in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were a = 8.439 (4) Å,[10] b = 7.423 (2) Å, c = 18.032 (9) Å, and V = 1129.5 (8) Å^3. The calculated density of 1.199 g cm^{-3} for 4 formula units per unit cell agrees with the experimental density of 1.198 g cm^{-3} measured by the flotation method using a mixture of pentane and CCl_4. ω scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.19°, indicating a satisfactory mosaic spread for the crystal. Axial photographs indicated that the crystal belonged to the orthorhombic system. Intensity data for zero and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of $h00$ ($h = 2n + 1$), $0k0$ ($k = 2n + 1$), and $00l$ ($l = 2n + 1$) reflections is consistent with only space group $P2_12_12_1$ (No. 19).[11]

Intensity data were collected by using θ–2θ scans with X-ray source and monochromator settings identical with those used for determination of the unit cell parameters. A variable scan rate from 2.02 to 29.3°/min was used and a scan width of 2° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (bdg1) and at the end (bgd2) of each scan with a total background to scan time ratio, TR, of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (008, 200, 020) monitored every 97 reflections. Intensities were calculated as described above. From a total of 1186 reflections collected in a complete octant of data out to 2θ = 50°, 1006 were accepted as statistically above background on the basis that F was greater than $3\sigma(F)$. Lorentz and polarization corrections were made in the usual way.

B. Solution and Refinement of the Structure. Computations were performed as described above. In all least-squares refinements, the quantity minimized was $w(|F_o| - |F_c|)^2$. A weighting scheme based on counting statistics ($w = 1.0/[\sigma(F)^2 + 0.037F^2]$) was employed for calculating R_w and in least-squares refinement.

The structure was solved by using the multisolution tangent refinement direct methods program SHELX-76. The total number of parameters varied were 156 for 1006 observations. The full-matrix least-squares refinement converged at R = 0.0548 and R_w = 0.0691. The final atomic coordinates and thermal parameters are available as supplementary material in Table 5 and the list of calculated and observed structure factors are available from us as Table 6; the list of bond angles and bond distances is available as supplementary material in Table 4.

Registry No. 5, 4949-44-4; 6, 74262-50-3; 7, 74262-51-4; 8, 74262-52-5; 9, 74262-53-6; 10, 74262-54-7; 11, 74345-29-2; 12, 74262-55-8; cyclohexenone, 930-68-7; diethyl malonate, 510-20-3; propionyl chloride, 79-03-8; furan, 110-00-9.

Supplementary Material Available: Tables of atomic coordinates and thermal parameters (Tables 2 and 5) and tables of bond distances and bond angles (Tables 1 and 4) (6 pages). Ordering information is given on any current masthead page.

Preparation of β-Hydroxy-α-phenylthio Esters via Condensation of Aldehydes with α-Phenylthio Ester Enolate Anions

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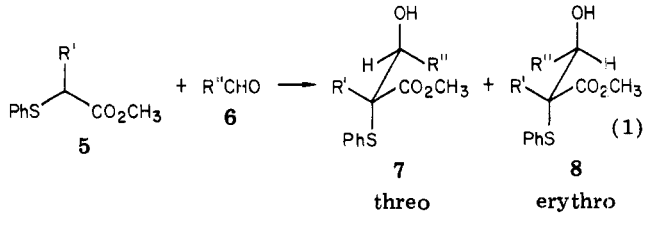
The lithium enolates of α-phenylthio esters **5** react with aldehydes **6** to give good yields of diastereomeric aldol products **7** and **8** provided that anhydrous zinc chloride is first added to the enolate solution. The threo or erythro nature of several of the aldol products (**7** and **8**) was determined by transforming them stereospecifically to *Z* and *E* olefins **15** through a net trans elimination of the elements of PhSOH. α-(Phenylthio)-γ-butyrolactone (**16**) also takes part in the aldol reaction.

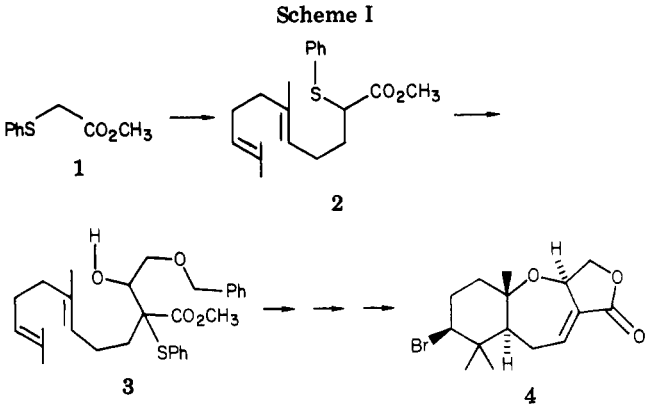
The use of α-sulfenylated carbonyl compounds in organic synthesis is well documented.[1] We recently invoked the sequential alkylation and aldolization of methyl α-(phenylthio)acetate (**1**) to prepare the β-hydroxy ester **3** (Scheme I), a key intermediate in a synthesis of *dl*-aplysistatin (**4**).[2] We have examined the aldol portion of that sequence (i.e., **2** → **3**) in some detail and now report the results of that study.

Initial attempts to condense the lithium enolates of α-sulfenylated esters of general structure **5** (R′ = alkyl) with aldehydes **6** (eq 1) at −78 °C or room temperature in



tetrahydrofuran met with limited success. In the best case (that leading to **7d** and **8d**; see Table I, entry 4), a 30% yield[3] of β-hydroxy-α-phenylthio esters **7** and **8** was obtained. In most instances, however, little if any quantity of aldol products could be detected by NMR analysis of the crude reaction mixtures, and the starting esters **5** were recovered. These results were surprising in view of the

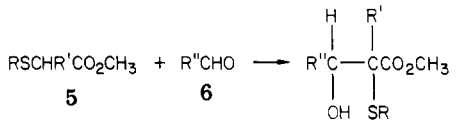
Scheme I



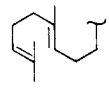
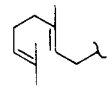
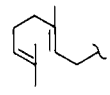
(1) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363.
(2) Hoye, T. R.; Kurth, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 5065.
(3) All yields refer to chromatographed or recrystallized material.

