Me) and **27** in 91% yield (from **23**). Isomerization of the double bond of **27** was carried out on treatment of the mixture of **26** (R = Me) and **27** with rhodium trichloride as a catalyst[16] at 95 °C in 2-propanol to give **26** (R = Me) in 88% yield. HPLC analysis of the products revealed that both the (+)- and (−)-cis isomers **26** (R = Me) are contaminated with less than 4% of their corresponding trans isomers (1*S*,3*S*)- and (1*R*,3*R*)-**1** (R = Me), respectively. However, the same treatment of a 1:2 mixture of **26b** (R = Me) and **27b** in methanol resulted in a 47:53 mixture of **26b** (R = Me) and **28b** in 98% yield. The cis isomers **26** (R = Me) can be



28a : (1S,3R)
b : (1R,3S)

smoothly converted into the corresponding trans isomers **1** (R = Me) in high yields.[5a,d]

Experimental Section

The boiling points are indicated by an air-bath temperature without correction, and the melting points are uncorrected. IR spectra were obtained with a JASCO IRA-1 grating spectrometer. ^1H NMR spectra were recorded on a Hitachi R-24 (60 MHz), and ^{13}C NMR spectra were obtained with a JEOL FX-100 (25.05 MHz). Samples were dissolved in $CDCl_3$, and the chemical shift values are expressed in δ values (ppm) relative to Me_4Si as an internal standard. Current–potential measurements were performed by using Kowa Electronics Model PGS-1550 potentiogalvanostat and an FG-102A function generator. Optical rotations were taken on a JASCO DIP-140 digital polarimeter in $CHCl_3$ as a solvent. Elemental analyses were performed in our laboratory. After the desired reaction period, unless otherwise noted, the mixture was poured into a separatory funnel with benzene–AcOEt (1:1) and brine. The organic layer was separated and washed twice with brine. The extracts were dried (Na_2SO_4) and concentrated on a rotary evaporator.

(5*R*)-2,3-Dimethyl-5-isopropenylcyclohex-2-en-1-one (9a). To a solution of **7a**[17] (2.0 g, 13.3 mmol) in ether (10 mL) was added ethereal 1.1 M MeLi (13.2 mL, 14.5 mmol) at −30 °C. The mixture was stirred at 0 °C for 1 h, quenched with cold 10% NH_4Cl, and worked up in the usual manner to give 2.1 g (95%) of (5*S*)-**8a**. Without further purification, this material was dissolved in ether (39 mL), and to this solution was added a solution of CrO_3 (3.4 g, 34 mmol) in 5% H_2SO_4 (34 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and diluted with water. The organic layer was worked up in the usual manner, and the crude product was distilled at 74 °C (10 mm) to give 1.85 g (85% yield) of (5*R*)-**9a** whose analytical sample (t_R = 4.5 min) was obtained by preparative GLC (silicon GE, SE-30, 10%, 3 mm × 4 m column, carrier gas H_2, 42 mL, 145 °C): $[\alpha]^{26}_D$ −104.5° (*c* 2.1); IR (neat) 3055, 1662 (C=O), 1650 (C=C), 1635 (C=C), 889 cm^{-1}; ^1H NMR δ 1.75 (br s, 6, CH_3), 1.94 (s, 3, CH_3), 2.10–2.85 (m, 5, CH_2, CH), 4.73 (br s, 2, H_2C=C). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.26; H, 9.67.

Similarly, (5*S*)-**9b** was obtained in 81% yield from **7b**: bp 74 °C (10 mm); $[\alpha]^{26}_D$ +103.5° (*c* 2.1). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.49; H, 9.76.

(5*R*)-5-(1-Chloro-1-methylethyl)-2,3-dimethylcyclohex-2-en-1-one (10a). Into a solution of (5*R*)-**9a** (58 mg, 0.35 mmol) in ether (6 mL) was passed dry gaseous HCl at 0–5 °C for 4 h. The mixture was poured into cold aqueous $NaHCO_3$ and worked up in the usual manner to give 62 mg (87%) of (5*R*)-**10a**: bp 130–132 °C (4 mm); $[\alpha]^{23}_D$ −103.3° (*c* 1.0); IR (neat) 1665 (C=O), 1638 cm^{-1} (C=C); ^1H NMR δ 1.58 (s, 6, CH_3CCl), 1.76, 1.95 (s, 6, CH_3), 1.95–2.85 (m, 5, CH_2, CH). Anal. Calcd for $C_{11}H_{17}ClO$: C, 65.83; H, 8.54. Found: C, 65.98; H, 8.63.

Similarly, (5*S*)-**10b** was obtained in 87% yield from (5*S*)-**9b**: bp 119–121 °C (2.5 mm); $[\alpha]^{21}_D$ +103.5° (*c* 1.3). Anal. Calcd for $C_{11}H_{17}ClO$: C, 65.83; H, 8.54. Found: C, 65.65; H, 8.49.

(5*R*)-5-(1-Chloro-1-methylethyl)-2,3-epoxy-2,3-dimethylcyclohexan-1-one (5a). To a solution of (5*R*)-**10a** (46 mg, 0.23 mmol) and 6 M aqueous NaOH (0.021 mL) in MeOH (5 mL) was added 30% H_2O_2 (0.07 mL). The mixture was stirred at 2–5 °C for 2 h and at room temperature for 1 h and extracted with benzene–AcOEt (1:1). The usual workup and chromatography (SiO_2; hexane–AcOEt, 7:1) gave 44 mg (89%) of (5*R*)-**5a**: mp 109–110 °C (from hexane); $[\alpha]^{25}_D$ +49° (*c* 1.7); IR (Nujol) 1700 cm^{-1} (C=O); ^1H NMR δ 1.42, 1.47, 1.52, 1.59 (s, 12, CH_3), 1.20–2.75 (m, 5, CH_2, CH); ^{13}C NMR δ 11.5 (q, C-3 Me), 19.4 (q, C-2 Me), 30.5 (q), 30.7 (q), 31.7 (t, C-4), 38.6 (t, C-6), 39.8 (d, C-5), 63.4 (s, C-3), 64.3 (s, C-2), 72.4 (s, CCl), 205.6 (s, C-1). Anal. Calcd for $C_{11}H_{17}ClO_2$; C, 60.97; H, 7.91. Found: C, 61.18; H, 7.97.

