Intramolecular Cyclization of (ω-Carboxyalkyl)sulfonium Salts. A Novel Synthesis of Macrocyclic Lactones

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A useful method for the synthesis of macrocyclic lactones using (ω-carboxyalkyl)sulfonium salts was developed. Base-catalyzed intramolecular cyclization of (ω-carboxyalkyl)diphenylsulfonium salts **2** gave simple macrocyclic lactones **6** in high yields at high dilution conditions. (ω-Carboxyalkyl)alkylphenylsulfonium salts **8** afforded simple macrocyclic lactone **6a** and alkyl carboxylates **9**. The reactions of (ω-carboxyalkyl)dialkylsulfonium salts **10** gave only esters without lactonization product **6a**. The cyclization of *S*-(ω-carboxyalkyl)thiolanium salts **3** and *S*-(ω-carboxyalkyl)-2-methylthiolanium salts **4** took place readily under similar conditions to afford sulfur-containing macrocyclic lactones **13** and **15**, respectively, in good yields. To investigate the reaction mechanism, sulfonium salt **25**, having an optically active carbon atom, was prepared. The intramolecular cyclization of **25** took place with an inversion of configuration at chiral carbon atom to give ricinelaidic acid lactone (**26**; optical purity 66%).

Macrocyclic lactones are attractive compounds, since they have biological activities and are useful as perfumes. A variety of synthetic approaches to macrocyclic lactones, involving mainly intramolecular esterification,[1] have been developed.[2,3] Although simple macrocyclic lactones have been prepared by many workers, it is difficult to prepare medium-membered rings such as 12- and 13-membered lactones in good yields because of the formation of diolides.[4]

We have been interested in the use of cyclic sulfur compounds for the synthesis of natural compounds.[5] It is well-known that alkylsulfonium salts act as good alkylating reagents for nucleophiles such as carboxylate anions. Badet et al. reported that alkyldiphenylsulfonium salts alkylated benzoic acid to give esters quantitatively.[6] Interestingly, Eliel et al. reported that alkylation of nucleophiles with *S*-alkylthiolanium salts occurred preferentially on the α-methylene carbon of the five-membered ring.[7] Therefore, we synthesized sulfonium salts **2** and **3**, which have a nucleophilic carboxyl group at the ω-carbon atom, and examined their intramolecular cyclization.

In this paper, we wish to report novel syntheses of sulfur-containing lactones from *S*-(ω-carboxyalkyl)-thiolanium salts **3** and simple macrocyclic lactones from (ω-carboxyalkyl)diphenylsulfonium salts **2** by intramolecular cyclization[8] and a possible mechanism of this reaction.

Table I. Lactonization of Sulfonium Salt 2a

solvt	condtn[a]	yield,[b] % 6a	7a
CH_2Cl_2[c]	A	6	46
CH_3CN	A	13	87
$(CH_3)_2C{=}O$	A	7	70
CH_2Cl_2[c]	B	17	26
CH_3CN	B	78	14
$(CH_3)_2C{=}O$	B	87	10

[a] A: A suspension of **2a** (1 mmol) and K_2CO_3 (3 mmol) in solvent (30 mL) was refluxed for 1 day. B: A solution (100 mL) of **2a** (2 mmol) was added to a basic solution (100 mL) containing K_2CO_3 (6 mmol) over 1.5 days under reflux conditions. [b] Isolated yield. [c] Unreacted salt **2a** (40%) was recovered.

Table II. Lactonization of Sulfonium Salts 2

sulfonium salt	ring size of 6	yield,[a] % 6	7
2a	12	87	10
2b	13	86	8
2c	14	86	0
2d	15	85	11
2e	16	92	trace

[a] Isolated yield.

Results and Discussion

Synthesis of Macrocyclic Lactones. Diphenylsulfonium salts **2** were prepared from diphenyl sulfide and ω-iodocarboxylic acids (**1a–e**) in the presence of silver perchlorate (eq 1). *S*-(ω-Carboxyalkyl)thiolanium salts **3** and **4** were readily prepared from tetrahydrothiophene or 2-methyltetrahydrothiophene and **1a–d** in the presence of silver perchlorate in acetonitrile (eq 2). Sulfonium salts **5** were similarly prepared from pentamethylene sulfide and **1a–d**.

The lactonization of **2a** was carried out in dichloromethane in the presence of potassium carbonate as a base under reflux conditions to give 12-membered lactone **6a** and diolide **7a** in 6% and 46% yields, respectively. On the other hand, under high-dilution conditions in acetone, the

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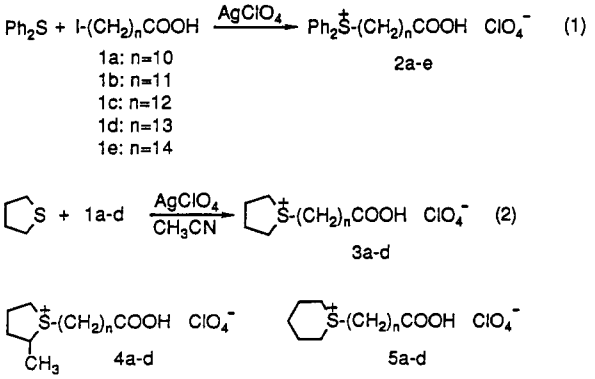
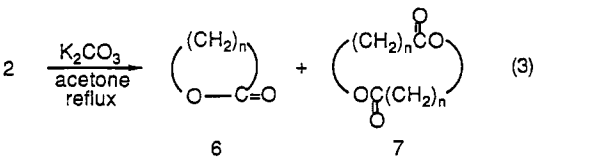


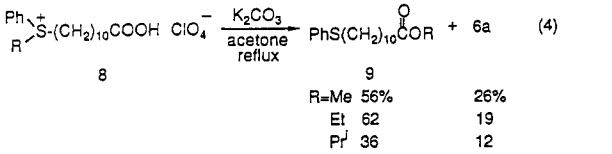
desired lactone **6a** was obtained in good yield (87%) and the formation of diolide **7a** was prevented (Table I). Therefore, subsequent cyclizations of diphenylsulfonium salts were carried out under these conditions.

The intramolecular cyclizations of diphenylsulfonium salts **2** (eq 3) took place readily to give simple macrocyclic lactones **6** in high yields (Table II). An important char-

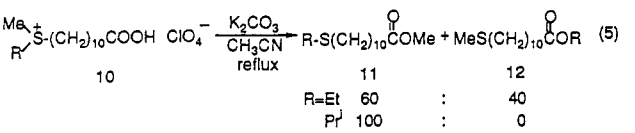


acteristic of this reaction is that 12- and 13-membered lactones **6a** and **6b**, which were not obtained in good yields by conventional methods,[4] are afforded in good yields. In this case the carboxylate anion can attack only the α-methylene carbon of the side chain.

