Bakers' Yeast Reduction of Alkyl 6-Chloro-3-oxohexanoates: Synthesis of (*R*)-(+)-α-Lipoic Acid†

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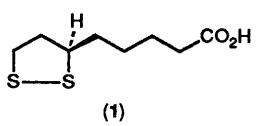
A number of alkyl 6-chloro-3-oxohexanoates were synthesized and their reduction with bakers' yeast studied. The enantioselectivity of these reductions was found to be influenced by the nature of the ester alkoxy substituent. The ethyl ester was reduced to the (3*R*)-6-chloro-3-hydroxyhexanoate (49% yield, 30% e.e.) while the octyl ester gave the (3*S*)-6-chloro-3-hydroxyhexanoate (62% yield, 90% e.e.). The latter product was then converted into (*R*)-(+)-α-lipoic acid, a cofactor in the biochemical decarboxylation of α-keto acids, *via* a sequence of seven steps.

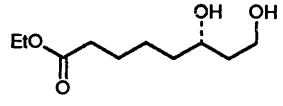
The reduction of functionalized β-keto esters by bakers' yeast can be a valuable procedure for the preparation of a variety of chiral trifunctional synthons.[1,2] Hence there has been much interest in understanding the scope of these reductions and in particular in predicting and controlling their stereochemical outcome.[3–7] The production of chiral alcohols of varying optical purities in these reductions can be attributed to competing oxidoreductases in bakers' yeast that have opposite enantioselectivity[8] and which generate products at different rates, or to a single enzyme of poor specificity. Hence, application of Prelog's rule[9] for predicting the absolute configuration of the chiral alcohols has had only limited success in many cases. Further, to obtain both high optical purity and good yields of the desired product is often difficult in these reductions.

Substrate modification has been suggested as a major method for controlling the stereochemical outcome of these reductions. Hirama *et al.* found that a number of potassium 3-oxoalkanoates[3] were reduced in high enantiomeric excess (e.e.) to the (*R*)-alcohols better than were their corresponding ester derivatives. The preparation of the potassium salts *via* alkaline hydrolysis of the corresponding esters limits this procedure to base-stable substrates.[10] Sih and co-workers discovered a stereochemical reversal from *S* to *R* in the reduction of alkyl 4-chloro-3-oxobutanoates,[6] on increasing the length of the ester chain. Going from ethyl to octyl, a trend was observed with the configuration changing from *S* to *R* with the octyl ester giving the *R*-alcohol of highest e.e. In contrast, butyl 5-methoxy-[10] and hexyl 5-benzyloxy-[4] 3-oxo esters are reduced in higher e.e. and yields than were their higher homologues.

We have been interested in the study of bakers' yeast reductions of functionalized β-keto esters for the production of trifunctional chiral synthetic intermediates and their applications to the synthesis of some natural products.[11] Here we would like to report our studies on the bakers' yeast reduction of readily prepared alkyl 6-chloro-3-oxohexanoates. Almost all of the published work so far has focussed on 4-chloro-3-oxo esters, and we desired to study the effect of the chloro atom elsewhere in the molecule. The usefulness of this study has been demonstrated by enantioselective synthesis of a key chiral intermediate (**2**) and its conversion into (**R**)-(+)-α-lipoic acid (**1**).



(1)



(2)

(*R*)-(+)-α-Lipoic acid (**1**) is a cofactor in the biochemical decarboxylation of a α-keto acids and has also been reported to be a growth factor for a variety of micro-organisms.[12] Recently, a number of reports have appeared describing the enantiospecific synthesis of (*R*)-(+)-α-lipoic acid.[13] Some of these syntheses utilize naturally available chiral starting materials[13a–e] while others use asymmetric synthetic methodology.[13f–h] A chiral synthesis of the intermediate (**2**) based on bakers' yeast reduction of octyl 7-cyano-3-oxoheptanoate has recently been published.[11] Also, an intermediate for (*S*)-(−)-α-lipoic acid has been synthesized using a bakers' yeast reduction.[4]