Similarly, (5*S*)-**5b** was obtained in 89% yield from (5*S*)-**10b**: mp 109–110 °C (from hexane); $[\alpha]^{25}_D$ −49.2° (*c* 1.8). Anal. Calcd for $C_{11}H_{17}ClO_2$: C, 60.97; H, 7.91. Found C, 61.13; H, 8.07.

(5*S*)-5-(1-Chloro-1-methylethyl)-2,3-epoxy-2-methylcyclohexan-1-one (6a). Similar epoxidation of **13a**[9] ($[\alpha]^{30}_D$ +43.1° (*c* 4.22); 138 mg, 0.74 mmol) as described for **5a** gave 130 mg (87%) of **6a**: mp 73.5 °C (from hexane); $[\alpha]^{23}_D$ −64.2° (*c* 3.8); IR (Nujol) 1700 (C=O), 1370, 1235, 1112, 884, 810 cm^{-1}; ^1H NMR

(15) Trost, B. M.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 7910.
(16) Andrieux, J.; Barton, D. H. R.; Patin, H. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 359.

(17) We are grateful to Dr. H. Tsuruta, Takasago Perfumary Co., and Mr. M. Ishihara, Shiono Koryo Co., for generous gifts of (−)- and (+)-carvones used in this work.

δ 1.20–2.80 (m, 5, CH_2, CH), 1.40, 1.53, 1.59 (s; 9, CH_3), 3.48 (m, 1, CHO). Anal. Calcd for $C_{10}H_{15}ClO_2$: 59.26; H, 7.46. Found: C, 59.43; H, 7.35.

Similarly, (5*R*)-**6b** was obtained in 87% yield from **13b**[9] ($[\alpha]^{30}_D$ −43.0° (*c* 3.73)): mp 73.5–74.0 °C; $[\alpha]^{19}_D$ +64.5° (*c* 4.0). Anal. Calcd for $C_{10}H_{15}ClO_2$: C, 59.26; H, 7.46. Found: C, 59.53; H, 7.60.

(5*S*)-5-(1-Chloro-1-methylethyl)-3-hydroxy-2-methoxy-2-methylcyclohexan-1-one (14a) and (5*S*)-5-(1-Chloro-1-methylethyl)-2-hydroxy-3-methoxy-2-methylcyclohexan-1-one (15a). A solution of **6a** (200 mg, 0.99 mmol) in MeOH (3 mL) containing concentrated H_2SO_4 (0.1 mL) or 70% $HClO_4$ (0.1 mL) was stirred at room temperature for 12 h, quenched with aqueous $NaHCO_3$, and worked up in the usual manner to give 190 mg (82%) of a mixture of **14a** and **15a** (R_f 0.32; Merck F254, hexane–AcOEt, 2:1).

Separation of 14a and 15a via Their Tetrahydropyranyl Ethers. A solution of **14a** and **15a** (209 mg, 0.89 mmol), dihydropyran (209 mg, 2.5 mmol), and PPTS (10 mg) in CH_2Cl_2 (2 mL) was stirred at room temperature for 12 h. The usual workup and chromatography (SiO_2; hexane–AcOEt, 5:1) gave 176 mg (62%) of the THP ether of **14a** (R_f 0.65 and 0.55) and 68.6 mg (24%) of the THP ether of **15a** (R_f 0.4). The subsequent hydrolysis of each THP ether with PPTS in EtOH at 60 °C for 10 h gave **14a** (90%) and **15a** (85%), respectively. **14a**: bp 94–95 °C (0.02 mm); $[\alpha]^{23}_D$ −17.5° (*c* 3.3); IR (neat) 3460 (OH), 2814, 1715 (C=O), 1395, 1377, 1150, 1125, 1075, 1045 cm^{-1}; ^1H NMR δ 1.26 (s, 3, CH_3), 1.55 (s, 6, CH_3), 1.65–2.65 (m, 5, CH_2, CH), 2.37 (br s, 1, OH), 3.12 (s, 3, OCH_3), 4.03 (m, 1, CHO). Anal. Calcd for $C_{11}H_{19}ClO_3$: C, 56.29; H, 8.16. Found: C, 56.45; H, 8.31. **15a**: bp 77–78 °C (0.02 mm); $[\alpha]^{29}_D$ −61.5° (*c* 4.2); IR (neat) 3460 (OH), 1708 (C=O), 1382, 1364, 1135, 1005, 980 cm^{-1}; ^1H NMR δ 1.32 (s, 3, CH_3), 1.50–2.70 (m, 5, CH_2, CH), 1.57, 1.60 (s, 6, CH_3), 3.05–3.35 (m, 1, CHO), 3.50 (s, 3, OCH_3), 3.96 (br, 1, OH). Anal. Calcd for $C_{11}H_{19}ClO_3$: C, 56.29; H, 8.16. Found: C, 56.39; H, 8.33.