Lactonization or Ester Formation Reaction from (ω-Carboxyalkyl)sulfonium Salts. Reactions of (ω-carboxyalkyl)diphenylsulfonium salts **2** afforded simple macrocyclic lactones **6** in high yields as described above. We also investigated an intramolecular cyclization of (ω-carboxyalkyl)alkylphenylsulfonium salts **8**. The reactions were carried out in acetone as solvent and under high-dilution conditions, and the results are shown in eq 4.



Sulfonium salts **8** gave lactone **6a** and esters **9**. (ω-Carboxyalkyl)dialkylsulfonium salts **10** very slowly give esters without lactone **6a** (eq 5). The relative reactivity



of alkyl groups on the sulfur atom of **8** and **10** estimated from the product ratio of esters was the following: methyl > ethyl > isopropyl. This result means that attack of carboxylate anions toward a sterically hindered secondary carbon atom is not favorable.[7a]

Synthesis of Sulfur-Containing Macrocyclic Lactones. The lactonization of **3a** was carried out in dichloromethane in the presence of potassium carbonate as a base under reflux conditions to give sulfur-containing 17-membered lactone **13a** and diolide **14a** (R = H) in 19% and 31% yields, respectively. On the other hand, under high-dilution conditions in acetone, the desired lactone **13a** was obtained in good yield (86%) and the formation of diolide **14a** (R = H) was prevented (Table III). Therefore, subsequent cyclizations of *S*-(ω-carboxyalkyl)thiolanium salts were carried out under these conditions.

Table III. Lactonization of Sulfonium Salt 3a

solvt	condtn[a]	yield,[b] % 13a	14a
CH_2Cl_2	A	19	31
CH_3CN	A	24	16
$(CH_3)_2C{=}O$	A	33	
CH_2Cl_2	B	73	0
CH_3CN	B	74	0
$(CH_3)_2C{=}O$	B	86	8

[a] A: A suspension of **3a** (2 mmol) and K_2CO_3 (6 mmol) in solvent (30 mL) was refluxed for 1 day. B: A solution (100 mL) of **3a** (2 mmol) was added to a basic solution (100 mL) containing K_2CO_3 (6 mmol) over 1.5 days under reflux conditions. [b] Isolated yield.

Table IV. Lactonization of Sulfonium Salts 3 or 4

sulfonium salt	ring size of 13 or 15	yield,[a] % 13 or 15	6	diolides[b]
3a	17	**13a** 86	3	8
3b	18	**13b** 81	10	2
3c	19	**13c** 84	10	4
3d	20	**13d** 80	8	1
4a	17	**15a** 82	4	4
4b	18	**15b** 72	7	4
4c	19	**15c** 73	17	2
4d	20	**15d** 77	14	5

[a] Isolated yield. [b] Diolides are the following compounds **7**, **14**, and **16**:

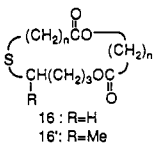
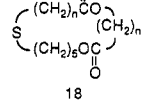


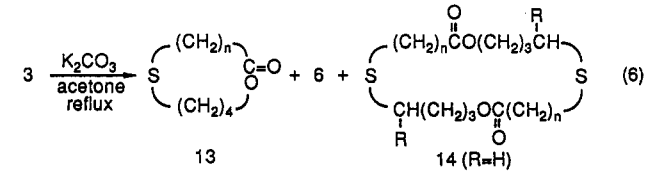
Table V. Lactonization of Sulfonium Salts 5

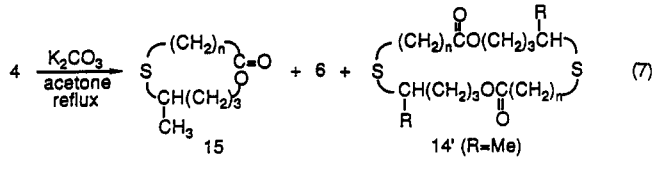
sulfonium salt	yield,[a] % 17	6	diolides[b]
5a	27	18	18
5b	30	43	6
5c	15	36	3
5d	22	45	7

[a] Isolated yield. [b] Diolides are the following compounds **7** and **18**:



In the case of intramolecular cyclization of thiolanium salts **3** or **4** (eq 6 and 7), carboxylate anions attack the





unhindered α-methylene carbon atom of the five-membered ring to afford sulfur-containing macrocyclic lactones

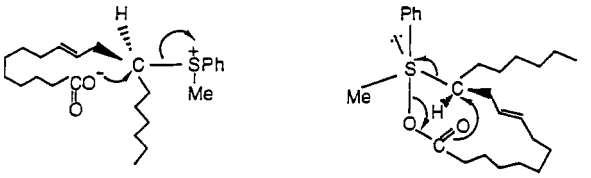
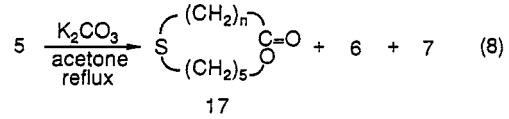


Figure 1. Inversion of configuration (left) via a 13-membered transition state and (right) via a 5- or 14-membered transition state.

13 or **15** in good yields, together with minor amounts of **6** and diolides (Table IV). This result is consistent with the absence of carboxylate anion attack on the secondary carbon atom in the case of **10**. Interestingly, sulfur-containing 17-membered lactones **13a** and **15a** have a musk odor.[9]

However, thianium salts **5** did not undergo attack on the α-methylene carbon atom of the six-membered ring regiospecifically (eq 8). The yield of **6** increased at the



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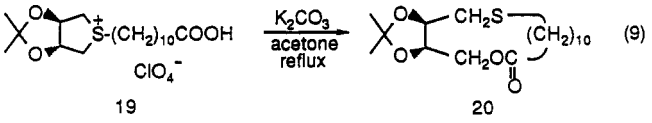
expense of sulfur-containing lactones **17** (Table V). It is possible to introduce chiral carbon atoms into a lactone ring by means of this method. As indicated in eq 9, an



(9)

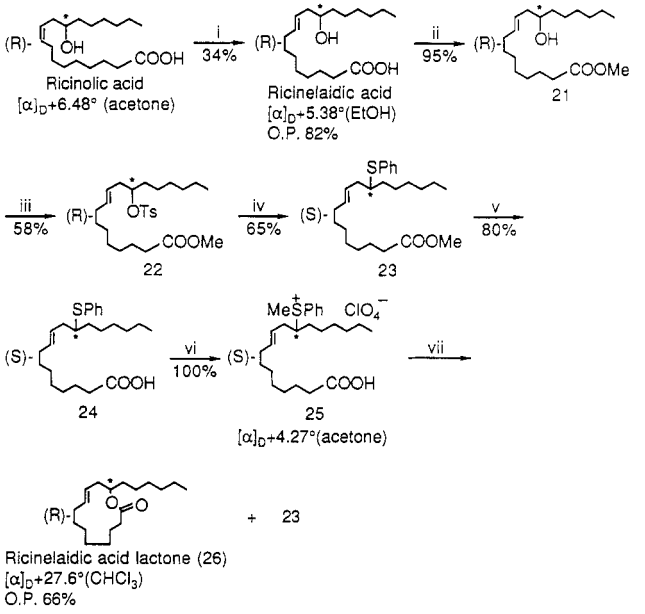
intramolecular cyclization of sulfonium salt **19**, which was prepared from 2,4-dioxa-3,3-dimethyl-7-thiabicyclo-[3.3.0]octane, **1a**, and silver perchlorate, afforded lactone **20** (10%) having two chiral carbon atoms in the lactone ring.

