Chemoenzymatic Synthesis of (2*S*)- and (2*R*)-2-(1,3-Dithian-2-ylmethyl)oxirane

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Lipase-catalyzed transesterifications and biological reductions were used to obtain the (*S*)-enantiomers of 3-chloro-1-(1,3-dithian-2-yl)-2-propanol and 1-(1,3-dithian-2-yl)-3-fluoro-2-propanol and their (*R*)-acetates. (*S*)-3-Chloro-1-(1,3-dithian-2-yl)-2-propanol and (*R*)-3-chloro-1-(1,3-dithian-2-yl)-2-propyl acetate were converted into the respective enantiomers of 2-(1,3-dithian-2-ylmethyl)oxirane. During this work we also isolated a new *gem*-disubstituted epoxide, 2-(chloromethyl)-2-(1,3-dithian-2-yl)oxirane.

Introduction

Since the introduction of lithiated dithianes as acyl anion equivalents by Corey and Seebach in 1965,[1] numerous synthons have been developed for the preparation of α- and β-hydroxy carbonyl compounds and their derivatives.[2]

Chiral building blocks with a C_4 skeleton are used as starting compounds for a large variety of bioactive substances. We have shown previously that enantiopure secondary alcohols containing 1,3-dithianes and thiophenes may be successfully prepared by biocatalytic methods possibly because of the bulkiness of the sulfur-containing rings.[3,4] Additionally, enantiomers of 1-(1,3-dithian-2-yl)-2-propanol have been kinetically resolved previously using lipases.[5]

The utility of chiral synthons depends on the number of functional groups present and how they can be manipulated chemically. Examples of such synthons are the enantiomers of 2-(1,3-dithian-2-ylmethyl)oxirane (**1**), which have been obtained previously in enantiomerically enriched form from malic acid and glycidol. They have been used to construct fragments of the cytotoxic macrolide Spongistatin 1,[6] the antiviral agent Hennoxazole A[7] and derivatives of maytansine.[8] We present here an alternative chemoenzymatic synthesis of both enantiomers of **1**.

Results and Discussion

Synthesis of Substrates

2-(1,3-Dithian-2-ylmethyl)oxirane (**1**) was synthesized by treating lithiated dithiane with epibromohydrin at −78 °C (Scheme 1). Initially, yields of this reaction were very low, but improved considerably following coordination of lithium by the addition of DMPU as a cosolvent.[9] Regioselective opening of the epoxide by known methods[10−12] gave racemic 3-chloro-1-(1,3-dithian-2-yl)-2-propanol (**2**) and 1-(1,3-dithian-2-yl)-3-fluoro-2-propanol (**3**) in good yields with no trace of the other regioisomers.

A number of attempts to synthesize the corresponding bromo alcohol using a similar procedure were unsuccessful. Moreover, attempts to prepare 3-bromo-1-(1,3-dithian-2-yl)-2-propanone by α-bromination of 1-(1,3-dithian-2-yl)-2-propanone, obtained by transacetalization of 1,1-dimethoxy-2-propanone,[4] also failed. These products proved to be very unstable, possibly because of an intramolecular alkylation,[8] and further syntheses of these substrates were not attempted.

Attempts to synthesize 3-chloro-1-(1,3-dithian-2-yl)-2-propanone (**4**) directly from lithiated dithiane and 1,3-dichloro-2-propanone failed. However, a *gem*-disubstituted epoxide, 2-(chloromethyl)-2-(1,3-dithian-2-yl)oxirane (**6**, Scheme 2), which has not been described previously, was isolated.

Reactions using 2,2-bis(chloromethyl)-1,3-dioxolane and lithiated 1,3-dithiane gave only unreacted starting material. Apparently, the dithiane anion is not sufficiently nucleophilic to displace the α-chloro substituent. This has been reported previously.[13]

Swern oxidation of the alcohols **2** and **3** gave good yields of the ketones **4** and **5**, respectively. Singh and co-workers[14,15] have reported a modified Swern reaction for the synthesis of α-chloro ketones from terminal epoxides. In our hands, this reaction gave low yields of the desired products and even these low yields were not reproducible.