0022-3263/80/1945-3549$01.00/0

Table I. Reaction of α-Sulfenylated Esters 5 with Aldehydes 6 To Give Diastereomers 7 (Threo)[9] and 8 (Erythro)[9]

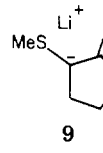


7 (threo) or 8 (erythro)

entry	5	6	7 (threo)	8 (erythro)	R	R'	R''	% yield[3] (7 + 8)	ratio[a] of 7/8
1	5a	6a	7a	8a	Ph	H	CH_3	77	50/50
2	5a	6b	7b	8b	Ph	H	Ph	82	40/60
3	5b	6b	7c	8c	Ph	CH_3	Ph	65	25/75
4	5b	6c	7d	8d	Ph	CH_3	$PhCH_2OCH_2$	29[b]	35/65
5	5c	6c	7e	8e	Ph		$PhCH_2OCH_2$	75	35/65
6	5d	6c	7f	8f	Ph		$PhCH_2OCH_2$	79	0/100
7	5e	6c	7g	8g	Ph	n-C_5H_{11}	$PhCH_2OCH_2$	78	40/60
8	5f	6c	7h	8h	CH_3		$PhCH_2OCH_2$	80	30/70

[a] As noted[13] these ratios were relatively reproducible as well as insensitive to changes in reaction conditions. Because the reactions varied widely in the degree of stereoselectivity and because it was not determined whether product ratios were kinetic or thermodynamic, we chose not to investigate the various factors, the most obvious of which would be the determination of the *E*/*Z* nature of the enolate derived from 5 by trapping with Me_3SiCl (see: Wissner, A. *J. Org. Chem.* **1979**, *44*, 4617; Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247) which is responsible for these ratios. [b] Condensation performed in absence of $ZnCl_2$ (see Experimental Section).

report of Uda and co-workers,[4] who successfully obtained aldol products in excellent yield from the reaction of the lithium enolate of **5** (R = H) with both aldehydes and ketones. However, the more hindered lithium enolate of α-(methylthio)-γ-butyrolactone (**9**) fails to add to cyclohexanone.[5] Other literature precedents also seemed to bear on the problem. The lithium and sodium enolates of methyl α-(phenylsulfinyl)acetate (**10**) are "unreactive" toward aldehydes and ketones (in as much as aldol adducts were not isolated), whereas the corresponding magnesium enolates of **10** add efficiently to these electrophiles.[6] The intramolecular aldol reaction of the α-methylsulfonyl ketone **11**, when mediated by the action of sodium *tert*-amyl oxide, yields the corresponding β-hydroxy ketone as the minor component in an equilibrium with the starting material.[7a] In contrast, substrate **12** cyclizes in high yield



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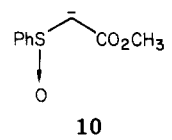

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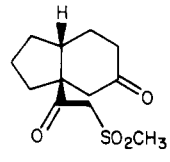
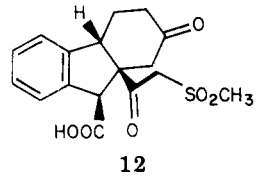


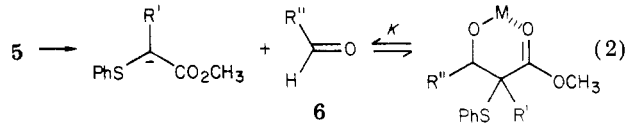
11



12

to its aldol product when treated with *tert*-butylmagnesium chloride.[7b] These observations, along with the frequently cited use of added zinc or magnesium salts to drive the equilibrium of simple aldol condensations toward products,[8] suggested that similar modifications might favorably alter the course of the coupling of **5** with **6**. This proved to be so, for when the lithium enolates of **5** (R = alkyl; from LDA at −78 °C in THF) were first treated with anhydrous zinc chloride and then allowed to react with aldehydes **6** at 0 °C for 10 min, high yields (65–82%)[3] of aldol products **7** and **8** were routinely obtained. Table I records the results of the condensations of esters **5a–f** with aldehydes **6a–c** under these conditions.

That a shift in equilibrium in favor of product **13** (larger *K* in eq 2) is at least partially responsible for the success



(2)

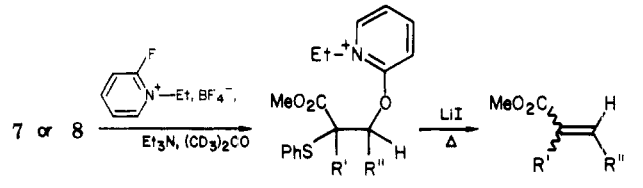
13a, M = Zn
b, M = Li
c, M = H

of this condensation reaction for M = Zn vs. M = Li was suggested by the observation that treatment of compound **7c** (**13c**; R' = CH_3, R'' = Ph) with lithium diisopropylamide in THF at −78 °C, warming the mixture to 0 °C for 10 min, and quenching the reaction led to a nearly quantitative generation of ester **5b**, the product of retroaldol reaction of the initially formed lithium alkoxide (see **13b**). Thus, the equilibrium is apparently sensitive to the metal ion, the degree of steric hindrance present in adduct **13** [cf. results of Uda[4] using **5** (R = H) with those reported here with **5** (R = alkyl) and with **9**], and the stability of the

(4) Yamagiwa, S.; Hoshi, N.; Sato, H.; Kosugi, H.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1978**, 214.
(5) Trost, B. M.; Arndt, H. C. *J. Org. Chem.* **1973**, *38*, 3140.
(6) Kunieda, N.; Nokami, J.; Kinoshita, M. *Tetrahedron Lett.* **1974**, 3997.
(7) (a) House, H. O.; Larson, J. K. *J. Org. Chem.* **1968**, *33*, 61. (b) House, H. O.; Melillo, D. G.; Sauter, F. J. *Ibid.* **1973**, *38*, 741.
(8) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.

enolate itself [i.e., **5** (R = H) leads to aldol products in the absence of strongly chelating metals whereas the more highly stabilized carbanions **10**, **11**, and **12** require these metals].

We were interested in unambiguously assigning threo or erythro stereochemistry[9] to the isomeric hydroxy esters **7e** and **8e** used in the aplysistatin synthesis.[2] We thus turned to the method of Mukaiyama[10] for a chemical means of structure determination. This involved the reaction of each pure diastereomer **7e** and **8e** with *N*-ethyl-2-fluoropyridinium tetrafluoroborate and triethylamine in hexadeuterioacetone to give the diastereomeric salts **14** (eq 3). Each of these was treated with lithium

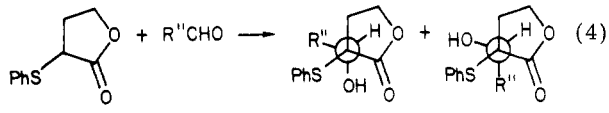


(3)