The differences in regioselectivity between **3** and **5** depend on the ring size (five- or six-membered ring). The carboxylate anions of **3** attack selectively on the α-methylene carbon atom of the five-membered ring, and the ring is easily cleaved by ring strain to give **13**. In contrast to the five-membered ring, the six-membered ring of **5** is so stable that the carboxylate anion attacks the side-chain's methylene carbon preferentially. These results are consistent with the reactivity of methylthianium salts with nucleophiles such as azide anion reported by Eliel et al.[7]

Mechanism of the Intramolecular Cyclization. To investigate this intramolecular cyclization mechanism, we synthesized sulfonium salt **25** ($[\alpha]_D$ +4.27° (acetone)), having an optically active secondary carbon atom as illustrated in Scheme I, from commercially available ricinolic acid ($[\alpha]_D$ +6.48° (acetone)) and studied its intramolecular cyclization. Ricinelaidic acid lactone (**26**, ($[\alpha]_D$ +27.6° ($CHCl_3$), optical purity (OP) 66%[10]) was obtained with inversion of configuration at the chiral carbon atom by an intramolecular alkylation of **25**, and methylated product **23** ($[\alpha]_D$ −13.5° ($CHCl_3$)) was also formed in 16% yield. The optical purity (66%) of **25** means that the stereoselectivity of this reaction is 80% based on the optical purity of ricinelaidic acid (OP 82%).

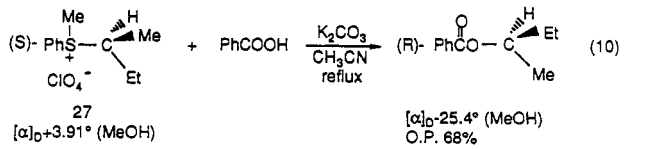
Two explanations for the inversion of configuration are possible. One route is S_N2 reaction as shown in Figure 1, left; the other is an inversion process via a sulfurane intermediate (Figure 1, right).[11] At present, it is difficult to determine which mechanism is correct.

Scheme I[a]



[a] Reagents: (i) $h\nu$, Ph_2S_2, hexane; (ii) CH_2N_2, ether; (iii) TsCl, pyridine; (iv) PhSNa, MeOH; (v) KOH, aqueous MeOH; (vi) MeI, $AgClO_4$, CH_3CN; (vii) K_2CO_3, CH_3CN, reflux.

We also synthesized sulfonium salt **27** having a (*S*)-*sec*-butyl group, and the esterification of benzoic acid with a mixture of diastereomeric salt **27** ($[\alpha]_D$ +3.91° (MeOH)) was carried out (eq 10). Treatment of benzoic acid with



(10)

27 in the presence of K_2CO_3 in acetonitrile gave (*R*)-*sec*-butyl benzoate ($[\alpha]_D$ −25.4° (MeOH), OP 68%) with an inversion of configuration at the chiral carbon atom. The optical purity was determined by comparison with an authentic sample ($[\alpha]_D$ +37.1° (MeOH)) that was prepared independently from benzoyl chloride and (*S*)-2-butanol.

In conclusion, intramolecular cyclization of sulfonium salts having a carboxyl group at ω-carbon atom is a useful method for the synthesis of macrocyclic lactones: (1) Sulfur-containing macrocyclic lactones via ring-expansion reactions were obtained from thiolanium salts in good yields. (2) Simple macrocyclic lactones were obtained from diphenylsulfonium salts in high yields. Of particular note, 12- and 13-membered lactones, difficult to prepare by conventional methods, are obtained in good yields.

Experimental Section

Proton magnetic resonance spectra were recorded on a JEOL PMX 60SI 60-MHz spectrometer. Infrared spectra were recorded on a Hitachi 260-10 spectrometer. Mass and high-resolution mass spectra were determined with a JEOL JMX-DX 300 mass spectrometer with JEOL JMA 5000 mass data system at an ionizing voltage of 70 eV. Optical rotations were measured in a 1.0- or 0.5-dm cell on a JASCO DIP-140 polarimeter. Melting points (uncorrected) were determined on a Yamato MP-21 apparatus in open capillary tubes. GLPC were recorded on a Hitachi

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G-3000 with 10% SE-30 1-m column. Column chromatography was performed with Wako gel C-200 (Wako Pure Chemical Ind.). Thin-layer chromatography was performed on 0.25-mm silica gel (Merck $60F_{254}$).

Materials. Dry solvents were obtained as follows: Acetone and methylene chloride were dried over molecular sieves (4 A, Wako Pure Chemical Ind.); acetonitrile was distilled from calcium hydride.

11-Bromoundecanoic acid, 12-bromododecanoic acid, pentamethylene sulfide, and (*S*)-2-butanol from Aldrich Chemical Co. and ricinolic acid from Wako Pure Chemical Ind. were used without purification.

Phenyl isopropyl sulfide and methyl isopropyl sulfide were prepared by the usual methods.

13-Bromotridecanoic acid and 14-bromotetradecanoic acid were prepared from 1,12-dibromododecane with sodium cyanide or the sodium salt of dimethyl malonate according to the literature procedures[12] and purified by recrystallization from ether–hexane as colorless crystals.

13-Bromotridecanoic acid: mp 52–54 °C (lit.[13] mp 58 °C); ^{1}H NMR ($CDCl_3$) δ 1.27–2.13 (m, 20 H), 2.18–2.50 (m, 2 H), 3.37 (t, J = 6.1 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1695 cm^{-1} (C=O); MS, m/z 294 (M^+ + 1), 249, 213.

14-Bromotetradecanoic acid: mp 59–60 °C (lit.[13] mp 63 °C); ^{1}H NMR ($CDCl_3$) δ 1.27–2.10 (m, 22 H), 2.22–2.44 (m, 2 H), 3.36 (t, J = 6.5 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1693 cm^{-1} (C=O).

ω-Iodocarboxylic acids **1a–d** were prepared by treatment of the corresponding ω-bromocarboxylic acids with KI (3 equiv) in boiling acetone for 6 h. Recrystallization from ether–hexane yielded pure **1a–d** as colorless crystals (**1a**, 98%; **1b**, 96%; **1c**, 97%; **1d**, 88%).

11-Iodoundecanoic acid (1a): mp 65 °C, ^{1}H NMR ($CDCl_3$) δ 1.30–1.92 (m, 16 H), 2.22–2.47 (m, 2 H), 3.17 (t, J = 6.6 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1695 cm^{-1} (C=O).