Asymmetric Reductions of 4 and 5

3-Chloro-1-(1,3-dithian-2-yl)-2-propanone (**4**) and 1-(1,3-dithian-2-yl)-3-fluoro-2-propanone (**5**) were biotransformed

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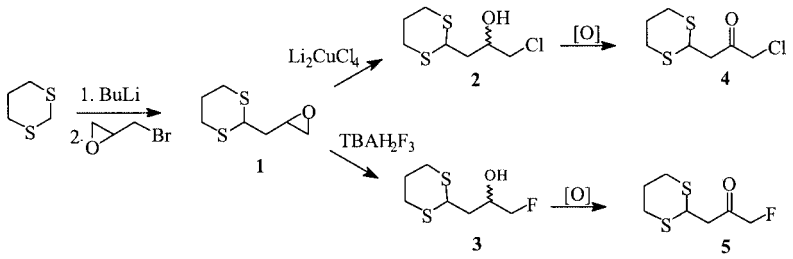
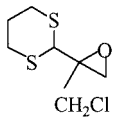


Scheme 1. Synthesis of 3-chloro-1-(1,3-dithian-2-yl)-2-propanol (**2**) and 1-(1,3-dithian-2-yl)-3-fluoro-2-propanol (**3**) and the corresponding ketones



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Scheme 2. 2-(Chloromethyl)-2-(1,3-dithian-2-yl)oxirane (**6**)

in the presence of fermenting baker's yeast, fermenting cells of *Geotrichum candidum* (IFO 4597) or the corresponding acetone powder (APG4).[16] The results are summarized in Table 1.

Table 1. Bioreductions of **4** and **5** using *G. candidum* and baker's yeast

Reduction system	Substrate	Product (*ee*)[a]
Fermenting baker's yeast	5	(*S*)-**3** (99%)
Fermenting *Geotrichum candidum*	5	**3** (0%)
APG4/NAD^+/2-propanol	5	(*S*)-**3** (98%)
APG4/$NADP^+$/2-propanol	5	(*S*)-**3** (83%)
Fermenting baker's yeast	4	(*S*)-**2** (85%)[b]

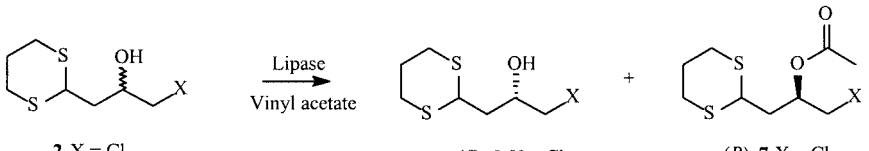
[a] No starting substrate was observed by GC after 24 h. [b] Small aliquots added over a 10 h period were required to achieve *ee* = 85%.

The fluoro ketone **5** was readily accepted as a substrate by both organisms, but only baker's yeast was able to catalyze the reduction of the chloro ketone **4**. The substrate requirement of a small alkyl group in ketones when using *Geotrichum candidum* (IFO 4597) is quite strict. Usually, methyl ketones undergo fast conversions with large enantiomeric excesses. Ethyl ketones give lower yields, and elongation of the alkyl chain to propyl and beyond gives no reaction in the systems studied.[3,16] Since the van der Waals radii of fluorine and hydrogen atoms are similar,[17] the sizes of CH_3 and CH_2F are also similar. On the other hand, CH_2Cl is slightly larger than an ethyl group, which probably explains why **4** was not accepted by *Geotrichum candidum.* This might also be the reason why the enantiomeric excesses for the products of the baker's yeast reductions decreased from > 99% to an optimized value of 85% when going from an α-fluoro to an α-chloro substituent.

The reduction of **4** and **5** with *Geotrichum candidum* gave (*S*)-**2** and (*S*)-**3**, respectively, and so the reactions do not follow Prelog's rule.[18] These findings disagree with previous reports by Nakamura et.al.,[19] who observed inversion of enantioselectivity in fluorinated acetophenone derivatives using *Geotrichum candidum*. However, for the inversion of enantioselectivity to take place, a di- and trifluoro-substituted substrate was needed. In order to examine these results further, bioreductions of di- and trifluoro-substituted 1-(1,3-dithian-2-yl)-2-propanone should be investigated.