	R′	R″	olefin geometry
8c → **15a**	CH_3	Ph	*E*
7c → **15b**	CH_3	Ph	*Z*
8e → **15c**	homogeranyl	CH_2OCH_2Ph	*E*
7e → **15d**	homogeranyl	CH_2OCH_2Ph	*Z*
8f → **15e**	geranyl	CH_2OCH_2Ph	*E*

iodide and warmed to 60 °C to effect trans elimination[10] of "PhSI" and *N*-ethyl-2-pyridone. The readily determined *E* or *Z* nature of the purified olefins **15** then allowed assignment of stereochemistry to **7e** and **8e**. This entire process could be monitored by periodic NMR analysis. Equation 3 summarizes the reactions of the hydroxy esters **7** and **8** whose structures were uniquely determined in this fashion.[11] The major isomer resulting from the aldol condensation was in all three instances the erythro form (**8**) which eluted more slowly than the threo isomer (**7**) upon short-column silica gel chromatography.[12] Unfortunately, once these unambiguous stereochemical assignments were determined, no systematic trend in NMR spectral data could be identified that allowed structural determination on that basis alone, even though in several instances markedly different R″**CHOH** coupling constants were observed for the two isomers as might be expected for hydrogen-bonded species of type **13c**. Therefore, the remaining *threo*-**7**/*erythro*-**8** ratios noted in Table I (entries 1, 2, 4, 7, 8) are based upon the assumption that the major and more polar isomer has the erythro (**8**) stereochemistry as was observed for the examples shown in eq 3. It should be noted that these ratios are reasonably reproducible under the stated reaction conditions. A brief attempt to alter the relative amounts of *threo*-**7** and *erythro*-**8** products by varying these conditions[13] again revealed no particularly useful or systematic trends.

The condensations of α-(phenylthio)-γ-butyrolactone (**16**) with acetaldehyde (**6a**) and benzaldehyde (**6b**) (eq 4)



(4)

$$\mathbf{16} + \mathbf{6a} \xrightarrow{70\%} \mathbf{17a}\ (R'' = CH_3) + \mathbf{18a}\ (R'' = CH_3)$$

$$\mathbf{16} + \mathbf{6b} \xrightarrow{68\%} \mathbf{17b}\ (R'' = Ph) \text{ or } \mathbf{18b}\ (R'' = Ph)$$

in the presence of $ZnCl_2$ were also examined. In the former case a 1:1 mixture of threo and erythro adducts **17a** and **18a** was obtained whereas the benzaldehyde condensation under otherwise identical conditions afforded a single crystalline isomer. This was assigned structure **18b**, but only on the basis that the erythro isomer always predominated in the reactions of **5**.

In conclusion, β-hydroxy-α-phenylthio esters can be efficiently prepared through the zinc chloride mediated aldol condensation of α-phenylthio ester enolates and aldehydes. Further synthetic applications of these intermediates are under investigation.

Experimental Section

General Methods. Melting points were determined on a Kofler hot stage and are uncorrected. Elemental analyses were performed by M-H-W Laboratories. Column chromatography was carried out under pressure (ca. 5 psi) on silica gel H for TLC (EM 7736, Type 60) by using a modification of the short-column chromatography technique.[12] Infrared spectra were recorded on a Perkin-Elmer 237 instrument, nuclear magnetic resonance spectra were obtained on a Varian HFT-80 instrument in the Fourier transform mode, and mass spectra were determined on AE1 MS-30 (electron impact, EI, at 70 eV unless otherwise indicated) and Finnigan 4000 (chemical ionization, CI) instruments. All chromatographed products were colorless oils unless otherwise indicated.

General Procedure for the Preparation of α-Phenylthio Esters 5c–f. Into a dry 25 × 150 mm test tube containing 8.4 mL of a THF solution of lithium diisopropylamide (5.6 mmol, prepared from *n*-butyllithium and diisopropylamine in THF, 0.67 M, standardized with menthol and phenanthroline[14]) under nitrogen at −78 °C was transferred by cannula a THF (7 mL) solution of methyl 2-(phenylthio)acetate [or 2-(methylthio)acetate in the case of **5f**] which had been precooled to −78 °C. Enolate formation was judged complete by D_2O/DCl quench after 40 min at −78 °C. The resulting solution was transferred by cannula under N_2 into a solution of alkylating agent [2.92 mmol of homogeranyl toluenesulfonate (for **5c**), geranyl bromide (for **5d** and **5f**), or *n*-pentyl bromide (for **5e**)] in 6 mL of dry Me_2SO. The resulting brown solution was stirred at room temperature under N_2 for the indicated time, and the reaction was quenched by the addition of saturated aqueous ammonium chloride (25 mL). A standard workup with ether extraction and water and brine washing gave a light yellow oil which was chromatographed on silica gel to afford compound **5** in yields of 42–76%.

(*E*)-Methyl 6,10-Dimethyl-2-(phenylthio)-5,9-undecadienoate (5c). The reaction was quenched after 18 h and provided **5c**: 64% yield; ^1H NMR ($CDCl_3$) δ 1.57 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.98 (m, 8 H, 4 CH_2's), 3.66 (s, 3 H, OCH_3), 3.66 (t, *J* = 7 Hz, 1 H, SCH), 5.05 (br t, 2 H, 2 HC=C's), 7.30 (m, 5 H, Ar H); IR (neat) 3070, 2930, 2860, 1740, 1670, 1590, 1485, 1440, 1260, 1155, 750, 695 cm^{-1}; mass spectrum (EI), *m/e* (relative

(9) The terms threo and erythro are used here to describe structures **7** and **8**, respectively, and are assigned on the basis of Cahn–Ingold–Prelog priorities of the various substituents.

(10) Mukaiyama, T.; Imaoka, M. *Chem. Lett.* **1978**, 413.

(11) It should be noted that this method[10] failed to distinguish threo and erythro isomers **17a** and **18a** as well as **7b** and **8b**. In the former case, both isomers gave the thermodynamically more stable (*E*)-α-ethylidene-γ-butyrolactone. In the latter instance, both isomers afforded (*Z*)-methyl 2-(phenylthio)cinnamate [^1H NMR ($CDCl_3$) δ 3.66 (OCH_3), 7.23 (br s, 5 H, SAr**H**), 7.25–7.45 (m, 3 H, ArH), 7.65–7.95 (m, 2 H, Ar H), 8.09 (s, 1 H, HC=C); IR (neat) 3040, 3010, 2940, 1710, 1630, 1585, 1485, 1480, 1430, 1255, 1230, 1190, 1070, 1030, 760, 730, 685 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 270 (10), 211 (8), 142 (49), 131 (100), 103 (56), 77 (32). Anal. Calcd for $C_{16}H_{14}O_2S$: *m/e* 270.0713. Found: *m/e* 270.0707], presumably as a result of competing β elimination of a proton and *N*-ethylpyridone from the intermediate pyridinium salt (see ref 4).

(12) Hunt, B. J.; Rigby, W. *Chem. Ind. (London)* **1967**, 1868.

(13) Basically the same ratios of **7b**/**8b** were observed when zinc chloride was added as an ethereal solution[14] to the lithium enolate in THF at 0 °C in either the absence or presence of HMPA (3 equiv). If the entire reaction (**5a**/THF, LDA, $ZnCl_2/Et_2O$, **6b**, NH_4Cl quench) was carried out at −78 °C, the ratio of **7b**/**8b** was again unchanged although ca. 25% starting material (**5a**) remained in the crude reaction mixture.