Results and Discussion

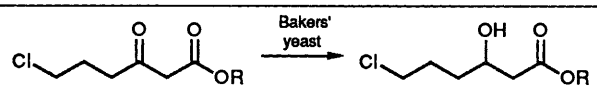
A number of alkyl 6-chloro-3-oxohexanoates (**3**) were synthesized in good yield (50–75%) by acylation of the anion obtained from deprotonation of alkyl acetates with lithium isopropylcyclohexylamide [tetrahydrofuran (THF); −76 °C] with 4-chlorobutanoyl chloride.[14] The β-keto esters (**3**) were then reduced with bakers' yeast and the e.e. of the chiral alcohols was ascertained by derivatization with Mosher's reagent,[15] (+)-methoxy(trifluoromethyl)phenylacetyl chloride (MTPA),‡ followed by ^{1}H NMR studies using Eu(fod)$_3$. Table 1 summarizes the results of these reductions.

Ethyl 6-chloro-3-oxohexanoate (**3a**) on reduction with bakers' yeast gave the alcohol (**4a**) in 49% yield and 30% e.e. The absolute configuration of the alcohol (**4a**) was determined to be *R* by dehalogenation with tributyltin hydride to the known compound ethyl 3-hydroxyhexanoate and comparison of its sign of rotation with published literature values.[16] Hence, reduction of compound (**3a**) is not only of poor enantioselectivity but also gives the alcohol (**4a**) having the wrong configuration for the synthesis of (*R*)-(+)-α-lipoic acid (**1**).

However, variation of the ester moiety in compounds (**3**) had a substantial effect in the stereochemical outcome of these reductions. The reduction of t-butyl, butyl, octyl, and decyl 6-chloro-3-oxohexanoates with bakers' yeast gave the corresponding (*S*)-alcohols (**4**) of increasing optical purity (see Table). The absolute configuration of the alcohols (**4b–d**) was determined by comparison of the ^{1}H NMR spectrum of their respective MTPA esters and the sign of optical rotation with those of the ethyl ester (**4a**). The configuration of octyl 6-chloro-

† Portions of this work were presented at the 197th meeting of the American Chemical Society, Dallas, TX, April 9–14, 1989.
‡ 3,3,3-Trifluoro-2-methoxy-2-phenylpropionyl chloride.

Table. Enantioselective reduction of alkyl 6-chloro-3-oxohexanoates (3) with bakers' yeast[a,b]



(3) (4)

R	Yield (%)	E.e. (%)	$[\alpha]_D$ (c, $CHCl_3$)	Absolute configuration
(4a) Et	49	30	−4.3° (1.6)	*R*
(4b) Bu	45	33	+4.2° (1.3)	*S*
(4c) Bu^t	29	25	+3.9° (1.4)	*S*
(4d) Octyl	62[c]	90	+10.6° (2.1)	*S*
	50	85	+8.6° (1.8)	*S*
(4e) Decyl	14	94	+9.3° (1.0)	*S*

[a] The reduction studies were carried out using Budweiser or Fleischmann's bakers' yeast with no significant difference in the results. [b] Reductions were carried out at room temperature (1–5 days), with a substrate concentration of 2 g l^{-1} in a 20 g l^{-1} sucrose solution in deionized water, and yeast (25 g per gram of substrate). [c] Substrate concentration was 3 g l^{-1} in a 30 g l^{-1} sucrose solution.

3-hydroxyhexanoate (**4d**) was established unequivocally to be (*S*) by its conversion into (*R*)-(+)-ethyl lipoate (**9**).

Although the decyl ester (**3e**) was reduced to the (*S*)-alcohol (**4e**) with highest optical purity, the reduction was slow and gave poor yields. A substantial amount of starting material (60–70%) was recovered even after 5 days of reduction.