12-Iodododecanoic acid (1b): mp 59–61 °C; ^{1}H NMR ($CDCl_3$) δ 1.27–2.29 (m, 20 H), 3.15 (t, J = 6.7 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1690 cm^{-1} (C=O).

13-Iodotridecanoic acid (1c): mp 67–69 °C; ^{1}H NMR ($CDCl_3$) δ 1.27–2.03 (m, 20 H), 2.12–2.17 (m, 2 H), 3.13 (t, J = 6.5 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1690 cm^{-1} (C=O); MS, m/z 341 (M^+ + 1), 323, 294.

14-Iodotetradecanoic acid (1d): mp 65–67 °C; ^{1}H NMR ($CDCl_3$) δ 1.27–2.07 (m, 22 H), 2.21–2.44 (m, 2 H), 3.14 (t, J = 6.9 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1690 cm^{-1} (C=O); MS, m/z 355 (M^+ + 1), 337, 308.

15-Iodopentadecanoic Acid (1e). A mixture of 15-pentadecanolactone (4.81 g, 20 mmol) and 57% hydroiodic acid in AcOH (150 mL) was refluxed for 6 h. After distillation of hydroiodic acid and AcOH, the residue was extracted with ether. The combined extracts were washed with aqueous $Na_2S_2O_3$, dried over Na_2SO_4, and concentrated. Recrystallization from ether–hexane gave **1e** [6.82 g (93%)] as colorless crystals: mp 78 °C; ^{1}H NMR ($CDCl_3$) δ 1.27–1.90 (m, 24 H), 2.05–2.47 (m, 2 H), 3.15 (t, J = 7.0 Hz, 2 H), 11.6 (br s, 1 H); IR (KBr) 2770–3460 (OH), 1695 cm^{-1} (C=O).

Sulfonium Salts 3, 4, 5, 8, and 10. In a 30-mL round-bottomed flask, cooled in an ice bath, were placed **1** (10 mmol) and silver perchlorate (2.29 g, 11 mmol). The sulfide (11 mmol) in CH_3CN (15 mL) was added dropwise and then the ice bath was removed. The flask was covered with aluminum foil and then stirred for 3 days at room temperature. The reaction mixture was passed through a silica gel short column and eluted with acetone. After removal of solvent, the residue was washed with ether. The crude products obtained were recrystallized from acetone–ether to yield sulfonium salts **3**, **4**, **5**, **8**, and **10** as colorless crystals.

3a: yield 80%; mp 76–78 °C; ^{1}H NMR (d_6-acetone) δ 1.34–2.50 (m, 22 H), 3.07–3.73 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1732 (C=O), 1090 cm^{-1} (ClO_4^-).

3b: yield 100%; mp 95–98 °C; ^{1}H NMR (d_6-acetone) δ 1.31–2.50 (m, 24 H), 3.25–3.77 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1727 (C=O), 1113 cm^{-1} (ClO_4^-).

3c: yield 84%; mp 94–96 °C; ^{1}H NMR (d_6-acetone) δ 1.28–2.57 (m, 26 H), 3.17–3.83 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1730 (C=O), 1090 cm^{-1} (ClO_4^-).

3d: yield 80%; mp 108–110 °C; ^{1}H NMR (d_6-acetone) δ 1.29–2.55 (m, 28 H), 3.23–3.74 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1725 (C=O), 1095 cm^{-1} (ClO_4^-).

4a: yield 77%; mp 75 °C; ^{1}H NMR (d_6-acetone) δ 1.33–2.63 (m, 25 H), 3.35–3.76 (m, 5 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1720 (C=O), 1080 cm^{-1} (ClO_4^-).

4b: yield 81%; mp 85–87 °C; ^{1}H NMR (d_6-acetone) δ 1.32–2.71 (m, 27 H), 3.35–3.76 (m, 5 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1720 (C=O), 1080 cm^{-1} (ClO_4^-).

4c: yield 86% mp 92–93 °C; ^{1}H NMR (d_6-acetone) δ 1.28–2.83 (m, 29 H), 3.23–4.40 (m, 5 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1730 (C=O), 1095 cm^{-1} (ClO_4^-).

4d: yield 78%; mp 100–102 °C; ^{1}H NMR (d_6-acetone) δ 1.28–2.83 (m, 31 H), 3.31–4.40 (m, 5 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1725 (C=O), 1100 cm^{-1} (ClO_4^-).

5a: yield 90%; mp 70–72 °C; ^{1}H NMR (d_6-acetone) δ 1.33–2.40 (m, 24 H), 3.13–4.62 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1740 (C=O), 1100 cm^{-1} (ClO_4^-).

5b: yield 87%; mp 84–87 °C; ^{1}H NMR (d_6-acetone) δ 1.30–2.40 (m, 26 H), 2.87–3.83 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1730 (C=O), 1100 cm^{-1} (ClO_4^-).

5c: yield 86%; mp 93–95 °C; ^{1}H NMR (d_6-acetone) δ 1.28–2.48 (m, 28 H), 3.27–3.73 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1740 (C=O), 1100 cm^{-1} (ClO_4^-).

5d: yield 83%; mp 104–106 °C; ^{1}H NMR (d_6-acetone) δ 1.29–2.42 (m, 30 H), 3.23–3.77 (m, 6 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1725 (C=O), 1105 cm^{-1} (ClO_4^-).

8 (R = Me): yield 88%; mp 62–64 °C; ^{1}H NMR (d_6-acetone) δ 1.26–2.53 (m, 18 H), 3.41 (s, 3 H), 3.63–4.07 (m, 2 H), 7.65–7.93 (m, 3 H), 7.97–8.27 (m, 2 H), 9.73 (br s, 1 H); IR (CH_2Cl_2) 3000–3600 (OH), 1705 (C=O), 1090 cm^{-1} (ClO_4^-).

8 (R = Et): yield 91%; ^{1}H NMR (d_6-acetone) δ 1.26–2.47 (m, 21 H), 3.67–4.13 (m, 4 H), 7.67–7.95 (m, 3 H); 7.95–8.27 (m, 2 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1705 (C=O), 1085 cm^{-1} (ClO_4^-).

8 (R = Pr^i): yield 59%; ^{1}H NMR (d_6-acetone) δ 1.10–2.42 (m, 24 H), 3.47–5.82 (m, 3 H), 7.23–8.13 (m, 5 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1685 (C=O), 1085 cm^{-1} (ClO_4^-).

10 (R = Et): yield 99%; mp 55–57 °C; ^{1}H NMR (d_6-acetone) δ 1.32–2.47 (m, 21 H), 2.95 (s, 3 H), 3.13–3.70 (m, 4 H), 9.73 (br s, 1 H); IR (CH_2Cl_2) 3000–3600 (OH), 1707 (C=O), 1097 cm^{-1} (ClO_4^-).