(14) Posner, G. H.; Lentz, C. M. *J. Am. Chem. Soc.* **1979**, *101*, 934.

intensity) 332 (7), 289 (9), 263 (16), 123 (47), 109 (36), 77 (14), 69 (100), 55 (22). Anal. Calcd for $C_{20}H_{28}O_2S$: *m/e* 332.1808. Found: *m/e* 332.1803.

(*E*)-Methyl 5,9-Dimethyl-2-(phenylthio)-4,8-decadienoate (5d). The reaction was quenched after 15 min and provided **5d**: 76% yield; ^{1}H NMR ($CDCl_3$) δ 1.59 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.98 (br s, 4 H, 2 CH_2's), 2.50 (m, 2 H, CH_2CHS), 3.64 (s, 3 H, OCH_3), 3.64 (m, 1 H, CHS), 5.10 (m, 2 H, 2 CH=C's), 7.35 (m, 5 H, Ar H); IR (neat) 3050, 2910, 2840, 1740, 1665, 1585, 1480, 1440, 1260, 1155, 1020, 740, 685 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 318 (10), 275 (10), 249 (5), 209 (24), 208 (22), 194 (30), 182 (66), 69 (100). Anal. Calcd for $C_{19}H_{26}O_2S$: *m/e* 318.1653. Found: *m/e* 318.1660.

Methyl 2-(Phenylthio)heptanoate (5e). The reaction was quenched after 18 h and provided **5e**: 42% yield; ^{1}H NMR ($CDCl_3$) δ 0.86 (br t, 3 H, CH_2CH_3), 1.05–1.55 (m, 6 H, 3 CH_2's), 1.55–1.95 (m, 2 H, CH_2CHS), 3.61 (br t, 1 H, CHS), 3.63 (s, 3 H, OCH_3), 7.30 (m, 5 H, Ar H); IR (neat) 3050, 2950, 2930, 2850, 1735, 1580, 1480, 1465, 1440, 1260, 1155, 1020, 740, 690 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 252 (52), 193 (70), 143 (19), 109 (34). Anal. Calcd for $C_{14}H_{20}O_2S$: *m/e* 252.1184. Found: *m/e* 252.1196.

(*E*)-Methyl 5,9-Dimethyl-2-(methylthio)-4,8-decadienoate (5f). The reaction was quenched after 15 min and provided **5f**: 76% yield; ^{1}H NMR ($CDCl_3$) δ 1.59 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.98 (br s, 4 H, 2 CH_2's), 2.13 (s, 3 H, SCH_3), 2.46 (m, 2 H, CH_2CHS), 3.25 (dd, J = 7, 15 Hz, 1 H, CHS), 3.72 (s, 3 H, OCH_3), 5.07 (m, 2 H, 2 CH=C's); IR (neat) 2960, 2920, 2850, 1735, 1655, 1440, 1275, 1155 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 256 (4), 241 (3), 208 (8), 187 (4), 176 (19), 120 (62), 81 (46), 69 (100), 61 (68). Anal. Calcd for $C_{14}H_{24}O_2S$: *m/e* 256.1495. Found: *m/e* 256.1489.

General Procedure for the Aldol Condensation of 5 with 6 To Give 7 and 8. Formation of the lithium enolate of **5** was performed as described above in the preparation of **5**. On a 6.59-mmol scale, the solution of the enolate in 27 mL of THF was transferred by cannula into another test tube containing freshly fused zinc chloride (9.23 mmol). After the mixture was stirred for 10 min at 0 °C, nearly all of the $ZnCl_2$ had dissolved, and aldehyde **6** (11.8 mmol) in 4 mL of THF was added. After 10 min at 0 °C, saturated ammonium chloride was added. Workup as described above gave a light yellow oil which was chromatographed on silica gel to afford **7** and **8** in the amounts noted in Table I.

(2*RS*,3*SR*)- and (2*RS*,3*RS*)-Methyl 3-Hydroxy-2-(phenylthio)butanoates (7a and 8a). Short-column chromatography (5:1 hexanes–EtOAc) on silica gel provided in 77% yield equal amounts of the less polar (assigned **7a**) and more polar (assigned **8a**) isomers. For **7a**: ^{1}H NMR ($CDCl_3$) δ 1.33 (d, J = 7 Hz, 3 H, $CHCH_3$), 3.05 (br d, J = 2 H, 1 H, OH), 3.56 (d, J = 7 Hz, 1 H, CHS), 3.69 (s, 3 H, OCH_3), 4.10 (m, 1 H, CHOH 7.34 (m, 5 H, Ar H); IR (neat) 3490, 3050, 2970, 2940, 1730, 1605, 1480, 1460, 1160, 1120, 1085, 1020, 1000, 940, 740, 690 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 244 (M + NH_4^+), 227 (M + H^+), 226, 209, 200. For **8a**: ^{1}H NMR ($CDCl_3$) δ 1.37 (d, J = 7 Hz, 3 H, $CHCH_3$), 2.71 (d, J = 6 Hz, 1 H, OH), 3.54 (d, J = 7 Hz, 1 H, CHS), 3.67 (s, 3 H, OCH_3), 4.05 (br heptet, 1 H, CHOH), 7.32 (m, 5 H, Ar H); IR (neat) 3450, 3050, 2980, 2950, 1730, 1590, 1480, 1440, 1380, 1270, 1200, 1160, 1120, 1090, 1015, 940, 880, 745, 690 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 244 (M + NH_4^+), 227 (M + H^+), 226, 209, 200.

(2*RS*,3*SR*)- and (2*RS*,3*RS*)-Methyl 3-Hydroxy-2-(phenylthio)benzenepropanoates (7b and 8b).[4] Chromatography (6:1 hexanes–EtOAc) afforded in 82% yield a 2:3 mixture of the less polar (assigned **7b**) and more polar (assigned **8b**) isomers. For **7b**: ^{1}H NMR ($CDCl_3$) δ 3.38 (br s, 1 H, OH), 3.55 (s, 3 H, OCH_3), 3.82 (d, J = 8 Hz, 1 H, CHS), 5.00 (br d, J = 8 Hz, 1 H, CHOH), 7.33 (br s, 10 H, Ar H); IR (neat) 3450, 3040, 3010, 2930, 1950, 1880, 1810, 1730, 1580, 1490, 1480, 1450, 1435, 1140, 1080, 1040, 1015, 910, 740, 690 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 306 (M + NH_4^+), 288 (M + NH_4^+ – H_2O), 271 (M + H^+ – H_2O). For **8b**: mp 99.5–100 °C (from hexanes–EtOAc) (lit.[4] mp 99–100 °C); ^{1}H NMR ($CDCl_3$) δ 3.12 (br s, 1 H, OH), 3.65 (s, 3 H, OCH_3), 3.92 (d, J = 8 Hz, 1 H, CHS), 5.01 (br d, J = 8 Hz, 1 H, CHOH), 7.24 (s, 5 H, Ar H), 7.33 (s, 5 H, Ar H); IR (neat) 3460, 3050, 3020, 2950, 1950, 1880, 1805, 1730, 1580, 1490, 1480, 1450, 1435, 1263, 1145, 1015, 910, 760, 740, 685 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 306 (M + NH_4^+), 288 (M + NH_4^+ – H_2O), 271 (M + H^+ – H_2O). Anal. Calcd for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59. Found: C, 66.92; H, 5.62.