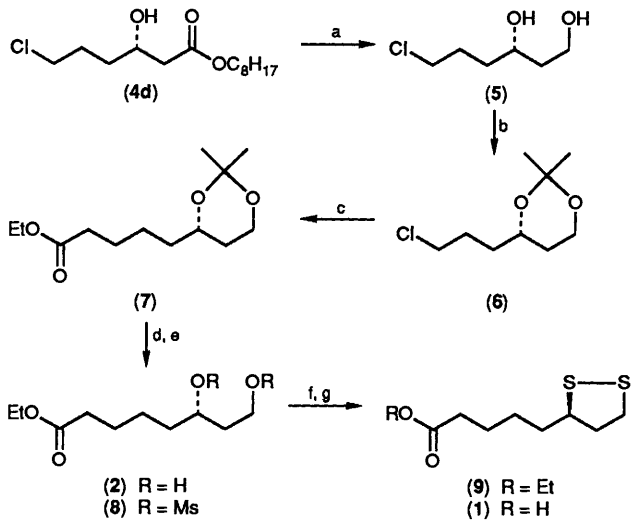
The octyl β-keto ester (**3d**) was reduced by bakers' yeast to the (*S*)-alcohol (**4d**) in good yield (55–62%) and high e.e. (86–90%) and therefore was the substrate of choice for the synthesis of compound (**1**). Further, we have found that increasing the concentration of ester (**3d**) from 2 g to 3 g l^{-1} in the yeast reduction improved both the optical purity and the yield of the hydroxy ester (**4d**). This reduction has been carried out several times in our laboratory and is quite reproducible.

The alcohol (**4d**) was then converted into (*R*)-(+)-ethyl lipoate (**9**) as shown in Scheme 1. The ester moiety in compound (**4d**) underwent smooth reduction with lithium borohydride in dry THF to give the diol (**5**), which was protected as its acetonide (**6**). Alkylation of compound (**6**) with excess of sodium diethyl malonate followed by de-ethoxycarbonylation gave the ester (**7**). After purification by column chromatography, compound (**7**) was deprotected to the diol (**2**) and this was in turn converted into the dimesyl ester (**8**) following published procedures.[13b,c] The absolute configuration of (**8**) was confirmed to be *S* by comparison with literature values[13c] of its optical rotation. The conversion of the dimesyl ester (**8**) into (*R*)-(+)-α-lipoic acid (**1**) in two steps has been previously described by two other groups[13b,c] and proceeds with inversion of the chiral centre. Reaction of compound (**8**) with sodium sulphide and sulphur in dimethylformamide (DMF) at 90 °C gave (*R*)-(+)-ethyl lipoate (**9**). The ethyl ester (**9**) has been hydrolysed[13c] with 0.1M-potassium hydroxide in ethanol at room temperature to (*R*)-(+)-α-lipoic acid (**1**).

In conclusion, the enantioselectivity of the bakers' yeast reduction of 6-chloro-3-oxohexanoate esters can be controlled by selection of a suitable ester alkoxy group. The resulting (*S*)-octyl 6-chloro-3-hydroxyhexanoate (**4d**) has been shown to be a valuable chiral intermediate for the synthesis of (*R*)-(+)-α-lipoic acid, a biologically important enzyme cofactor.

Experimental

General Procedures.—IR spectra were recorded on a Perkin-Elmer 283B Spectrophotometer. ^1H NMR spectra were obtained on a Varian XL 200 MHz spectrometer in $CDCl_3$ with



Scheme. *Reagents and conditions:* (a) $LiBH_4$, THF, 80%; (b) $Me_2C(OMe)_2$, *p*-TsOH, CH_2Cl_2, 60%; (c) $CH_2(CO_2Et)_2$, NaH, DMF, 75 °C; NaCN, DMSO, 165 °C, 43%; (d) 10% H^+–EtOH, 98%; (e) MsCl, Et_3N, CH_2Cl_2, 0 °C, 69%; (f) $Na_2S{\cdot}9H_2O$, S, DMF, 85 °C, 79%; (g) ref. 13*c*.