Lipase-Catalyzed Kinetic Resolution

The two secondary alcohols were subject to lipase-catalyzed kinetic resolution, using vinyl acetate as the acyl donor, to give the acetates (*R*)-**7** and (*R*)-**8** (Scheme 3). The unchanged alcohols were (*S*)-**2** and (*S*)-**3**. The enantiomeric ratios, *E*, were very high for both substrates (> 300). This is very convenient as no monitoring is required — the reaction stops, when complete, at 50% conversion. However, the reaction time was very long, especially for the chloro alcohol **2**. By varying the ratio of hexane and toluene in the reaction medium — the substrate is insoluble in pure hexane — we were able to reduce the reaction time from five weeks to 24 h without a significant reduction in the enantiomeric ratio (Table 2).



2 X = Cl
3 X = F

(*S*) -**2** X = Cl
(*S*) -**3** X = F

(*R*) -**7** X = Cl
(*R*) -**8** X = F

Scheme 3. Lipase-catalyzed transesterification of 1-(1,3-dithian-2-yl)-3-halo-2-propanol

Table 2. Effects of variation of solvent on the resolution of **2** and **3** using CALB and vinyl acetate

Substrate	Solvent	Reaction time[a]
2	toluene	4−5 weeks
2	benzene	4−5 weeks
2	toluene/hexane (90:10)	3 weeks
2	toluene/hexane (60:40)	108 h
2	toluene/hexane (50:50)	84 h
2	toluene/hexane (10:90)	24 h
3	toluene	48 h

[a] Until 50 % conversion. $E > 300$ for all of the reactions.

Synthesis of (2*S*)- and (2*R*)-2-(1,3-Dithian-2-ylmethyl)oxirane

Preparative lipase-catalyzed kinetic resolution of **2** gave (2*R*)-3-chloro-1-(1,3-dithian-2-yl)-2-propyl acetate [(*R*)-**7**] and (*S*)-**2**. The alcohol was separated from the ester by column chromatography and they were individually treated with potassium carbonate in dichloromethane to give the respective enantiomers of 2-(1,3-dithian-2-ylmethyl)oxirane (**1**) (Scheme 4).

Absolute Configuration of the Enantiomers of 2 and 3

Although a synthesis of (*S*)-**2** has been published,[8] no value for the optical rotation was reported. However, the optical rotation of (*S*)-**1** is known,[8] so the absolute configuration of the enantiomers of **2** was verified after transformation into the epoxides.

The slow-reacting enantiomer of the fluoro alcohol **3** in the kinetic resolution was determined to be (*S*)-**3**, based on the known stereo-preference of lipase B from *Candida antarctica* and the elution order of its acetate and trimethylsilyl derivatives on a CP Chirasil-Dex CB column.[20]

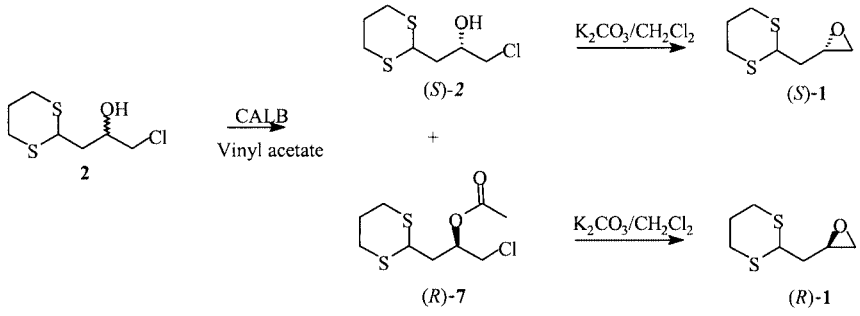
Conclusion

1-(1,3-Dithian-2-yl)-3-halo-2-propanones and 1-(1,3-dithian-2-yl)-3-halo-2-propanols are ideal substrates for enzymatic reductions and esterifications, respectively. Efficient chemoenzymatic methods have been developed for the preparation of both enantiomers of 2-(1,3-dithian-2-ylmethyl)oxirane.