(2*RS*,3*SR*)- and (2*RS*,3*RS*)-Methyl 3-Hydroxy-2-methyl-2-(phenylthio)benzenepropanoates (7c and 8c). Chromatography (6:1 hexanes–EtOAc) afforded in 65% yield a 1:3 mixture of less polar (**7c**) and more polar (**8c**) isomers. For **7c**: ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3 H, CH_3), 3.37 (d, J = 2 Hz, 1 H, OH), 3.56 (s, 3 H, OCH_3), 5.11 (d, J = 2 Hz, 1 H, CHOH), 7.2–7.6 (m, 10 H, Ar H); IR (neat) 3480, 3070, 3040, 3000, 2950, 1960, 1890, 1810, 1730, 1605, 1585, 1575, 1495, 1475, 1455, 1440, 1380, 1250, 1110, 1085, 1045, 1028, 980, 900, 745, 695 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 320 (M + NH_4^+), 302 (M + NH_4^+ – H_2O), 285 (M + H^+ – H_2O). For **8c**: mp 99.5–101 °C (from hexanes–EtOAc); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H, CH_3), 3.51 (d, J = 5 Hz, 1 H, OH), 3.63 (s, 3 H, OCH_3), 5.07 (d, J = 5 Hz, 1 H, CHOH), 7.26–7.52 (m, 10 H, Ar H); IR (KBr) 3460, 3060, 3020, 3000, 2950, 2940, 2890, 1710, 1570, 1490, 1470, 1450, 1415, 1250, 1150, 1100, 1040, 905, 760, 750, 710, 690 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 320 (M + NH_4^+), 302 (M + NH_4^+ – H_2O), 285 (M + H^+ – H_2O). Anal. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 6.00. Found: C, 67.74; H, 6.10.

(2*RS*,3*SR*)- and (2RS,3RS)-Methyl 4-(Benzyloxy)-3-hydroxy-2-methyl-2-(phenylthio)butanoates (7d and 8d). This reaction was carried out as described above except that the solution of lithium enolate was not treated with $ZnCl_2$ but was reacted with aldehyde **6c** directly. Chromatography (6:1 hexanes–EtOAc) afforded in 29% yield a 35:65 mixture of less polar (assigned **7d**) and more polar (assigned **8d**) isomers. For **7d**: ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3 H, CH_3), 3.02 (br s, 1 H, OH), 3.52 (s, 3 H, OCH_3), 3.56 (m, 2 H, OCH_2CHOH), 4.17 (br dd, J = 6, 5 Hz, 1 H, CHOH); 4.49 (s, 2 H, CH_2Ph), 7.28 (s, 5 H, CH_2ArH), 7.3–7.6 (m, 5 H, SArH); IR (neat) 3500, 3060, 3020, 3000, 2970, 2930, 1970, 1890, 1810, 1730, 1580, 1490, 1495, 1445, 1430, 1245, 1100, 1020, 1110, 740, 690 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 346 (1), 196 (5), 109 (9), 107 (11), 91 (100). Anal. Calcd for $C_{19}H_{22}O_4S$: *m/e* 346.1238. Found: *m/e* 346.1252. For **8d**: ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3 H, CH_3), 3.15 (br d, J = 7 Hz, 1 H, OH), 3.58 (s, 3 H, OCH_3), 3.59 (dd, J = 13, 7 Hz, 1 H, OCH_aH_bCHOH), 3.97 (dd, J = 13, 3 Hz, 1 H, OCH_aH_bCHOH), 4.15 (m, simplifies to dd upon D_2O addition, J = 7, 3 Hz, 1 H, CHOH), 4.55 (s, 2 H, CH_2Ph), 7.32 (br s, 10 H, Ar H); IR (neat) 3450, 3060, 3030, 3000, 2870, 2840, 1970, 1890, 1810, 1730, 1580, 1490, 1470, 1450, 1435, 1250, 1110, 1060, 1020, 970, 910, 740, 690 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 346 (0.1), 196 (3), 109 (10), 107 (12), 91 (100). Anal. Calcd for $C_{19}H_{22}O_4S$: *m/e* 346.1238. Found: *m/e* 346.1216.

(*E*)-(2*RS*,1′*SR*)- and (*E*)-(2*RS*,1′*RS*)-Methyl 6,10-Dimethyl-2-[2′-(benzyloxy)-1′-hydroxyethyl]-2-(phenylthio)-5,9-undecadienoates (7e and 8e). Chromatography (9:1 hexanes–EtOAc) afforded in 75% yield a 35:65 mixture of the less polar (**7e**) and more polar (**8e**) isomers. For **7e**: ^{1}H NMR ($CDCl_3$) δ 1.57 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.74–2.35 (m, 3 H, 4 CH_2's), 3.20 (d, J = 7 Hz, 1 H, OH), 3.55 (s, 3 H, OCH_3), 3.64–4.15 (m, 3 H, OCH_2CHOH), 4.53 (br s, 2 H, CH_2Ph), 4.99 (br t, 2 H, two HC=C's), 7.32 (m, 10 H, Ar H); IR (neat) 3500, 3070, 3020, 2930, 2870, 1960, 1880, 1810, 1730, 1670, 1590, 1495, 1470, 1450, 1435, 1210, 1100, 750, 695 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 482 (0.3), 413 (3), 373 (0.3), 361 (0.2), 332 (2), 123 (26), 109 (22), 107 (42), 91 (100), 89 (89). Anal. Calcd for $C_{24}H_{24}O_4S$ (M^+ – CH_2CH=$C(CH_3)_2$): *m/e* 413.1785. Found: *m/e* 413.1755. For **8e**: ^{1}H NMR ($CDCl_3$) δ 1.57 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.75–2.50 (m, 8 H, 4 CH_2's), 3.43 (d, J = 6 Hz, 1 H, OH), 3.59 (s, 3 H, OCH_3), 3.60–4.20 (m, 3 H, OCH_2CHOH), 4.54 (s, 2 H, CH_2Ph), 4.98 (br t, 2 H, 2 HC=C's), 7.31 (m, 10 H, Ar H); IR (neat) 3500, 3060, 3030, 2930, 2860, 1960, 1880, 1810, 1730, 1670, 1590, 1495, 1470, 1450, 1435, 1215, 1100, 750, 690 cm^{-1}; mass spectrum (EI), *m/e* (relative intensity) 482 (0.2), 413 (2), 373 (0.1), 361 (0.3), 332 (2), 123 (23), 109 (21), 107 (33), 91 (100), 89 (82). Anal. Calcd for $C_{23}H_{31}O_3$ (M^+ – H_2O – PhS): *m/e* 355.2272. Found: *m/e* 355.2321.