$SiMe_4$ as internal standard. Mass spectroscopic analyses were carried out on a Hitachi RMU6 mass spectrometer. Optical rotations were measured using a Perkin-Elmer 241 polarimeter. Elemental analyses were carried out by Desert Analytics, Tucson, AZ. THF was freshly distilled from sodium–benzophenone prior to use. Dichloromethane was distilled from CaH_2. Dimethyl sulphoxide (DMSO) and DMF were dried over 4 Å molecular sieves. Bakers' yeast (Budweiser or Fleischmann's) was obtained from Busch's Bakery, Las Cruces, NM. Column chromatography was performed on silica gel 60 (70–230 mesh), unless otherwise indicated, with HPLC grade solvents obtained from Fisher Scientific. Analytical and preparative TLC was done on silica 60/F254 plastic or glass backed plates obtained from E.M. Science.

Representative Procedure for the Preparation of Alkyl 6-Chloro-3-oxohexanoates.—Synthesis of octyl 6-chloro-3-oxohexanoate (**3d**). 1.6M-Butyl-lithium in hexane (35.2 ml, 56.3 mmol) was added to a solution of distilled isopropylcyclohexylamine (9.27 ml, 56.3 mmol) in dry THF (70 ml) at 0 °C under nitrogen and the mixture was stirred for 45 min. The reaction mixture was cooled to −76 °C, and octyl acetate (5.6 ml, 28.2 mmol) was added dropwise. After 45 min, 4-chlorobutanoyl chloride (3.16 ml, 28.2 mmol) was added and the reaction mixture was stirred for 20 min. The reaction was quenched by addition of 2M-HCl (60 ml) and the product was extracted into ethyl acetate (2 × 100 ml). The combined extracts were washed successively with saturated aq. $NaHCO_3$ (2 × 100 ml) and water (2 × 100 ml), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. Kugelrohr distillation (0.25 mm, 105–120 °C) of the crude product gave the ester (**3d**) as an oil (5.22 g, 67%), ν_{max} 2 920s, 1 740s, and 1 720s cm^{-1}; δ_H 0.94 (3 H, t, Me), 1.24–1.4 (10 H, br s, $[CH_2]_5Me$), 1.6–1.75 (2 H, m, OCH_2CH_2), 2.00–2.10 (2 H, m, 5-H_2), 2.83 (2 H, t, *J* 7 Hz, 4-H), 3.52 (2 H, s, 2-H), 3.65 (2 H, t, *J* 7 Hz, 6-H), and 4.2 (2 H, t, *J* 7 Hz, OCH_2); *m/z* 278 (M^+, ^{37}Cl) and 276 (M^+, ^{35}Cl).

Representative Procedure for Bakers' Yeast Reduction.—Synthesis of (S)*-octyl 6-chloro-3-hydroxyhexanoate* (**4d**). To a suspension of bakers' yeast (Fleischmann's, 25 g) and sucrose (10 g) in deionized water (333 ml) in a shaker was added compound (**3d**) (1.0 g). The suspension was shaken at room

temperature and at 250 rpm and the reduction was followed by TLC. After 76 h, the product was extracted into ethyl acetate (3 × 200 ml) followed by separation of the layers by centrifugation (8000 rpm; 10 min). The combined organic extracts were dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The crude product was purified by chromatography on silica gel (ethyl acetate–hexane 3–10%) to give the *hydroxy ester* (**4d**) as an oil (0.63 g, 62%), $[\alpha]_D$ +10.6° (*c* 2.12 in $CHCl_3$) (Found: C, 60.6; H, 9.85. $C_{14}H_{27}ClO_3$ requires C, 60.3; H, 9.7%); ν_{max} 3 450br, 2 925s, 2 860s, and 1 725s cm^{-1}; δ_H 0.89 (3 H, t, Me), 1.24–1.42 (10 H, br, s, $[CH_2]_5Me$), 1.60–1.65 (4 H, m, 5-H_2 and OCH_2CH_2), 1.8–2.10 (2 H, m, 4-H), 2.39–2.61 (2 H, m, 2-H), 3.08–3.16 (1 H, br s, OH), 3.60 (2 H, t, *J* 7 Hz, 6-H), 4.0–4.1 (1 H, m, 3-H), and 4.12 (2 H, t, *J* 7 Hz, OCH_2).