10 (R = Pr^i): yield 34%; ^{1}H NMR (d_6-acetone) δ 1.32–2.43 (m, 24 H), 2.94 (s, 3 H), 3.26–3.48 (m, 2 H), 3.64–4.15 (m, 1 H), 9.73 (br s, 1 H); IR (CH_2Cl_2) 3000–3600 (OH), 1726 (C=O), 1090 cm^{-1} (ClO_4^-).

***(S)-sec*-Butylmethylphenylsulfonium Salt (27).** This reaction was carried out using 223 mg (1.3 mmol) of (*S*)-*sec*-butyl phenyl sulfide ($[\alpha]_D$ +16.2° (*c* 1.50, MeOH) that was prepared from (*S*)-*sec*-butyl bromide ($[\alpha]_D$ +11.8° (*c* 5.2, MeOH)) and sodium thiophenoxide in EtOH, methyl iodide (1.92 g, 14 mmol), and silver perchlorate (314 mg, 1.5 mmol) in CH_3CN (5 mL), in a manner similar to that described for preparation of **3** to give **27** [377 mg (100%)]: $[\alpha]_D$ +3.91° (*c* 2.44, MeOH); ^{1}H NMR (d_6-acetone) δ 0.83–1.97 (m, 8 H), 3.43 (s, 3 H), 3.77–4.30 (m, 1 H), 7.49–7.88 (m, 3 H), 7.91–8.22 (m, 2 H); IR (neat) 1090 cm^{-1} (ClO_4^-).

Sulfonium Salts 2. In a 30-mL round-bottomed flask were placed **1a–e** (10 mmol) and silver perchlorate (2.29 g, 11 mmol); this was cooled in an ice bath. Phenyl sulfide (18.6 g, 0.1 mol) was added dropwise and then the ice bath was removed. The flask was covered with aluminum foil and then stirred for 3 days at room temperature. The reaction mixture was worked up as described for the preparation of **3** to yield **2** (**2a**, 70%; **2b**, 83%; **2c**, 99%; **2d**, 87%; **2e**, 46%).

2a: oil; ^{1}H NMR (d_6-acetone) δ 1.27–3.20 (m, 18 H), 4.38 (t, J = 7.0 Hz, 2 H), 7.25–7.80 (m, 6 H), 7.98–8.20 (m, 4 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1710 (C=O), 1080 cm^{-1} (ClO_4^-).

2b: oil; ^{1}H NMR (d_6-acetone) δ 1.27–1.90 (m, 18 H), 1.95–2.38 (m, 2 H), 4.22–4.48 (m, 2 H), 7.53–7.80 (m, 6 H), 7.95–8.15 (m, 4 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1707 (C=O), 1092 cm^{-1} (ClO_4^-).

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2c: oil; ^{1}H NMR (d_6-acetone) δ 1.25–1.90 (m, 20 H), 2.14–2.43 (m, 2 H), 4.13–4.50 (m, 2 H), 7.48–7.81 (m, 6 H), 7.90–8.17 (m, 4 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1707 (C=O), 1095 cm^{-1} (ClO_4^-).

2d: oil; ^{1}H NMR (d_6-acetone) δ 1.25–1.90 (m, 22 H), 2.13–2.43 (m, 2 H), 4.25–4.53 (m, 2 H), 7.53–7.83 (m, 6 H), 7.97–8.20 (m, 4 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1705 (C=O), 1095 cm^{-1} (ClO_4^-).

2e: mp 69–72 °C; ^{1}H NMR (d_6-acetone) δ 1.27–2.40 (m, 26 H), 4.25–4.49 (m, 2 H), 7.55–7.80 (m, 6 H), 8.00–8.17 (m, 4 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1730 (C=O), 1095 cm^{-1} (ClO_4^-).

General Procedure of Intramolecular Cyclization. To a stirred suspension of K_2CO_3 (831 mg, 6 mmol) in refluxing acetone (100 mL) was added sulfonium salt in acetone (100 mL) over 1.5 days. After the mixture was refluxed for an additional 12 h, the solution was cooled to room temperature, diluted with ether (100 mL), and passed through a silica gel short column. The solvent was removed, and the residue was chromatographed on silica gel (hexane–ether) to give pure products.

The following lactones **6a–e** were characterized by ^{1}H NMR, IR, and mass spectral data.

6a: ^{1}H NMR ($CDCl_3$) δ 1.33–1.91 (m, 16 H), 2.26–2.63 (m, 2 H), 4.07–4.23 (m, 2 H); IR (neat) 1734 cm^{-1} (C=O) [lit.[14] IR 1727 cm^{-1} (C=O)]; MS, m/z 185 ($M^+ + 1$), 166, 148.

6b: ^{1}H NMR ($CDCl_3$) δ 1.30–1.80 (m, 18 H), 2.13–2.42 (m, 2 H), 4.01–4.17 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 198 (M^+), 180, 168.

6c: ^{1}H NMR ($CDCl_3$) δ 1.32–2.00 (m, 20 H), 2.23–2.50 (m, 2 H), 3.97–4.23 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 212 (M^+), 194, 176.

6d: ^{1}H NMR ($CDCl_3$) δ 1.32–1.93 (m, 22 H), 2.19–2.43 (m, 2 H), 3.97–4.20 (m, 2 H); IR (neat) 1732 cm^{-1} (C=O); MS, m/z 226 (M^+), 208, 166.

6e: mp 32–34 °C; ^{1}H NMR ($CDCl_3$) δ 1.30–1.87 (m, 24 H), 2.20–2.43 (m, 2 H), 4.01–4.18 (m, 2 H); IR (neat) 1735 cm^{-1} (C=O).

The esters **9** obtained from reaction of sulfonium salt **8** were characterized by ^{1}H NMR, IR, and mass spectra.

9 (R = Me): ^{1}H NMR ($CDCl_3$) δ 1.25–1.92 (m, 16 H), 2.08–2.47 (m, 2 H), 2.67–3.07 (m, 2 H), 3.57 (s, 3 H), 6.93–7.33 (m, 5 H); IR (CCl_4) 1735 cm^{-1} (C=O); MS, m/z 308 (M^+), 277, 207.

9 (R = Et): ^{1}H NMR ($CDCl_3$) δ 1.05–1.93 (m, 19 H), 2.07–2.47 (m, 2 H), 2.71–3.00 (m, 2 H), 4.03 (q, J = 7.0 Hz, 2 H), 6.92–7.31 (m, 5 H); IR (CCl_4) 1735 cm^{-1} (C=O); MS, m/z 322 (M^+), 277, 235.

9 (R = Pr^i): ^{1}H NMR ($CDCl_3$) δ 1.05–1.93 (m, 22 H), 2.10–2.34 (m, 2 H), 2.73–3.03 (m, 2 H), 4.72–5.20 (m, 1 H), 6.94–7.41 (m, 5 H); IR (neat) 1728 cm^{-1} (C=O); MS, m/z 336 (M^+), 294, 277.