Experimental Section

General Remarks: Solvents were dried with molecular sieves. The cultivation of *Geotrichum candidum* (IFO 4597) and preparation of its acetone powder (AGP) are described elsewhere.[16] Column chromatography was performed using silica gel 60 from Fluka. Enzymatic reactions were performed in a shaker incubator (New Brunswick, Edison, NJ, USA).

Analyses: Optical rotations were determined using an Optical Activity Ltd. AA-10 automatic polarimeter. Concentrations are given in g/100 mL. NMR spectra of $CDCl_3$ solutions were recorded using Bruker DPX 300 and 400 spectrometers operating at 300 and 400 MHz for ^1H, and 75 and 100 MHz, for ^{13}C, respectively. Chemical shifts are in ppm relative to TMS and coupling constants are given in Hertz. Enantiomeric ratios, *E*, were calculated on the basis of enantiomeric excesses of both substrate (ee_s) and product (ee_p) at several degrees of conversion (c), using the computer program E & K calculator version 2.03. Chiral analyses were performed using a Varian 3400 gas chromatograph (Varian Instrument Group, Walnut Creek, California, USA). The CP-Chirasil-Dex CB



Scheme 4. Synthesis of (*R*) and (*S*) enantiomers of 2-(1,3-dithian-2-ylmethyl)oxirane (**1**)

Table 3. GLC properties of alcohols **2** and **3**, and acetates **7** and **8**; column: Chirasil-dex

	Temperature program	Pressure (split)	t_1[b]	t_2[b]	R_s[c]
2[a]	150 °C (20 min), 180 °C (15 °C/min)	8 psi (60)	14.85	15.48	2.49
7[a]	130 °C (90 min), 180 °C (15 °C/min)	8 psi (60)	69.73	72.18	1.52
3	150 °C (20 min), 180 °C (15 °C/min).	8 psi (60)	7.93	8.26	2.63
8	140 °C (20 min), 180 °C (15 °C/min).	8 psi (60)	19.25	19.83	1.80

[a] As the trimethylsilyl ether. [b] t_1 and t_2 are retention times [min] for the two enantiomers. [c] Resolution factor.

column (25 m, 0.32 mm ID, 0.25 μm film thickness) was obtained from Chrompack, Chrompack Norge A.S., Sandvika, Norway. The gas chromatographs were pressure-regulated (carrier gas: hydrogen 5.0, purity: 99.999%) with an outlet pressure of 3 bar (7 psi). Injection was performed in split mode at 200 °C with split ratio = 60. Detection was by an FID detector at 200 °C with air (300 mL/min) and hydrogen (30 mL/min) as flame gases. The chromatographic details are given in Table 3.

Biocatalytic reactions (Small Scale): Reaction conditions for the transesterifications and enzymatic reductions by baker's yeast, *Geotrichum candidum*, and its acetone powder, are described elsewhere.[3] In the kinetic resolutions, the enantiomeric excesses of substrate (ee_s) and product (ee_p) were obtained by chiral GLC from which conversion, c, was calculated by $c = ee_s/(ee_s + ee_p)$. In control experiments without enzyme, no acylation was observed using vinyl acetate as the acyl donor.

2-(1,3-Dithian-2-ylmethyl)oxirane (1): 1,3-Dithiane (5 g, 41.66 mol) was dissolved in dry THF (50 mL) and cooled to −40 °C under N_2. *n*-Butyllithium (1.6 M in hexane, 10.00 mL) was added over a period of 50 min and the mixture was stirred at −25 °C for 2.5 h. The mixture was then cooled to −78 °C, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) (5.01 mL, 41.66 mmol) was added over a period of 5 min and stirring was continued for 1 h. Epibromohydrin (3.56 mL, 41.66 mmol in 75 mL dry THF) was then added cautiously and the mixture was stirred at −78 °C overnight. The mixture was hydrolyzed by pouring it into water (250 mL); the organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (4 × 50 mL). The combined organic phases were dried with $MgSO_4$, filtered and the solvents evaporated. The crude product was subject to column chromatography (hexane/acetone, 4:1) to give **1** in 66.6% yield. ^{1}H NMR: δ = 1.96 (m, 3 H, Me-H and 5′-H), 2.15 (m, 1 H, 5′-H), 2.55 (m, 1 H, 1-H), 2.81 (m, 1 H, 1-H), 2.89 (m, 4 H, 4′-H_2 and 6′-H_2), 3.15 (m, 1 H, 2-H), 4.26 (t, 1 H. 2′-H, J = 7.0 Hz and 13.6 Hz) ppm. ^{13}C NMR: δ = 25.6, 30.2, 30.4, 38.6, 44.7, 47, 49.6 ppm. GC/MS (EI): m/z =176 [$M^{\cdot+}$], 159, 145, 133, 119.