(*E*)-(2*RS*,1′*RS*)-Methyl 5,9-Dimethyl-2-[2′-(benzyloxy)-1′-hydroxyethyl]-2-(phenylthio)-4,8-decadienoate (8f). This lone example afforded a single isomer in 79% yield which was subsequently shown to be **8f**: ^{1}H NMR ($CDCl_3$) δ 1.46, 1.59, 1.66 (3 br s, 3 H each, 3 CH_3's), 2.00 (br s, 4 H, 2 CH_2's), 2.41 (d, J

= 6 Hz, 2 H, CH_2CS), 3.54 (s, 3 H, OCH_3), 3.71 (m, 3 H, OCH_2CHOH), 4.02 (m, 1 H, CHOH), 4.48 (s, 2 H, CH_2Ph), 5.04 (m, 1 H, HC=C), 5.38 (br t, J = 6 Hz, 1 H, HC=C), 7.28 (s, 5 H, CH_2ArH), 7.32 (m, 5 H, SArH); IR (neat) 3500, 3070, 3030, 2930, 2870, 1960, 1880, 1810, 1730, 1590, 1580, 1495, 1470, 1455, 1435, 1215, 1100, 1010, 750, 690 cm^{-1}; mass spectrum (CI, NH_3), m/e 486 ($M + NH_4^+$), 469 ($M + H^+$), 451 ($M + H^+ - H_2O$).

(2*RS*,1′*SR*)- and (2RS,1′RS)-Methyl 2-[2′-(Benzyloxy)-1′-hydroxyethyl]-2-(phenylthio)heptanoates (7g and 8g). Chromatography (9:1 hexanes–EtOAc) afforded in 78% yield a 40:60 mixture of less polar (assigned **7g**) and more polar (assigned **8g**) isomers. For **7g**: ^1H NMR ($CDCl_3$) δ 0.85 (br t, J = 7 Hz, 3 H, CH_2CH_3), 1.0–2.05 (m, 8 H, 4 CH_2's), 3.21 (d, J = 6 Hz, 1 H, OH), 3.54 (s, 3 H, OCH_3), 3.75–4.13 (m, 3 H, OCH_2CHOH), 4.54 (AB, J_{ab} = 11 Hz, 2 H, CH_2Ph), 7.31 (s, 5 H, CH_2ArH), 7.43 (m, 5 H, SArH); IR (neat) 3520, 3070, 3030, 2980, 2970, 2870, 1960, 1890, 1810, 1730, 1590, 1580, 1500, 1470, 1460, 1440, 1230, 1120, 1030, 750, 695 cm^{-1}; mass spectrum (CI, NH_3), m/e 420 ($M + NH_4^+$), 403 ($M + H^+$), 385 ($M = H^+ - H_2O$). For **8g**: ^1H NMR ($CDCl_3$) δ 0.85 (br t, J = 7 Hz, 3 H, CH_2CH_3), 1.0–2.05 (m, 8 H, 4 CH_2's), 3.46 (d, J = 6 Hz, 1 H, OH), 3.59 (s, 3 H, OCH_3), 3.62–4.19 (m, 3 H, OCH_2CHOH), 4.54 (s, 2 H, CH_2Ph), 7.36 (m, 10 H, Ar H); IR (neat) 3500, 3060, 3030, 2970, 2930, 2870, 1950, 1880, 1810, 1730, 1580, 1570, 1495, 1465, 1450, 1435, 1230, 1200, 1105, 1020, 740, 690 cm^{-1}; mass spectrum (CI, NH_3), m/e 420 ($M + NH_4^+$), 403 ($M + H^+$), 385 ($M + H^+ - H_2O$).

(*E*)-(2*RS*,1′*SR*)- and (*E*)-(2*RS*,1′*RS*)-Methyl 5,9-Dimethyl-2-[2′-(benzyloxy)-1′-hydroxyethyl]-2-(methylthio)-4,8-decadienoates (7h and 8h). Crude chromatography (6:1 hexanes–EtOAc) gave in 80% yield a purified but unseparated mixture of **7h** and **8h** in a 30:70 ratio as judged from analysis of the NMR spectrum of the mixture: ^1H NMR ($CDCl_3$) δ 1.49 (br s, 6 H, 2 CH_3's), 1.66 (br s, 3 H, CH_3), 1.98 (br s, 4 H, 2 CH_2's), 2.05 (major) and 2.08 (minor) (2 s, 3 H, SCH_3), 2.57 (d, J = 7 Hz, 2 H, CH_2CS), 2.97 (minor) and 3.21 (major) (2 d, J = 5 and 7 Hz, 1 H, OH), 3.55–3.80 (m, 2 H, OCH_2CH), 3.67 (s, 3 H, OCH_3), 4.14 (m, 1 H, CHOH), 4.51 (s, 2 H, CH_2Ph), 5.04 (m, 1 H, HC=C), 5.26 (br t, J = 7 Hz, 1 H, $SCCH_2CH$=C), 7.30 (br s, 5 H, Ar H); IR (neat) 3500, 3070, 3040, 2920, 2860, 1970, 1900, 1810, 1730, 1670, 1590, 1580 1495, 1470, 1450, 1430, 1220, 1100, 1020, 740, 685 cm^{-1}.

Preparation of Lactones 17 and 18. The procedure used to condense **16** with **6a** and **6b** was identical with that described above for conversion of **5** plus **6** to **7** and **8**.