Intramolecular Reaction of 10. A suspension of **10** (1 mmol) and K_2CO_3 (838 mg, 6 mmol) in CH_3CN (20 mL) was refluxed for 6 h. The reaction mixture was diluted with ether (30 mL) and passed through a silica gel short column. After removal of solvent, the residue was extracted with ether to remove the esters from the unreacted salt. The extract was analyzed by ^{1}H NMR and gas chromatography. A mixture of **11** and **12** (R = Et): ^{1}H NMR ($CDCl_3$) δ 3.62 (s, –OMe)/2.08 (s, –SMe) = 6:4. **20** (R = Pr^i): ^{1}H NMR ($CDCl_3$) δ 1.13–1.90 (m, 22 H), 2.03–2.34 (m, 5 H), 3.60 (s, 3 H).

13a: ^{1}H NMR ($CDCl_3$) δ 1.31–1.80 (m, 20 H), 2.20–2.60 (m, 6 H), 3.97–4.15 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 272 (M^+), 231, 213; HRMS calcd for $C_{15}H_{28}O_2S$ 272.1810, found 272.1830.

13b: ^{1}H NMR ($CDCl_3$) δ 1.25–1.77 (m, 22 H), 2.13–2.58 (m, 6 H), 3.93–4.13 (m, 2 H); IR (neat) 1733 cm^{-1} (C=O); MS, m/z 286 (M^+), 258, 245; HRMS calcd for $C_{16}H_{30}O_2S$ 286.1966, found 286.1962.

13c: ^{1}H NMR ($CDCl_3$) δ 1.28–1.93 (m, 24 H), 2.08–2.65 (m, 6 H), 3.90–4.17 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 300 (M^+), 259, 241; HRMS calcd for $C_{17}H_{32}O_2S$ 300.2123, found 300.2120.

13d: ^{1}H NMR ($CDCl_3$) δ 1.29–2.03 (m, 26 H), 2.10–2.35 (m, 6 H), 3.93–4.23 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 314 (M^+), 273, 255; HRMS calcd for $C_{18}H_{34}O_2S$ 314.2279, found 314.2298.

15a: ^{1}H NMR ($CDCl_3$) δ 1.30–1.68 (m, 23 H), 2.13–2.58 (m, 5 H), 3.97–4.17 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 286 (M^+), 271, 245; HRMS calcd for $C_{16}H_{30}O_2S$ 286.1967, found 286.1971.

15b: ^{1}H NMR ($CDCl_3$) δ 1.32–1.88 (m, 25 H), 2.15–2.87 (m, 5 H), 3.98–4.18 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 300 (M^+), 259, 241; HRMS calcd for $C_{17}H_{32}O_2S$ 300.2123, found 300.2079.

15c: ^{1}H NMR ($CDCl_3$) δ 1.13–1.90 (m, 27 H), 2.07–2.67 (m, 5 H), 3.90–4.17 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 314 (M^+), 281, 259; HRMS calcd for $C_{18}H_{34}O_2S$ 314.2279, found 314.2266.

15d: ^{1}H NMR ($CDCl_3$) δ 1.17–2.08 (m, 29 H), 2.12–2.67 (m, 5 H), 3.93–4.20 (m, 2 H); IR (neat) 1728 cm^{-1} (C=O); MS, m/z 328 (M^+), 273, 257; HRMS calcd for $C_{19}H_{36}O_2S$ 328.2436, found 328.2432.

The following diolides **7**, **14**, and **18** were characterized by ^{1}H NMR, IR, and mass spectral data.

7a: ^{1}H NMR ($CDCl_3$) δ 1.30–1.92 (m, 32 H), 2.21–2.43 (m, 4 H), 3.98–4.17 (m, 4 H); IR (CCl_4) 1735 cm^{-1} (C=O); MS, m/z 368 (M^+), 350, 332.

7b: ^{1}H NMR ($CDCl_3$) δ 1.28–1.81 (m, 36 H), 2.14–2.41 (m, 4 H), 3.97–4.13 (m, 4 H); IR (CCl_4) 1730 cm^{-1} (C=O); MS, m/z 396 (M^+), 378, 360.

7c: ^{1}H NMR ($CDCl_3$) δ 1.26–1.93 (m, 40 H), 2.15–2.47 (m, 4 H), 3.90–4.19 (m, 4 H); IR (CCl_4) 1733 cm^{-1} (C=O); MS, m/z 424 (M^+), 406, 388.

7d: ^{1}H NMR ($CDCl_3$) δ 1.27–2.02 (m, 44 H), 2.13–2.47 (m, 4 H), 3.92–4.20 (m, 4 H); IR (CCl_4) 1731 cm^{-1} (C=O); MS, m/z 452 (M^+), 434, 269.

14a: ^{1}H NMR ($CDCl_3$) δ 1.27–1.80 (m, 40 H), 2.20–2.60 (m, 12 H), 3.97–4.15 (m, 4 H); IR (CCl_4) 1734 cm^{-1} (C=O); MS, m/z 456 (M^+), 415, 397.

14b: MS, m/z 572 (M^+), 517, 373.

14′a: ^{1}H NMR ($CDCl_3$) δ 1.27–1.68 (m, 46 H), 2.17–2.77 (m, 10 H), 3.93–4.13 (m, 4 H); IR (CCl_4) 1732 cm^{-1} (C=O); MS, m/z 572 (M^+), 558, 514.

16′c: ^{1}H NMR ($CDCl_3$) δ 1.27–2.00 (m, 47 H), 2.12–2.45 (m, 7 H), 3.87–4.17 (m, 4 H); IR (CCl_4) 1731 cm^{-1} (C=O); MS, m/z 526 (M^+), 467, 406.

16d: ^{1}H NMR ($CDCl_3$) δ 0.67–1.83 (m, 48 H), 1.98–2.42 (m, 8 H), 3.88–4.23 (m, 4 H); IR (CCl_4) 1732 cm^{-1} (C=O); MS, m/z 540 (M^+), 481, 435.

16′d: ^{1}H NMR ($CDCl_3$) δ 1.27–1.93 (m, 51 H), 2.12–2.60 (m, 7 H), 3.93–4.27 (m, 4 H); IR (CCl_4) 1730 cm^{-1} (C=O); MS, m/z 554 (M^+), 495, 434.

17a: ^{1}H NMR ($CDCl_3$) δ 1.32–1.87 (m, 22 H), 2.17–2.60 (m, 6 H), 3.98–4.17 (m, 2 H); IR (neat) 1730 cm^{-1} (C=O); MS, m/z 286 (M^+), 231, 213; HRMS calcd for $C_{16}H_{30}O_2S$ 286.1966, found 286.1981.