Similarly, **14b** and **15b** were obtained in 45% and 16% yields from **6b**. **14b**: bp 94–95 °C (0.02 mm); $[\alpha]^{27}_D$ +17.4° (*c* 2.32). Anal. Calcd for $C_{11}H_{19}ClO_3$: C, 56.29; H, 8.16. Found: C, 56.45; H, 8.21. **15b**: bp 77–78 °C (0.02 mm); $[\alpha]^{20}_D$ +62.6° (*c* 3.1). Anal. Calcd for $C_{11}H_{19}ClO_3$: C, 56.29; H, 8.16. Found: C, 56.42; H, 8.26.

(5*S*)-5-(1-Chloro-1-methylethyl)-3-hydroxy-2-methoxy-2,3-dimethylcyclohexan-1-one (11b) and (5*S*)-5-(1-Chloro-1-methylethyl)-2-hydroxy-3-methoxy-2,3-dimethylcyclohexan-1-one (12b). Similar acid-catalyzed methanolysis of **5b** as described for **14a** and **15a** gave a mixture of **11b** (39%) and **12b** (55%). **11b**: bp 91–93 °C (0.04 mm); $[\alpha]^{17}_D$ −3.6° (*c* 1.7); IR (neat) 3430 (OH), 2820, 1717 (C=O), 1370, 1040, 915, 865 cm^{-1}; ^1H NMR δ 1.22, 1.30, 1.58, 1.59 (s, 12, CH_3), 1.50–2.76 (m, 6, CH_2, CH, OH), 3.12 (s, 3, OCH_3). Anal. Calcd for $C_{12}H_{21}ClO_3$: C, 57.94; H, 8.51. Found: C, 58.08; H, 8.74. **12b**: mp 53.0–54.0 °C (from hexane); $[\alpha]^{17}_D$ −4.36° (*c* 0.9); IR (Nujol) 3440, 3320 (OH), 1712 (C=O), 1372, 1148, 1038, 798 cm^{-1}; ^1H NMR δ 1.10, 1.41, 1.57, 1.61 (s, 12, CH_3), 1.50–2.22 (m, 3, CH_2, CH), 2.55–2.76 (m, 2, CH_2CO), 3.41 (s, 3, OCH_3), 3.96 (s, 1, OH). Anal. Calcd for $C_{12}H_{21}ClO_3$: C, 57.94; H, 8.51. Found: C, 58.18; H, 8.61.

Electrolysis Apparatus. An undivided cell was equipped with a gas lead pipe, a stirring bar, a thermometer, and two platinum foil electrodes (3 cm^2), being placed parallel to each other and 4 mm apart. The vessel was immersed in an ice–water bath at 2–5 °C. The integration of the current was carried out by accumulating the amount of electric current recorded on the time–current diagrams. The typical experimental procedure is as follows.

Methyl (3*R*)-3-(1-Chloro-1-methylethyl)-5-oxohexanoate (3a). A solution of (5*R*)-**5a** (750 mg, 3.46 mmol) in MeOH (14 mL) and AcOEt (2 mL) containing $LiClO_4$ (80 mg) as a supporting electrolyte was electrolyzed under a constant current at 30 mA/cm^2 (applied voltage 6.0–8.0 V, cell voltage 2.10–2.23 V vs. Ag/0.1 M AgCl) at 2–5 °C. After 12 F/mol of electricity was passed, the reaction mixture was concentrated and the residue was taken up in benzene–AcOEt (1:1). The usual workup and chromatography (SiO_2; hexane–AcOEt, 6:1) gave 665 mg (87%) of (3*R*)-**3a**: bp 71–73 °C (2.5 mm); $[\alpha]^{17}_D$ +4.28° (*c* 1.1); IR (neat) 1739 (ester C=O), 1720 cm^{-1} (C=O); ^1H NMR δ 1.59 (s, 6, CH_3), 2.05–3.10 (m, 5, CH_2, CH), 2.21 (s, 3, $COCH_3$), 3.67 (s, 3, OCH_3); ^{13}C NMR δ 30.0 (q, C-6), 30.7 (q), 31.2 (q), 36.3 (t, C-4), 42.0 (d, C-3), 45.6 (t, C-2), 51.8 (q, OMe), 73.3 (s, CCl), 170.3 (s, C-1), 206.6 (s, C-5). Anal. Calcd for $C_{10}H_{17}ClO_3$: C, 54.42; H, 7.77. Found: C, 54.59; H, 7.82.

Similarly, (3*S*)-**3b** was obtained in 88% yield by the electrolysis of (5*S*)-**5b**: bp 71–73 °C (2.5 mm); $[\alpha]^{10}_D$ −4.24° (*c* 1.7). Anal. Calcd for $C_{10}H_{17}ClO_3$: C, 54.42; H, 7.77. Found: C, 54.60; H, 7.75.

Methyl (3*S*)-3-(1-chloro-1-methylethyl)-5,5-dimethoxypentanoate (4a): bp 78–79 °C (0.02 mm); $[\alpha]^{29}_D$ −0.6° (*c* 3.04); IR (neat) 2804, 1732 (ester C=O), 1432, 1385, 1369, 1192, 1152, 1110, 1054 cm^{-1}; ^1H NMR δ 1.25–2.70 (m, 5, CH_2, CH), 1.57 (s, 6, CH_3), 3.30 (s, 6, OCH_3), 3.68 (s, 3, OCH_3), 4.41 (t, *J* = 6 Hz, 1, CHO); ^{13}C NMR δ 30.5 (q), 30.8 (q), 35.0 (t), 36.5 (t), 43.5 (d), 51.7 (q), 52.8 (q), 53.7 (q), 74.0 (s), 104.0 (d), 173.5 (s). Anal. Calcd for $C_{11}H_{21}ClO_4$: C, 52.28; H, 8.38. Found: C, 52.25; H, 8.23. (3*R*)-**4a**: bp 78–79 °C (0.02 mm); $[\alpha]^{29}_D$ +0.6° (*c* 2.4). Anal. Calcd for $C_{11}H_{21}ClO_4$: C, 52.28; H, 8.38. Found: C, 52.52; H, 8.48.