(3*RS*,1′*SR*)- and (3*RS*,1′*RS*)-4,5-Dihydro-3-(1′-hydroxyethyl)-3-(phenylthio)furan-2(3*H*)-ones (17a and 18a). Chromatography (3:1 hexanes–EtOAc) afforded in 70% yield a 1:1 mixture of the less polar (assigned **17a**) and more polar (assigned **18a**) isomers. For **17a**: ^1H NMR ($CDCl_3$) δ 1.39 (d, J = 7 Hz, CH_3), 1.99 (m, 1 H, $SCCH_aH_mCH_xH_yO$), 2.28 (br d, J = 4 Hz, 1 H, OH), 2.77 (m, 1 H, $SCCH_aH_mCH_xH_yO$), 4.07 (dq, J = 7, 4 Hz, 1 H, CHOH), 4.26 (m, 2 H, $SCCH_2CH_2O$), 7.2–7.6 (m, 5 H, ArH); IR (CCl_4) 3600, 3520, 3070, 2990, 2930, 1765, 1590, 1480, 1450, 1380, 1270, 1220, 1180, 1090, 1040, 990, 740, 695 cm^{-1}; mass spectrum (EI), m/e (relative intensity) 238 (7), 194 (100), 161 (14), 149 (18), 121 (26), 117 (18), 115 (13), 110 (15), 109 (22), 105 (14), 91 (12). Anal. Calcd for $C_{12}H_{14}O_3S$: m/e 238.0661. Found: m/e 238.0667. For **18a**: mp 59–60 °C (from hexanes–EtOAc); ^1H NMR ($CDCl_3$) 1.28 (d, J = 7 Hz, CH_3), 1.90–2.73 (m, 2 H, $SCCH_2$), 3.19 (br s, 1 H, OH), 4.00 (br q, 1 H, CHOH), 4.22 (m, 2 H, CH_2O), 7.30–7.45 (m, 3 H, Ar H), 7.45–7.65 (m, 2 H, Ar H); IR (CCl_4) 3520, 3070, 2980, 2910, 1765, 1580, 1480, 1440, 1375, 1275, 1220, 1175, 1035, 1005, 690 cm^{-1}; mass spectrum (EI), m/e (relative intensity) 238 (3), 194 (100), 161 (10), 149 (13), 121 (21), 117 (19), 115 (15), 110 (19), 109 (18), 105 (11), 91 (12). Anal. Calcd for $C_{12}H_{14}O_3S$: m/e 238.0661. Found: m/e 238.0679. Calcd: C, 60.48; H, 5.92. Found: C, 60.36; H, 6.04.

(3*RS*,1′*RS*)-4,5-Dihydro-3-(1′-hydroxy-1′-phenylmethyl)-3-(phenylthio)furan-2(3*H*)-one (18b). The condensation of **16** with benzaldehyde afforded a single crystalline diastereomer (assigned **18b** although the threo isomer **17b** cannot be excluded)[11] in 68% yield: mp 119–120.5 °C (from hexanes–EtOAc); ^1H NMR ($CDCl_3$) δ 1.85 (ddd, J = 14, 6, 3 Hz, 1 H, $SCCH_aH_mCH_2O$), 2.85 (br s, 1 H, OH), 2.97 (m, 1 H, J_{am} = 14 Hz, $SCCH_aH_mCH_2O$), 4.07 (m, 2 H, CH_2O), 5.12 (br s, 1 H, CHOH), 7.3–7.6 (m, 10 H, Ar H); IR ArH); (KBr) 3430, 3060, 3030, 2970, 2920, 2880, 1960, 1880, 1740, 1660, 1590, 1580, 1490, 1470, 1450, 1440, 1380, 1355, 1280, 1215, 1190, 1110, 1080, 1050, 1020, 960, 740, 690 cm^{-1}; mass spectrum (CI, NH_3), m/e 318 ($M + NH_4^+$), 300 ($M + NH_4^+ - H_2O$), 283 ($M + H^+ - H_2O$). Anal. Calcd for $C_{17}H_{16}O_3S$: C, 67.98; H, 5.37. Found: C, 67.78; H, 5.15.

Preparation of Substituted Acrylates 15a–e. In a typical experiment the β-hydroxy sulfide **7** or **8** (0.1 mmol) was dissolved in 300 μL of acetone-d_6, and *N*-ethyl-2-fluoropyridinium tetrafluoroborate (0.12 mmol) and triethylamine (freshly distilled, 0.12 mmol) were added sequentially. After the mixture had been allowed to stand ca. 5 min at room temperature, NMR analysis indicated complete conversion of the alcohol (presumably to pyridinium salt **14**), and LiI (0.13 mmol) was added. The mixture was warmed at 60 °C for ca. 40 min (until NMR analysis showed complete disappearance of **14**), and the dark brown solution was placed on a 0.25 × 100 × 200 mm silica gel plate and purified to give the acrylates **15**. Although the yields on this scale were between 45 and 65%, in all cases the purified product was virtually the only olefin that could be detected in the NMR spectrum of the crude reaction mixture before workup.

(*E*)-Methyl 2-Methylcinnamate (15a) from 8c. Chromatography (17:1 hexanes–EtOAc) afforded **15a**:[15] 55% yield; ^1H NMR ($CDCl_3$) δ 2.10 (d, J = 2 Hz, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 7.37 (s, 5 H, Ar H), 7.68 (q, J = 2 Hz, 1 H, HC=C).

(*Z*)-Methyl 2-Methylcinnamate (15b) from 7c. Chromatography (17:1 hexanes–EtOAc) afforded **15b**:[15] 55% yield; ^1H NMR ($CDCl_3$) δ 2.08 (d, J = 2 Hz, 3 H, CH_3), 3.64 (s, 3 H, OCH_3), 6.71 (q, J = 2 Hz, 1 H, HC=C), 7.25 (s, 5 H, Ar H).

(2(1′)*E*,5*E*)-Methyl 2-(2′-Benzyloxyethylidene)-6,10-dimethyl-5,9-undecadienoate (15c) from 8e. Chromatography (17:1 hexanes–EtOAc) afforded **15c**: 45% yield; ^1H NMR ($CDCl_3$) δ 1.54, 1.57, 1.66 (3 br s, 9 H, 3 CH_3's), 1.8–2.5 (m, 8 H, 4 CH_2's), 3.74 (s, 3 H, OCH_3), 4.19 (d, J = 6 Hz, 2 H, C=$CHCH_2O$), 4.51 (s, 2 H, CH_2Ph), 5.06 (br t, 2 H, 2 HC=C's), 6.85 (t, J = 6 Hz, 1 H, C=$CHCH_2O$), 7.32 (s, 5 H, Ar H); IR (neat) 3070, 3050, 3010, 2920, 2850, 1715, 1645, 1495, 1450, 1435, 1260, 1110, 735, 690 cm^{-1}; mass spectrum (EI, 20 eV), m/e (relative intensity) 356 (2), 205 (15), 137 (23), 123 (12), 107 (10), 91 (100), 69 (57).

(2(1′)*Z*,5*E*)-Methyl 2-(2′-Benzyloxyethylidene)-6,10-dimethyl-5,9-undecadienoate (15d) from 7e. Chromatography (17:1 hexanes–EtOAc) afforded **15d**: 43% yield; ^1H NMR ($CDCl_3$) δ 1.56 (br s, 6 H, 2 CH_3's), 1.64 (br s, 3 H, CH_3), 1.8–2.4 (m, 8 H, 4 CH_2's), 3.70 (s, 3 H, OCH_3), 4.43 (d, J = 6 Hz, 2 H, C=$CHCH_2O$), 4.49 (s, 2 H, CH_2Ph), 5.06 (m, 2 H, 2 HC=C's), 6.08 (t, J = 6 Hz, 1 H, C=$CHCH_2O$), 7.31 (s, 5 H, Ar H); IR (neat) 3060, 3030, 2920, 2860, 1715, 1645, 1500, 1455, 1435, 1365, 1210, 1155, 1115, 1070, 735, 695 cm^{-1}; mass spectrum (EI, 20 eV), m/e (relative intensity) 356 (2), 233 (28), 205 (25), 136 (82), 123 (14), 107 (13), 91 (89), 69 (100).