17b: ^{1}H NMR ($CDCl_3$) δ 1.28–1.87 (m, 24 H), 2.12–2.60 (m, 6 H), 4.00–4.17 (m, 2 H); IR (neat) 1732 cm^{-1} (C=O); MS, m/z 300 (M^+), 245, 227; HRMS calcd for $C_{17}H_{32}O_2S$ 300.2123, found 300.2141.

17c: ^{1}H NMR ($CDCl_3$) δ 1.28–1.93 (m, 26 H), 2.08–2.37 (m, 6 H), 3.93–4.23 (m, 2 H); IR (neat) 1733 cm^{-1} (C=O); MS, m/z 314 (M^+), 259, 241; HRMS calcd for $C_{18}H_{34}O_2S$ 314.2280, found 314.2292.

17d: ^{1}H NMR ($CDCl_3$) δ 1.27–2.00 (m, 28 H), 2.15–2.67 (m, 6 H), 3.90–4.22 (m, 2 H); IR (neat) 1732 cm^{-1} (C=O); MS, m/z 328 (M^+), 273, 255; HRMS calcd for $C_{19}H_{36}O_2S$ 328.2436, found 328.2416.

18d: ^{1}H NMR ($CDCl_3$) δ 1.25–1.99 (m, 50 H), 2.12–2.67 (m, 8 H), 3.87–4.21 (m, 4 H); IR (CCl_4) 1730 cm^{-1} (C=O); MS, m/z 554 (M^+), 452, 434.

2,4-Dioxa-3,3-dimethyl-7-thiabicyclo[3.3.0]octane. (*R*,*R*)-(–)-1,4-Di-*O*-tosyl-2,3-*O*-isopropylidene-L-threitol (4.71 g, 10 mmol, from Aldrich) in DMF (20 mL) was added to a mixture of DMF (20 mL) and water (10 mL) dropwise. To the mixture was added aqueous sodium sulfide (15 mmol) dropwise. After stirring for 12 days at room temperature, the reaction mixture was diluted with water (50 mL) and extracted with ether (2 × 100 mL). The organic layer was washed with water (5 × 30 mL) and dried over Na_2SO_4. After removal of solvent, the residue was purified by chromatography on silica gel (hexane–ether 10:1). The solvent was removed under atmospheric pressure to give the expected sulfide [940 mg (59%)] as a pale yellow oil: $[\alpha]_D$ +144° (*c* 1.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.33, 1.48 (s, 6 H), 2.22–2.87

(m, 4 H), 3.97–4.30 (m, 2 H); MS, m/z 160 (M^+), 145, 131.

Sulfonium Salt 19. Following the procedure described for **2**, the sulfide obtained above (901 mg, 5.6 mmol), **1a** (1.72 g, 5.5 mmol), and silver perchlorate (1.24 g, 6 mmol) in CH_3CN (9 mL) afforded **19** [1.74 g (71%)]: mp 104 °C; ^1H NMR (d_6-acetone) δ 1.33–1.88 (m, 22 H), 2.17–2.41 (m, 2 H), 3.43–4.09 (m, 8 H), 9.73 (br s, 1 H); IR (KBr) 3000–3600 (OH), 1725 (C=O), 1085 cm^{-1} (ClO_4^-).

Intramolecular Cyclization of 19. This reaction was carried out using 19 (897 mg, 2 mmol) and K_2CO_3 (834 mg, 6 mmol) in acetone under high-dilution conditions as described above for intramolecular alkylation. The reaction mixture was purified by chromatography on silica gel (hexane–ether 30:1) to give **20** [72 mg (10%)]: $[\alpha]_D$ −2.92° (c 1.22, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.31–1.93 (m, 22 H), 2.15–2.79 (m, 6 H), 3.85–4.17 (m, 4 H); IR (neat) 1735 cm^{-1} (C=O); MS, m/z 344 (M^+), 329, 301; HRMS calcd for $C_{18}H_{32}O_4S$ 344.2021, found 344.2006.

Ricinelaidic acid was prepared from ricinolic acid ($[\alpha]_D$ +6.48° (c 6.76, acetone)) according to the literature procedures[10] and purified by recrystallization from hexane as a colorless solid [12.2 g (34%)]: mp 45–47 °C [lit.[10] mp 51.0–51.5 °C]; $[\alpha]_D$ +5.38° (c 8.37, EtOH) [lit.[10] $[\alpha]_D$ +6.6° (c 10, EtOH) OP 82%]; ^1H NMR ($CDCl_3$) δ 0.85–1.80 (m, 23 H), 1.80–2.53 (m, 6 H), 3.44–3.80 (m, 1 H), 5.25–5.57 (m, 2 H), 11.6 (br s, 1 H); IR (CH_2Cl_2) 2770–3460 (OH), 1708 cm^{-1} (C=O); MS, m/z 299 ($M^+ + 1$), 281, 263.

Methyl [*R*-(*E*)]-12-Hydroxy-9-octadecenoate (21). In a round-bottomed flask was placed ricinelaidic acid (10.4 g, 35 mmol) in ether (50 mL), and this was cooled in an ice bath. To the stirred mixture was added diazomethane (ether solution) with a pipet, until evolution of N_2 was stopped. After removal of solvent, the residual oil was chromatographed on silica gel (hexane–AcOEt 5:1) to give **21** [10.4 g (95%)]. Recrystallization from hexane gave a colorless solid: mp 27–28 °C; $[\alpha]_D$ −0.20° (c 3.65, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.87–1.80 (m, 23 H), 1.80–2.57 (m, 6 H), 3.30–3.83 (m, 4 H), 5.31–5.57 (m, 2 H); IR (CCl_4) 1740 cm^{-1} (C=O); MS, m/z 313 ($M^+ + 1$), 294, 279; HRMS calcd for $C_{19}H_{36}O_3$ 312.2664, found 312.2709.

Methyl [*R*-(*E*)]-12-[(*p*-Tolylsulfonyl)oxy]-9-octadecenoate (22). To **21** (6.90 g, 22 mmol) in pyridine (35 mL) was added *p*-toluenesulfonyl chloride (5.10 g, 27 mmol) in pyridine (35 mL) dropwise. The mixture was stirred for 40 h at room temperature. After distillation of pyridine under reduced pressure, the residue was diluted with aqueous hydrochloric acid (100 mL) and extracted with ether (2 × 200 mL). The organic layer was dried over $MgSO_4$ and purified by chromatography on silica gel (hexane–AcOEt 10:1) to give **22** [5.95 g (58%)]: $[\alpha]_D$ +12.6° (c 7.19, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.78–2.07 (m, 23 H), 2.15–2.58 (m, 9 H), 3.60 (s, 3 H), 4.26–4.70 (m, 1 H), 5.10–5.43 (m, 2 H), 7.22 (ABq, J = 8.2 Hz, 2 H), 7.70 (ABq, J = 8.4 Hz, 2 H); IR (neat) 1735 (C=O), 1308 (SO_2), 1175 cm^{-1} (SO_2); MS, m/z 466 (M^+), 294, 263; HRMS calcd for $C_{26}H_{42}O_5S$ ($M^+ + 1$) 467.2831, found 467.2753.