(5*R*)-5-(1-Chloro-1-methylethyl)-2,2,7,7-tetramethoxyheptan-3-one (17b): bp 95–98 °C (0.03 mm); $[\alpha]^{28}_D$ −1.1° (*c* 1.8); IR (neat) 2810, 1710 (C=O), 1370, 1125, 1040 cm^{-1}; ^1H NMR δ 1.10–3.00 (m, 5, CH_2, CH), 1.37 (s, 3, CH_3), 1.50, 1.55 (s, 6, CH_3), 3.20, 3.22, 3.24, 3.29 (s, 12, OCH_3), 4.32 (t , *J* = 6 Hz, 1, CHO). Anal. Calcd for $C_{14}H_{27}ClO_5$: C, 54.10; H, 8.76. Found: C 54.22; H, 8.87.

Methyl (3*R*)-3-(1-chloro-1-methylethyl)-5-methoxy-6-oxoheptanoate (18b): bp 75–78 °C (0.02 mm); $[\alpha]^{28}_D$ −44.2° (*c* 1.7); IR (neat) 2810, 1735 (ester C=O), 1708 (C=O), 1435, 1374, 1108, 1005 cm^{-1}; ^1H NMR δ 1.25–2.75 (m, 5, CH_2, CH), 1.57 (s, 6, CH_3), 2.17 (s, 3, $COCH_3$), 3.34 (s, 3, OCH_3), 3.61 (d, d, *J* = 12, 4 Hz, 1, CHO), 3.68 (s, 3, OCH_3). Anal. Calcd for $C_{12}H_{21}ClO_4$: C, 54.44; H, 8.00. Found: C, 54.61; H, 8.17.

(3*R*)-3-(1-Chloro-1-methylethyl)-5-methylhexan-5-olide (2a). To a solution of (3*R*)-**3a** (100 mg, 0.45 mmol) in ether (5 mL) was added a solution of MeMgI, prepared from MeI (160 mg, 1.13 mmol) and Mg (22 mg, 0.9 mmol) in ether (3 mL) at −20 °C. The mixture was stirred at −20 °C for 20 min, quenched with aqueous NH_4Cl, and extracted with benzene–AcOEt (1:1). The usual workup and chromatography (SiO_2; hexane–AcOEt, 6:1) gave 76 mg (82%) of (3*R*)-**2a**: mp 86–87 °C (from hexane); $[\alpha]^{20}_D$ +15° (*c* 1.5); IR (Nujol) 1718 cm^{-1} (ester C=O); ^1H NMR δ 1.25–2.85 (m, 5, CH_2, CH), 1.39, 1.48 (s, 6, CH_3), 1.57, 1.59 (s, 6, CH_3); ^{13}C NMR δ 27.4 (q), 29.9 (q), 30.4 (q), 30.8 (q), 31.6 (t, C-4), 36.2 (t, C-2), 41.1 (d, C-3), 71.5 (s, CCl), 81.1 (s, C-5), 170.7 (s, C-1). Anal. Calcd for $C_{10}H_{17}ClO_2$: C, 58.68; H, 8.37. Found: C, 58.80; H, 8.59.

Similarly, (3*S*)-**2b** was obtained in 83% yield from (3*S*)-**3b**: mp 86–87 °C (from hexane); $[\alpha]^{17}_D$ −15.2° (*c* 1.3). Anal. Calcd for $C_{10}H_{17}ClO_2$: C, 58.68; H, 8.37. Found: C, 58.80; H, 8.50.

Methyl (*E*)-4,4-Dimethyl-6-oxo-2-heptenoate (24). A solution of **2a** (136 mg, 0.62 mmol) and DBU (240 mg, 1.56 mmol) in toluene (3 mL) was heated at 110 °C for 5 h. The usual workup and chromatography (SiO_2; hexane–AcOEt 4:1) gave 103 mg (91%) of **24**: bp 102–103 °C (23 mm); IR (neat) 1720 (ester C=O), 1704 (C=O), 1650 cm^{-1} (C=C); ^1H NMR δ 1.16 (s, 6, CH_3), 2.09 (s, 3, $COCH_3$), 2.52 (s, 2, CH_2), 3.71 (s, 3, OCH_3), 5.75 (d, *J* = 16 Hz, 1, HC=C), 7.05 (d, *J* = 16 Hz, 1, HC=C). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.11; H, 8.75.

(1*S*,3*R*)-Dihydrochrysanthemolactone (23a). To a solution of (3*R*)-**2a** (36.4 mg, 0.18 mmol) in THF (3 mL) was added a solution of $LiN(i\text{-}Pr)_2$ prepared from a hexane solution of 1.6 M BuLi (0.28 mL, 0.45 mmol) and $i\text{-}Pr_2NH$ (46.5 mg, 0.46 mmol) in THF (4 mL). The mixture was stirred at −78 °C for 5 min and at room temperature for 1 h, quenched with water, and worked up in the usual manner to give 29 mg (97%) of (1*S*,3*R*)-**23a**: mp 82–83 °C (from hexane) (lit.[5b] 82–83 °C); $[\alpha]^{25}_D$ −77.3° (*c* 1.4) (lit. −72°,[5b] −77.24°[5c]); ^{13}C NMR δ 15.9 (q), 22.7 (d, C-3), 24.4 (q), 26.2 (s), 27.1 (q), 27.3 (d, C-2), 28.9 (q), 30.2 (t, C-4), 83.2 (s, C-5), 170.9 (s, C-1).