(2(1′)*Z*,4*E*)-Methyl 2-(2′-Benzyloxyethylidene)-5,9-dimethyl-4,8-decadienoate (15e) from 8f. Chromatography (17:1 hexanes–EtOAc) afforded **15e**: 67% yield; ^1H NMR ($CDCl_3$) δ 1.55, 1.60, 1.65 (3 s, 9 H, 3 CH_3's), 1.94 (br s, 4 H, 2 CH_2's), 2.95 (d, J = 7 Hz, 2 H, C=$CHCH_2C$=C), 3.72 (s, 3 H, OCH_3), 4.20 (d, J = 6 Hz, 2 H, C=$CHCH_2O$), 4.51 (s, 2 H, CH_2Ph), 5.00 (m, 2 H, 2 HC=C's), 6.83 (t, J = 6 Hz, 1 H, C=$CHCH_2O$), 7.31 (s, 5 H, ArH); IR (neat) 3080, 3060, 3020, 2950, 2920, 2850, 1715, 1660, 1490, 1450, 1430, 1260, 1205, 1110, 1045, 740, 695 cm^{-1}; mass spectrum (EI, 20 eV), m/e (relative intensity) 300 (13), 299 (6), 233 (4), 209 (25), 194 (18), 191 (21), 181 (9), 163 (31), 149 (13), 147 (10), 137 (8), 136 (30), 135 (17), 110 (14), 105 (11), 91 (100), 69 (41).

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Registry No. 5a, 17277-58-6; **5b**, 21673-18-7; **5c**, 71841-09-3; **5d**, 74143-92-3; **5e**, 74143-93-4; **5f**, 74143-94-5; **6a**, 75-07-0; **6b**, 100-52-7; **6c**, 60656-87-3; **7a**, 74143-95-6; **7b**, 66716-31-2; **7c**, 74143-96-7; **7d**,

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74143-97-8; **7e**, 71841-11-7; **7g**, 74143-98-9; **7h**, 74165-58-5; **8a**, 74143-99-0; **8b**, 66716-32-3; **8c**, 74144-00-6; **8d**, 74144-01-7; **8e**, 71841-10-6; **8f**, 74144-02-8; **8g**, 74144-03-9; **8h**, 74175-89-6; **15a**, 22946-43-6; **15b**, 21370-57-0; **15c**, 74144-04-0; **15d**, 74144-05-1; **15e**, 74144-06-2; **16**, 35998-30-2; **17a**, 74144-07-3; **18a**, 74144-08-4; **18b**, 74144-09-5; methyl 2-(methylthio)acetate, 16630-66-3; homogeranyl toluenesulfonate, 71841-08-2; geranyl bromide, 6138-90-5; *n*-pentyl bromide, 110-53-2; (*Z*)-methyl 2-(phenylthio)cinnamate, 58808-66-5.

Synthesis of Diethyl, Di-*n*-octyl, and Mono- and Dicyclohexano Macrocyclic Polyether–Diester Ligands

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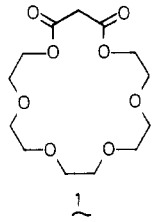
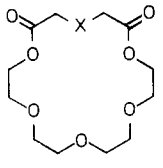
Three series of macrocyclic polyether–diester ligands have been prepared from the reaction of four diethyl-oligoethylene glycols, **24–27**, di-*n*-octyltetraethylene glycol **28**, and mono- and dicyclohexanotetraethylene glycols **29** and **30** with diglycolyl dichloride (products **6–11b**), thiadiglycolyl dichloride (products **12–17**), and 2,6-pyridinedicarbonyl chloride (products **18–23**). Compounds **11** and **17** formed trans-syn-trans and trans-anti-trans isomers, and in the case of compound **11** these isomers were isolated and characterized. The 18-membered-ring compounds **7**, **22**, and **23** formed solid potassium thiocyanate complexes.

Macrocyclic polyethers were first reported by Pedersen in 1967.[1,2] Since that time an intense interest in the synthesis and cation complexation properties of these macrocyclic compounds has developed. A number of excellent reviews have been published.[2-11]

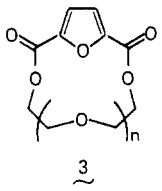
We have recently reported the synthesis of a large number of macrocyclic polyether–diester compounds.[12-16] We have also studied the cation complexation properties of compounds **1–5**.[17-21] Compound **1** shows a cation selectivity similar to that of valinomycin ($K^+ > Ba^{2+}$) whereas compound **2a** shows much the same complexing pattern as that of 18-crown-6 ($Ba^{2+} > K^+ > Na^+$) but with diminished stability.[17] Compound **2b** shows no heat of reaction except with Ag^+ as is seen with other sulfur macrocycles.[18] Compound **4b** shows excellent complexing properties, giving heats of reaction in methanol with alkali, alkaline earth, and silver cations on the order of 4.3–4.9 log *K* units.[18] Compounds **3–5** also complex strongly with alkylammonium cations as shown by significant chemical shift changes in the ^1H NMR spectra.[16,19-21] It is interesting to note that whereas the benzylammonium cation complex of **4b** (18-membered ring) was kinetically more stable than the complex of **4d** (24-membered ring), the benzylammonium cation complex of **3c** (24-membered ring) gave the most stable complex of the furan-containing ligands.[20] Clearly, different complexing parameters are operating in these two classes of compounds.



1

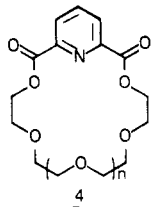


2
a,x = 0
b,x = S



3
a,n = 3
b,n = 4
c,n = 5

In order to study the complexing ability of the macrocyclic diester compounds more fully, we have synthesized a number of new alkyl-substituted macrocyclic polyether–diester compounds. A series of dimethyl- and tet-



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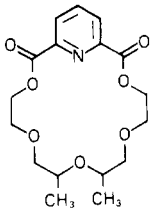
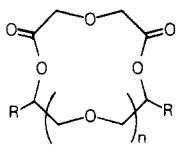
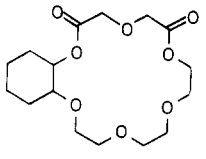
d,n = 3



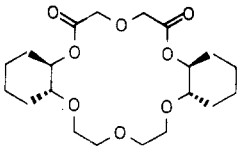
5



6 R = C_2H_5, n = 2
7 R = C_2H_5, n = 3
8 R = C_2H_5, n = 4
9 R = C_8H_{17}, n = 3



10



11a

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