Reductions of keto esters (**3a–c**), and (**3e**) were carried out using a similar procedure. The substrate concentration was 2 g l^{-1} in a 20 g l^{-1} sucrose solution, with 25 g of yeast per gram of substrate. Compound (**3a**) was reduced the fastest (1–2 days) while the reduction of the decyl ester (**3e**) was incomplete even after 5 days.

(R)-*Ethyl* 3-*Hydroxyhexanoate from Chloro Compound* (**4a**).—Tributyltin hydride (0.18 ml, 0.66 mmol) was added to a degassed solution of compound (−)-(**4a**) (0.107 mg, 0.55 mmol; e.e. 30%) in toluene (4 ml) under nitrogen. A catalytic amount of azoisobutyronitrile was then added and the solution was heated at 80 °C for 4 h. The solvent was removed under reduced pressure and the crude product was purified by chromatography on silica gel (ethyl acetate–hexane 0–4%). To obtain the ultrapure sample needed for determination of the absolute configuration, the chromatographed product was further purified by preparative TLC (1:2 ethyl acetate–hexane) to give the title compound 40 mg, 45%) as an oil. $[\alpha]_D$ −6.0° (*c* 1.0 in $CHCl_3$) (lit.,[16] $[\alpha]_D$ −21° (*c* 1.5 in $CHCl_3$; 90% e.e.); ν_{max} 3 450br, 2 960s, and 1 733s cm^{-1}; δ_H 0.92 (3 H, t, 6-H_3), 1.26 (3 H, t, *J* 7 Hz, OCH_2Me), 1.36–1.68 (4 H, m, 4- and 5-H_2), 2.34–2.60 (2 H, m, 2-H_2), 2.98 (1 H, br s, OH), 3.96–4.12 (1 H, m, 3-H), and 4.18 (2 H, q, *J* 7 Hz, OCH_2Me); *m/z* 160 (M^+) and 142 ($M^+ - 18$).

(S)-6-*Chlorohexane*-1,3-*diol* (**5**).—2.0M-$LiBH_4$ in THF (2.1 ml, 4.19 mmol) was added dropwise to a solution of compound (**4d**) (0.834 g, 2.99 mmol) in THF (8 ml) under nitrogen at 0 °C. The reaction mixture was allowed to warm to room temperature and was then stirred for 18 h. Excess of $LiBH_4$ was quenched by slow addition of methanol, after the reaction flask had been cooled in ice. Water was then added and the aqueous layer was washed with hexane (1 × 75 ml) to remove octanol. The diol (**5**) was then extracted into ethyl acetate (6 × 75 ml), the combined extracts were dried ($MgSO_4$), then filtered, and the solvent was removed under reduced pressure to give the diol (0.364 g, 80%), which was used in the next step without purification; ν_{max} 3 340br, 2 930s, 1 420s, 1 330s, and 1 055s cm^{-1}; δ_H 1.6–2.1 (6 H, m, 2-, 4-, and 5-H), 3.6 (2 H, t, *J* 6 Hz, 6-H), 3.8–4.1 (3 H, m, 1-H_2 and 3-H), and minor peaks due to impurities.

(S)-4-(3-*Chloropropyl*)-2,2-*dimethyl*-1,3-*dioxane* (**6**).—A catalytic amount of toluene-*p*-sulphonic acid was added to a solution of the diol (**5**) (0.235 g, 1.54 mmol) in a mixture of dry CH_2Cl_2 (3 ml) and 2,2-dimethoxypropane (1.6 ml, 13 mmol) and the mixture was stirred for 18 h. Saturated aq. $NaHCO_3$ was then added and the product was extracted into diethyl ether, the extract was dried ($MgSO_4$), then filtered, and the solvent was removed under reduced pressure. The crude product was purified by chromatography on neutral alumina 5% diethyl ether–hexane) to give the title compound (**6**) as an oil (0.178 g, 60%), $[\alpha]_D$ −16.2° (*c* 2.74 in $CHCl_3$); ν_{max} 2 995s, 2 950s, 2 860s, 1 380s, and 1 200s cm^{-1}; δ_H 1.37 (3 H, s, 2-Me), 1.44 (3 H, s, 2-Me), 1.50–1.66 (4 H, m, 5-H_2 and 4-CH_2), 1.72–2.00 (2 H, m, $ClCH_2CH_2$), 3.56 (2 H, t, *J* 7 Hz, $ClCH_2$), and 3.78–4.04 (3 H, m, 4-H and 6-H_2); *m/z* 179 ($M^+ - 15$, ^{37}Cl) and 177 ($M^+ - 15$, ^{35}Cl).