Similarly, (1*R*,3*S*)-**23b** was obtained in 96% yield from (3*S*)-**2b**: mp 82–83 °C (from hexane) (lit.[5a] mp 83 °C); $[\alpha]^{22}_D$ +77.6° (*c* 1.8) (lit.[5a] $[\alpha]^{22}_D$ +77°).

Methyl (+)-*trans*-Chrysanthemate ((1*R*,3*R*)-1a, R = Me). A solution of (1*S*,3*R*)-**23a** (100 mg, 0.6 mmol) and NaOH (109 mg, 2.7 mmol) in diethylene glycol (3 mL) was heated to 230–235 °C for 7 h. The esterification of the crude product with CH_2N_2 gave 79 mg (73%) of a mixture of (1*R*,3*R*)-**1a** (R = Me, 79.2%), (1*S*,3*R*)-**27a** (9.8%), and (1*S*,3*R*)-**26a** (R = Me, 11%).[5c] The analysis and their separation were carried out by HPLC (a Waters Associates Model 6000A solvent delivery system: column, μ-

Porasil 7.8 mm × 30 cm; hexane–AcOEt, 80:1, 1.5 mL/min; room temperature). **1a** (R = Me; t_R = 16.8 min): bp 97–99 °C (10 mm) [lit.[5c] bp 120–125 °C (5 mm)]; $[\alpha]^{23}_D$ +20.69° (*c* 1.1) (lit. $[\alpha]^{23}_D$ +20.74°,[18] +13.27°[5c]; ^{13}C NMR δ 18.5 (q), 20.4 (q), 22.2 (q), 25.5 (q), 28.6 (s), 32.8 (d), 34.7 (d), 51.4 (q), 121.1 (d), 135.5 (s), 173.0 (s). IR and ^1H NMR spectra data were identical with those reported.[19]

Similarly, the (–)-trans isomer (1*S*,3*S*)-**1b** (R = Me) was obtained in 59% yield from (1*R*,3*S*)-**23b**: bp 98–99 °C (10 mm); $[\alpha]^{22}_D$ –20.82 ° (*c* 1.0) [lit.[20] $[\alpha]^{22}_D$ –19° (EtOH)].

(4*R*)-4-(1-Chloro-1-methylethyl)-2-methoxy-6,6-dimethyltetrahydropyran (19a). To a solution of **4a** (700 mg, 2.77 mmol) in ether (8 mL) was added 0.95 M MeLi in ether (6.9 mL, 6.6 mmol) at –60 °C. The mixture was warmed gradually to –35 °C over about 30 min, quenched with aqueous NH_4Cl, and worked up in the usual manner. The crude product was dissolved in MeOH (3 mL) containing *p*-TsOH (3 mg) and stirred at room temperature for 1 h. The usual workup and chromatography (SiO_2; hexane–AcOEt, 5:1) gave 460 mg (75%) of **19a**: bp 88–89 °C (4 mm); IR (neat) 1370, 1198, 1122, 1056 cm^{-1}; ^1H NMR δ 1.10–2.40 (m, 5, CH_2, CH), 1.24, 1.31, 1.36 (s, 6, CH_3), 1.54 (s, 6, CH_3), 3.37, 3.46 (s, 3, OCH_3), 4.47–4.82 (m, 1, CHO). Anal. Calcd for $C_{11}H_{21}ClO_2$: C, 59.85; H, 9.59. Found: C, 59.86; H, 9.46.

Similarly, (4*S*)-**19b** was obtained in 75% yield from **4b**; bp 88–89 °C (4 mm). Anal. Calcd for $C_{11}H_{21}ClO_2$: C, 59.85; H, 9.59. Found: C, 59.92; H, 9.42.

Conversion of 19a to 2a. A solution of **19a** (190 mg, 0.86 mmol) in AcOH (1 mL), H_2O (0.5 mL), and 5% HCl (0.2 mL) was stirred at room temperature for 10 h. The usual workup and chromatography (SiO_2; hexane–AcOEt, 2:1) gave 137 mg (77%) of **20a**: bp 78–80 °C (0.025 mm); IR (neat) 3370 cm^{-1} (OH); ^1H NMR δ 1.00–2.60 (m, 5, CH_2, CH), 1.24, 1.33 (s, 6, CH_3), 1.57 (s, 6, CH_3), 3.95 (br, 1, OH), 4.73–5.45 (m, 1, CHO). Without further purification, **20a** (137 mg, 0.66 mmol) in ether (4 mL) was oxidized with a solution of CrO_3 (198 mg, 1.98 mmol) in 5% H_2SO_4 (2.0 mL) at 0 °C for 30 min to give 120 mg (89%) of **2a** after chromatography (SiO_2; hexane–AcOEt, 5:1): mp 86–87 °C; $[\alpha]^{26}_D$ +15.5° (*c* 2.44).

Similarly, **2b** was obtained in 68% yield from **19b**: mp 86–87 °C; $[\alpha]^{21}_D$ –15.3° (*c* 0.75).

Methyl Hydrogen (3*S*)-3-(1-Chloro-1-methylethyl)-glutarate (22a). A solution of **4a** (510 mg, 2.02 mmol) in AcOH (3 mL), H_2O (1.5 mL), and 5% HCl (0.3 mL) was stirred at 2–5 °C for 45 min. The usual workup and chromatography (SiO_2; hexane–AcOEt, 10:1) gave 376 mg (90%) of **21a**: $[\alpha]^{28}_D$ –3.7° (*c* 1.9); IR (neat) 2710, 1730 (ester C=O), 1715 (C=O), 1435, 1375, 1110 cm^{-1}; ^1H NMR δ 1.57 (s, 6, CH_3), 2.05–3.10 (m, 5, CH_2, CH), 3.66 (s, 3, OCH_3), 9.74 (t, *J* = 1 Hz, 1, CHO). Without further purification, the oxidation of **21a** (220 mg, 1.06 mmol) in ether (5 mL) with a solution of CrO_3 (320 mg, 3.2 mmol) in 5% H_2SO_4 (3.2 mL) at 4–5 °C for 2 h gave 192 mg (81%) of **22a** after chromatography (SiO_2; hexane–AcOEt, 1:1): $[\alpha]^{29}_D$ +1.6° (*c* 1.8); IR (neat) 3600–2600 (COOH) 1730 (ester C=O), 1708 (COOH), 1370, 1112 cm^{-1}; ^1H NMR δ 1.59 (s, 6, CH_3), 2.63–3.00 (m, 5, CH_2, CH), 3.65 (s, 3, OCH_3), 8.40 (br, 1, COOH). Anal. Calcd for $C_9H_{15}ClO_4$: C, 48.55; H, 6.79. Found: C, 48.68; H, 6.91.