Methyl [*S*-(*E*)]-12-(Phenylthio)-9-octadecenoate (23). Sodium (238 mg, 10 mmol) was added to stirred MeOH (10 mL), and then thiophenol (1.11 g, 10 mmol) in MeOH (10 mL) was added dropwise. After the mixture was stirred for 30 min at room temperature, **22** (4.67 g, 10 mmol) in MeOH (10 mL) was added dropwise. The mixture was refluxed for 3 h, and the solvent was removed. The product was diluted with water (80 mL) and extracted with ether (2 × 200 mL). The organic layer was dried over $MgSO_4$ and purified by chromatography on silica gel (hexane–AcOEt 30:1) to give **23** [2.63 g (65%)]: $[\alpha]_D$ −15.4° (c 4.03, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86–1.80 (m, 23 H), 1.80–2.50 (m, 6 H), 2.82–3.33 (m, 1 H), 3.60 (s, 3 H), 5.30–5.53 (m, 2 H), 7.03–8.87 (m, 5 H); IR (neat) 1735 cm^{-1} (C=O); MS, m/z 404 (M^+), 373, 327; HRMS calcd for $C_{25}H_{40}O_2S$ 404.2749, found 404.2732.

[*S*-(*E*)]-12-(Phenylthio)-9-octadecenoic Acid (24). A mixture of **23** (2.34 g, 5.8 mmol) in MeOH (7 mL) and 1 N sodium hydroxide (7.54 g, 7.5 mmol) was refluxed for 1.5 h. After removal of solvent, the residue was acidified with aqueous hydrochloric acid, and the product was extracted with ether (3 × 200 mL) and dried over $MgSO_4$. Removal of the solvent gave **24** [1.79 g (80%)]: $[\alpha]_D$ −16.2° (c 2.78, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.85–1.77 (m, 23 H), 1.79–2.53 (m, 6 H), 2.80–3.31 (m, 1 H), 5.17–5.53 (m, 2 H), 6.96–7.47 (m, 5 H), 11.6 (br s, 1 H); IR (neat) 2770–3460 (OH), 1702 cm^{-1} (C=O); MS, m/z 390 (M^+), 280, 207; HRMS calcd for $C_{24}H_{38}O_2S$ 390.2592, found 390.2550.

Sulfonium Salt 25. This reaction was carried out using **24** (1.47 g, 3.8 mmol), methyl iodide (5.33 g, 38 mmol), and silver perchlorate (936 mg, 4.5 mmol) in CH_3CN (10 mL) in a procedure similar to that described for preparation of **3** to give **25** [1.89 g (100%)]: $[\alpha]_D$ +4.27° (c 6.14, acetone); ^1H NMR (d_6-acetone) δ 0.63–1.74 (m, 23 H), 1.80–2.86 (m, 6 H), 3.43 (s, 3 H), 3.84–4.42 (m, 1 H), 5.10–5.82 (m, 2 H), 7.42–8.20 (m, 5 H), 9.73 (br s, 1 H); IR (neat) 3000–3600 (OH), 1702 (C=O), 1093 cm^{-1} (ClO_4^-).

Intramolecular Cyclization of 25. Sulfonium salt **25** (865 mg, 1.7 mmol) in CH_3CN (100 mL) was added to a suspension of K_2CO_3 (720 mg, 5.2 mmol) in refluxing CH_3CN (100 mL) over 1.5 days. The reaction mixture was worked up in a procedure similar to that described for the general procedure of intramolecular cyclization to give ricinelaidic acid lactone [**26**, 16 mg (3%)]: $[\alpha]_D$ +27.6° (c 0.82, $CHCl_3$, OP 66%) [lit.[10] $[\alpha]_D$ +42° (c 1, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 0.72–1.83 (m, 23 H), 1.83–2.48 (m, 6 H), 4.76–5.17 (m, 1 H), 5.27–5.57 (m, 2 H); IR (CCl_4) 1721 cm^{-1} (C=O); MS, m/z 280 (M^+, 46), 207 (91), 166 (42), 137 (40), 68 (100); HRMS calcd for $C_{18}H_{32}O_2$ 280.2403, found 280.2391. Methyl ester **23** [113 mg (16%)] was also obtained. **23**: $[\alpha]_D$ −13.5° (c 5.33, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.83–1.76 (m, 23 H), 1.78–2.42 (m, 6 H), 2.82–3.27 (m, 1 H), 3.58 (s, 3 H), 5.23–5.49 (m, 2 H), 6.95–7.40 (m, 5 H); IR (neat) 1740 cm^{-1} (C=O); MS, m/z 404 (M^+), 373, 327.

Intramolecular Alkylation of Benzoic Acid with 27. A suspension of **27** (351 mg, 1.25 mmol), benzoic acid (159 mg, 1.3 mmol), and K_2CO_3 (522 mg, 3.8 mmol) in CH_3CN (10 mL) was refluxed for 40 h. The reaction mixture was diluted with ether (20 mL) and passed through a silica gel short column. After removal of solvent, the residue was chromatographed on silica gel (hexane–AcOEt 50:1) to give methyl benzoate [28 mg (16%)] and (*R*)-*sec*-butyl benzoate [73 mg (33%)]: $[\alpha]_D$ −25.4° (c 2.85, MeOH, OP 68%); ^1H NMR ($CDCl_3$) δ 0.95 (t, J = 7.0 Hz, 3 H), 1.30 (d, J = 6.0 Hz, 3 H), 1.43–1.97 (m, 2 H), 4.73–5.33 (m, 1 H), 7.07–7.58 (m, 3 H), 7.77–8.13 (m, 2 H); IR (neat) 1715 cm^{-1} (C=O); MS, m/z 178 (M^+), 149, 123.

Preparation of Authentic (*S*)-*sec*-Butyl Benzoate. A mixture of (*S*)-2-butanol ($[\alpha]_D$ +13.2° (c 7.97, MeOH, 234 mg, 3.2 mmol) and pyridine (2.38 g, 30 mmol) in benzene (10 mL) was cooled in an ice bath. To this mixture was added benzoyl chloride (488 mg, 3.5 mmol) in benzene (10 mL) dropwise, and then the ice bath was removed. After the mixture was stirred for 18 h at room temperature, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 × 150 mL). The extracts were dried over $MgSO_4$ and purified by silica gel column chromatography (hexane–ether 35:1) to give (*S*)-*sec*-butyl benzoate [527 mg (94%)]: $[\alpha]_D$ +37.1° (c 6.83, MeOH); ^1H NMR ($CDCl_3$) δ 0.97 (t, J = 7.1 Hz, 3 H), 1.32 (d, J = 6.4 Hz, 3 H), 1.45–2.00 (m, 2 H), 4.73–5.33 (m, 1 H), 7.13–7.63 (m, 3 H), 7.90–8.20 (m, 2 H).