(S)-*Ethyl* 5-(2′,2′-*Dimethyl*-1′,3′-*dioxan*-4′-*yl*)*pentanoate* (**7**).—Diethyl malonate (0.43 ml, 2.8 mmol) was added dropwise to a suspension of 50% NaH–oil (0.135 g, 2.8 mmol) in dry DMF (1 ml) under nitrogen and the reaction mixture was stirred until gas evolution stopped. The protected diol (**6**) (0.18 g, 0.93 mmol) was added as a solution in dry DMF (1 ml). The mixture was then heated at 70–80 °C for 64 h. The reaction was quenched by addition of saturated aq. NH_4Cl (30 ml) and the product was extracted into hexane (3 × 40 ml), the extract was dried ($MgSO_4$), then filtered, and the hexane was removed under reduced pressure. Excess of diethyl malonate and traces of reactant (**6**) were removed by Kugelrohr distillation (0.25 mm, 80 °C) and the residual diester was used in the next step without further purification; ν_{max} 2 920s, 2 860s, 1 750s, 1 730s, 1 455m, and 1 365m cm^{-1}; δ_H 1.20–1.60 (6 H, complex 5′-H_2 and 4′-CH_2:CH_2), 1.27 (6 H, t, 2 × OCH_2Me), 1.37 (3 H, s, 2′-Me), 1.44 (3 H, s, 2′-Me), 1.86–2.00 (2 H, m, $CHCH_2$), 3.35 [1 H, t, *J* 7 Hz, $CH(CO_2Et)_2$], 3.78–4.04 (3 H, m, 4′-H and 6′-H_2), and 4.2 (4 H, q, 2 × OCH_2Me).

Sodium cyanide (0.18 g) was added to a solution of the crude diester from above in dry DMSO (8 ml) and the mixture was heated to 175–180 °C for 3.5 h. The reaction mixture was cooled and diluted with water. The product was extracted into hexane (3 × 25 ml), the extract was dried ($MgSO_4$), then filtered, and the solvent was removed under reduced pressure. The crude product was purified by chromatography on neutral alumina (hexane–20% ethyl acetate–hexane) to yield the *title compound* (**7**) as an oil [98 mg, 43% from (**6**)], $[\alpha]_D$ −8.75° (*c* 2.0 in $CHCl_3$) (Found: C, 64.0; H, 9.9. $C_{13}H_{24}O_4$ requires C, 63.9; H, 9.90%); ν_{max} 2 980s, 2 930s, 2 860s, and 1 760s cm^{-1}; δ_H 1.22–1.76 (8 H, m, 3-, 4-, 5-, and 5′-H_2), 1.26 (3 H, t, *J* 7 Hz, OCH_2Me), 1.37 (3 H, s, 2′-Me), 1.44 (3 H, s, 2′-Me), 2.30 (2 H, t, *J* 7 Hz, $COCH_2$), 3.78–4.04 (3 H, m, 4′-H and 6′-H_2), and 4.11 (2 H, q, *J* 7 Hz, OCH_2Me).