Similarly, **22b** was obtained in 80% yield from **4b** via **21b** ($[\alpha]^{19}_D$ +3.5° (*c* 3.14)); $[\alpha]^{29}_D$ –1.29 (*c* 2.2). Anal. Calcd for $C_9H_{15}ClO_4$; C, 48.55; H, 6.79. Found: C, 48.76; H, 6.97.

Conversion of 22a to 2a. To 0.68 M MeLi in ether (5.9 mL, 4.0 mmol) was added a solution of **22a** (90 mg, 0.4 mmol) in ether (2 mL) at –70 °C. After being stirred at –70 °C for 20 min, the mixture was warmed gradually to –30 °C over about 40 min, quenched with 10% NH_4Cl, and extracted with benzene–AcOEt (1:1). The usual workup and chromatography (SiO_2; hexane–AcOEt, 1:1) gave **2a**: 58 mg (71%); mp 86–87 °C; $[\alpha]^{26}_D$ +15.3 ° (*c* 3.2).

Similarly, **2b** was obtained in 70% yield from **22b**: mp 86–87 °C; $[\alpha]^{26}_D$ –15.3° (*c* 2.5).

Methyl (1*R*,3*S*)-3-(2-Hydroxy-2-methylpropyl)-2,2-dimethylcyclopropane-1-carboxylate (25b). Hydrolysis of (1*R*,3*S*)-**23b** (145 mg, 0.86 mmol) in MeOH (2 mL)–KOH (110 mg, 1.96 mmol)–H_2O (0.6 mL) was carried out at 40–45 °C for 48 h, and the mixture was acidified with cold 5% HCl and extracted with benzene–AcOEt (1:1). The usual workup, esterification with CH_2N_2 in ether, and chromatography (SiO_2; hexane–AcOEt, 3:1) gave 167 mg (97%) of (1*R*,3*S*)-**25b**: bp 84–86 °C (1.5 mm) [lit.[5h] bp 110 °C (1 mm)]; $[\alpha]^{23}_D$ –21.5° (*c* 1.9) (lit.[5h] $[\alpha]^{23}_D$ –16.3 °); ^{13}C NMR δ 14.6 (q), 25.0 (s), 28.7, 28.85, 28.93, 29.4 (2 C), 36.7 (t), 51.1 (q), 70.8 (s), 172.7 (s).

Similarly, (1*S*,3*R*)-**25a** was obtained in 96% yield from (1*S*,3*R*)-**23a**: bp 85–87 °C (1.5 mm) [lit.[5f] bp 105 °C (3.5 mm)]; $[\alpha]^{23}_D$ +21.0° (*c* 2.1) (lit.[5f] $[\alpha]^{23}_D$ +16.2°).

Methyl (+)-*cis*-Chrysanthemate ((1*R*,3*S*)-26b, R = Me). To a solution of (1*R*,3*S*)-**25b** (180 mg, 0.9 mmol) in HMPA (1.5 mL) was added $POCl_3$ (500 mg, 3.3 mmol). After the mixture was stirred at 50 °C for 1 h, pyridine (530 mg, 6.7 mmol) was added, and the mixture was heated at 50 °C for 1 h, at 75 °C for 30 min, and at 100 °C for 45 min. The reaction mixture was poured into cold aqueous $NaHCO_3$ and extracted with benzene–AcOEt (1:1). The usual workup and chromatography (SiO_2; hexane–AcOEt, 10:1) gave 156 mg (95%) of a 2:1 mixture of (1*R*,3*S*)-**27b** and (1*R*,3*S*)-**26b** (R = Me). The analytical sample of (1*R*,3*S*)-**27b** was obtained by preparative GLC (silicon GE, 10%, coated on 80–100-mesh Chamelite, 4 mm × 6 m column, 130 °C, carrier gas H_2 at 15 mL/min, t_R = 7.8 min): bp 96–98 °C (10 mm); $[\alpha]^{18}_D$ –42.1° (*c* 0.65); IR (neat) 3070, 1728 (ester C=O), 1648 (C=C), 1437, 1378, 1200, 1168, 1130, 1088, 885, 852 cm^{-1}; ^1H NMR δ 1.16–1.59 (m, 2, CH), 1.17 (s, 3, CH_3), 1.19 (s, 3, CH_3), 1.75 (br s, 3, CH_3C=C), 2.38 (d, *J* = 7 Hz, 2, CH_2), 3.62 (s, 3, OCH_3), 4.74 (m, 2, H_2C=C); ^{13}C NMR δ 14.2 (q), 23.1 (q), 25.5 (s), 28.4 (q), 29.0 (d), 31.0 (t), 32.1 (d), 51.0 (q), 109.3 (t), 145.6 (s), 172.3 (s). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.46; H, 9.87. Without separation of the double bond isomers, the mixture was dissolved in 2-propanol (1.7 mL) containing $RhCl_3 \cdot 3H_2O$ (3 mg, 0.01 mmol) and heated at 90–95 °C for 12 h. The mixture was concentrated, and the residue was chromatographed (SiO_2; hexane–AcOEt, 10:1) to give 153 mg (98%) of (1*R*,3*S*)-**26b** (R = Me) contaminated with 4% of (1*R*,3*S*)-**27b** and 6% of unidentified compounds. An analytical sample of (1*R*,3*S*)-**26b** (R = Me) was obtained by preparative HPLC (t_R 15.2 min) under the same conditions as for **1** (R = Me): bp 95–97 °C (10 mm) [lit.[5h] bp 105 °C (10 mm)]; $[\alpha]^{21}_D$ +59.8° (*c* 1.2) (lit.[5h] $[\alpha]^{21}_D$ +41°); ^{13}C NMR δ 14.8 (q), 18.3 (q), 25.9 (q), 26.4 (s), 28.8 (q), 31.0 (d), 32.3 (d), 51.0 (q), 118.1 (d), 134.6 (s), 171.6 (s). IR and ^1H NMR spectral data were identical with those reported.[19]

Similarly, the (–)-cis isomer (1*S*,3*R*)-**26a** (R = Me) was obtained in 83% yield from (1*S*,3*R*)-**25a**: bp 95–97 °C (10 mm); $[\alpha]^{21}_D$ –59.1° (*c* 1.8) (lit.[5e] $[\alpha]^{21}_D$ –41.5°).

The treatment of a 2:1 mixture of **27b** and **26b** (R = Me) with $RhCl_3 \cdot 3H_2O$ in MeOH gave a 47:53 mixture of **26b** (R = Me) and **28b** in 98% yield. An analytical sample of **28b** was obtained by preparative GLC (silicon GE, 10%, coated on 80–100-mesh Chamelite, 4 mm × 4 m column, 120 °C, H_2 at 30 mL/min, t_R = 11.6 min): bp 111–113 °C (9 mm); $[\alpha]^{18}_D$ –16.1° (*c* 0.7); IR (neat) 2804, 1723 (ester C=O), 1435, 1378, 1219, 1170, 1139, 1128, 1080, 847 cm^{-1}; ^1H NMR δ 1.12 (s, 6, CH_3), 1.16 (s, 3, CH_3), 1.17 (s, 3, CH_3), 1.20–1.56 (m, 2, CH), 1.70 (dd, *J* = 6, 3 Hz, 2, CH_2), 3.17 (s, 3, OCH_3), 3.60 (s, 3, OCH_3); ^{13}C NMR δ 14.6 (q), 24.7 (q), 25.0 (q), 25.1 (q), 28.6, 28.9, 29.0, 32.7 (t), 49.1 (q), 50.9 (q), 74.6 (s), 172.5 (s). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.26; H, 10.37.

2,3-Epoxy-2-methyl-3-nonylcyclopentan-1-one. To a solution of 3-ethoxy-2-methyl-2-cyclopenten-1-one (340 mg, 2.43 mmol) in ether (5 mL) was added a solution of *n*-$C_9H_{19}MgBr$ prepared from Mg (177 mg, 7.38 mmol) and bromononane (1.5 g, 7.24 mmol) in ether (7 mL) at 0 °C. After being stirred at room temperature for 3 h, the mixture was quenched with aqueous NH_4Cl and worked up in the usual manner to give 380 mg (70%) of 2-methyl-3-nonyl-2-cyclopenten-1-one: bp 132–134 °C (1 mm); IR (neat) 1700 (C=O), 1642 cm^{-1} (C=C); ^1H NMR δ 0.89 (t, 3, CH_3), 1.29 (br s, 14, CH_2), 1.70 (s, 3, CH_3), 2.25–2.65 (m, 6, CH_2). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.70. Found: C, 81.09; H, 11.86. The epoxidation of the enone with 30% H_2O_2–6 M NaOH in MeOH gave 2,3-epoxy-2-methyl-3-nonylcyclopentan-1-one: 57% yield; bp 137–139 °C (1.5 mm); IR (neat) 1740 cm^{-1} (C=O); ^1H

(18) Staudinger, H.; Ruzicka, L. *Helv. Chim. Acta* **1924**, *7*, 201.
(19) Bramwell, A. F.; Crombie, L.; Hemesley, P.; Pattenden, G.; Elliott, M.; Janes, N. F. *Tetrahedron* **1969**, *25*, 1727.
(20) Martel, J. Fr. Addn. 2076204; *Chem. Abstr.* **1972**, *77*, 34037. Martel, J. Nihhon Tokkyo Koho, 47–14563, 1972.

NMR δ 0.89 (t, 3, CH_3), 1.29 (br, 14, CH_2), 1.33 (s, 3, CH_3), 1.40–2.58 (m, 6, CH_2). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.58; H, 10.85.

Dimethyl (3*R*)-3-methyladipate: bp 102–104 °C (2 mm); $[\alpha]_D^{28}$ +6.1° (*c* 2.22) (lit.[21a] $[\alpha]^{28}_D$ +3.49°).

(21) (a) *Beilstein 4th ed. Hauptwerk* **1920**, *No. 176*, 674. (b) Semmler, F. W. *Chem. Ber.* **1892**, *25*, 3513.

Dimethyl 4-oxononanedioate: bp 118–119 °C (1.5 mm); IR (neat) 1733 (ester C=O), 1710 cm^{-1} (C=O); ^1H NMR δ 1.45–1.76 (m, 4, CH_2), 2.18–2.82 (m, 8, $COCH_2$), 3.63 (s, 6, OCH_3). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.37; H, 7.95.