(S)-*Ethyl* 6,8-*Dihydroxyoctanoate* (**2**).—A solution of compound (**7**) (40 mg, 0.16 mmol) in 10% ethanolic HCl (2 ml) was stirred for 2.5 h at room temperature. The solvent was removed under reduced pressure and the residue was pumped overnight to give the title compound (**2**) as a highly viscous oil (33 mg, 98%), which was used in the next step without purification; $[\alpha]_D$ −1.23° (*c* 1.62 in $CHCl_3$); ν_{max} 3 300br, 2 940s, and 1 730s cm^{-1}; δ_H 1.26 (3 H, t, *J* 7 Hz, OCH_2Me), 1.36–1.78 (8 H, m, 3-, 4-, 5-, and 7-H), 2.32 (2 H, t, *J* 7 Hz, 2-H), 2.50–2.62 (2 H, br s, OH), 3.82–4.00 (3 H, m, 6-H and 8-H_2), and 4.12 (2 H, q, *J* 7 Hz, OCH_2Me).

(S)-*Ethyl* 6,8-*Bis*(*methylsulphonyloxy*)*octanoate* (**8**).—Distilled methanesulphonyl chloride (0.04 ml, 0.4 mmol) was added to a solution of compound (**2**) (17 mg, 0.08 mmol) in a mixture of dry CH_2Cl_2 (0.33 ml) and triethylamine (0.16 ml) under nitrogen at 0 °C. After being stirred for 4 h at 0 °C, the reaction mixture was quenched by addition of saturated aq. $NaHCO_3$ and the product was extracted into CH_2Cl_2 (3 × 20 ml). The crude product was purified by chromatography on silica gel 20% ethyl acetate–hexane) to give the bis mesyl ester (**8**) as an oil (24 mg, 69%), $[\alpha]_D$ +19.3° (*c* 0.61 in $CHCl_3$) {lit.,[13c] $[\alpha]_D$ +17° (*c* 1.0 in $CHCl_3$)}; ν_{max} 2 940s, 1 730s, and 1 465m cm^{-1}; δ_H 1.26 (3 H, t, *J* 7 Hz, OCH_2Me), 1.40–1.85 (6 H, m, 3-, 4-, and 5-H_2), 2.04–2.20 (2 H, m, 7-H), 2.33 (2 H, t, *J* 7 Hz, 2-H), 3.07

(6 H, s, 2 × OSO_2Me), 4.12 (2 H, q, *J* 7 Hz, OCH_2Me), 4.36 (2 H, t, *J* 6 Hz, 8-H_2), and 4.84–5.00 (1 H, m, 6-H).

(R)-(+)-*Ethyl Lipoate* (**9**).—Sulphur (10.4 mg, 0.32 mmol) and sodium sulphate nonahydrate (78.3 mg, 0.32 mmol) were added to a solution of triester (**8**) (0.13 g, 0.32 mmol) in dry DMF (1 ml) and the mixture was heated at 85–90 °C for 24 h under nitrogen. The reaction mixture was quenched by addition of ice–water and extracted with hexane (3 × 40 ml). The combined extracts were washed with saturated aq. NaCl (2 × 40 ml), dried ($MgSO_4$), then filtered, and the solvent was removed under reduced pressure. The crude product was purified by chromatography on silica gel (5% ethyl acetate–hexane) to give the title compound (**9**) as an oil (60 mg, 79%), $[\alpha]_D$ +57.5° (*c* 1.5 in $CHCl_3$) {lit.,[13c] $[\alpha]_D$ +61° (*c* 0.3 in $CHCl_3$)} (Found: C, 51.0; H, 7.8. Calc. for $C_{10}H_{18}O_2S_2$: C, 51.25; H, 7.7%); ν_{max} 2 924s, and 1 732s cm^{-1}; δ_H 1.26 (3 H, t, *J* 7 Hz, OCH_2Me), 1.44–1.80 (6 H, m, 3-, 4-, and 5-H_2), 1.84–2.04 (1 H, m, $HCHCH_2S$), 2.32 (2 H, t, *J* 7 Hz, 2-H_2), 2.40–2.60 (1 H, m, $HCHCH_2S$), 3.10–3.32 (2 H, CH_2S), 3.56–3.71 (1 H, m, CHS), and 4.12 (2 H, q, *J* 7 Hz, OCH_2Me); *m/z* 234 (M^+), 235 ($M^+ + 1$), and 236 ($M^+ + 2$).

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