Methyl 4-oxotridecanoate: bp 132–133 °C (12 mm); IR (neat) 1739 (ester C=O), 1717 cm^{-1} (C=O); ^1H NMR δ 0.89 (t, 3, CH_3), 1.27 (br s, 14, CH_2), 2.00–2.70 (m, 6, $COCH_2$), 3.67 (s, 3, OCH_3). Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.30; H, 10.72.

New Binuclear NMR Shift Reagents for Olefins and Aromatics

Thomas J. Wenzel* and Daniel R. Lalonde, Jr.

Department of Chemistry, Bates College, Lewiston, Maine 04240

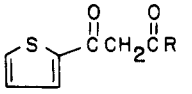
Received July 20, 1982

Binuclear complexes formed in solution from a lanthanide(III) β-diketonate and silver(I) β-diketonate have been studied as NMR shift reagents for olefinic and aromatic compounds. The shift reagent properties of a variety of silver β-diketonates with the praseodymium(III) or ytterbium(III) chelates of the ligands 4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione, H(tta), and 4,4,5,5,6,6,6-heptafluoro-1-(2-thienyl)-1,3-hexanedione, H(hfth), have been evaluated and compared to binuclear shift reagents that have already been reported in the literature. The complexes of silver with the tta and hfth ligands, when employed with certain chiral lanthanide chelates, have resulted in better resolution of the resonances of *d* and *l* enantiomers than previously reported chiral binuclear complexes. The Ag(tta) and Ag(hfth) complexes are considerably more stable than the silver β-diketonates used in prior studies. Representative spectra of the resolution achieved for a mixture of *dl*-camphene are presented.

A wide range of oxygen- and nitrogen-containing compounds have been studied with lanthanide nuclear magnetic resonance shift reagents.[1-7] Recently, binuclear shift reagents suitable for use with olefins, aromatics, halogenated compounds, and phosphines have been reported.[8-13] The binuclear reagents are formed in solution from a lanthanide(III) β-diketonate and silver(I) β-diketonate. The active species is believed to be an ion pair between Ag(I) and a lanthanide tetrakis(chelate) anion;[9] however, other structures are possible for these binuclear complexes.[14] The silver in this complex bonds to the olefinic or aromatic substrate, and the NMR spectrum of the substrate exhibits shifts because of the lanthanide ion. We report a new set of binuclear complexes that involve silver compounds with the ligands 4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione, H(tta), and 4,4,5,5,6,6,6-heptafluoro-1-(2-thienyl)-1,3-hexanedione, H(hfth). In certain instances, binuclear complexes with one or more of these ligands produced better shifts in the NMR spectra of olefins or aromatics than the binuclear complexes already reported in the literature. In addition, these new silver β-diketonates appear to be more stable than the previously reported examples.[8-10]

Table I. Shifts in the Proton NMR Spectrum of Cyclohexene (0.1 M) in $CDCl_3$ with Various Yb(III) Shift Reagents (0.05 M)

shift reagent	olefin	α	β
$Yb(fod)_3/Ag(fod)$	5.41	3.13	2.41
$Yb(fod)_3/Ag(hfth)$	3.08	1.91	1.48
$Yb(fod)_3/Ag(tta)$	1.50	1.01	0.79
$Yb(hfth)_3/Ag(fod)$	1.74	1.18	0.94
$Yb(hfth)_3/Ag(tfa)$	0.75	0.61	0.51
$Yb(hfth)_3/Ag(hfth)$	1.67	1.12	0.90
$Yb(hfth)_3/Ag(tta)$	0.65	0.53	0.44
$Yb(tta)_3/Ag(fod$	0.02	0.23	0.22
$Yb(tta)_3/Ag(tfa)$	−0.25	0.06	0.12
$Yb(tta)_3/Ag(hfth)$	−0.21	0.09	0.14
$Yb(tta)_3/Ag(tta)$	−0.18	0.06	0.09



R = $-CF_2CF_2CF_3$

R = $-CF_3$

Results and Discussion

The nature of the interaction between the silver and the lanthanide in these binuclear complexes remains unknown.

(1) Sievers, R. E., Ed.; "Nuclear Magnetic Resonance Shift Reagents"; Academic Press: New York, 1973.
(2) Mayo, B. C. *Chem. Soc. Rev.* **1973**, *2*, 49.
(3) Cockerill, A. F.; Davies, G. L. O.; Harden, R. C.; Rackham, D. M. *Chem Rev.* **1973**, *73*, 553.
(4) Reuben, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1975**, *9*, 1.
(5) Flockhart, B. D. *CRC Crit. Rev. Anal. Chem.* **1976**, *6*, 69.
(6) Hofer, O. *Top. Stereochem.* **1976**, *9*, 111.
(7) Inagaki, F.; Tatsuo, M. *Prog. Nucl. Magn. Reson. Spectrosc.* **1980**, *14*, 67.
(8) Wenzel, T. J.; Bettes, T. C. Sadlowski, J. E.; Sievers, R. E. *J. Am. Chem. Soc.* **1980**, *102*, 5904.
(9) Wenzel, T. J.; Sievers, R. E. *Anal. Chem.* **1981**, *53* 393.
(10) Wenzel, T. J.; Sievers, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 382.
(11) Offermann, W.; Mannschreck, A. *Tetrahedron Lett.* **1981**, *22*, 3227.
(12) Smith, W. B. *Org. Magn. Reson.* **1981**, *17* 124.
(13) Krasutsky, P. A.; Yurchenko, A. G.; Radionov, V. N. *Tetrahedron Lett.* **1982**, *23*, 3719.
(14) Peters, J. A.; Schuyl, P. J. W.; Bovee, W. M. M. J.; Alberts, J. A.; van Bekkum, H. *J. Org. Chem.* **1981**, *46*, 2784.

0022-3263/83/1948-1951$01.50/0