3-Chloro-1-(1,3-dithian-2-yl)-2-propanol) (2): LiCl (1.14 g, 26.9 mmol) and anhydrous $CuCl_2$ (1.81 g, 13.46 mol) were dissolved in dry THF (25 mL). The solution was stirred at room temp. under N_2 for 30 min. 2-(1,3-Dithian-2-ylmethyl)oxirane (**2**) (0.93 g, 5.28 mmol) in dry THF (5 mL) was added and stirring was continued overnight. The reaction mixture was hydrolyzed in phosphate buffer (25 mL, pH = 7.0) and THF removed in vacuo. Water (100 mL) was added to the remaining solution and the mixture extracted with EtOAc (4 × 50 mL). The combined organic phases were dried with $MgSO_4$, filtered and the solvents evaporated to give **2** in 79% yield. ^{1}H NMR: δ = 1.96 (m, 3 H, 1-H_2 and 5′-H), 2.13 (m, 1 H, 5′-H), 2.89 (m, 4 H, 4′-H_2 and 6′-H_2), 3.53 and 3.65 (2 dd, ^2J = 11.0 Hz, ^3J = 6.5, 4.0 Hz, 2 H, 3-H_2), 4.17 (m, 1 H, 2-H), 4.27 (dd, ^3J = 5.5 Hz and 9.0 Hz, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 26.0, 30.3, 30.8, 40.0, 44.1, 50.2, 68.5 ppm. GC/MS(EI): m/z = 214 [$M^{\cdot+}$], 212, 195, 176, 159, 145, 133, 119.

Preparative Kinetic Resolution of 2: Racemic 3-chloro-1-(1,3-dithian-2-yl)-2-propanol) (**2**, 500 mg, 2.36 mmol) was dissolved in hexane/toluene (9:1, 10 mL). Vinyl acetate (5 equiv.) was added and the reaction initiated by addition of immobilized CALB (100 mg) at 30 °C in a shaking incubator at 200 rpm. The reaction was monitored by chiral GLC. After 24 h, the reaction was practically complete and the enzyme was removed by filtration. The enantiomeric excess of both the product ester and the remaining alcohol was > 99% as shown by GLC. The ester and the alcohol were separated by column chromatography (EtOAc/hexane, 1:5) to give (*S*)-**2** (247 mg, 42% yield) and (*R*)-**7** (225 mg, 45% yield). Physical properties for (*S*)-**2** are identical with those of *rac*-**2**. $[\alpha]_D^{20}$ = +5.00 (c = 1.20, $CHCl_3$), +5.00 (c = 1.20, EtOH).

(*R*)-3-Chloro-1-(1,3-dithian-2-yl)-2-propyl Acetate [(*R*)-7]: ^{1}H NMR: δ = 2.13 (m, 4 H, 1-H_2 and 5′-H_2), 2.18 (s, 3 H, Ac-H_3), 2.89 (m, 4 H, 4′-H_2 and 6′-H_2), 3.55 (d, ^3J = 6.5 Hz, 2 H, 3-H_2), 4.30 (m, 1 H, 2′-H), 5.13 (m, 1 H, 2-H) ppm. $[\alpha]_D^{20}$ = +52.7 (c = 0.91, EtOH).

Tetrabutylammonium Dihydrogen Trifluoride ($TBAH_2F_3$): Tetrabutylammonium hydrogen sulfate (2.55 g, 7.5 mmol) was dissolved in $CHCl_3$ (60 mL). Saturated $NaHCO_3$ (0.1875 mL) was added and the solution was stirred for 15 min. KHF_2 (29.3 g in 51 mL H_2O) was added and stirring was continued for 1 h. The organic phase was then separated, dried with $MgSO_4$ and the solvents were evaporated to give $TBAH_2F_3$ in 75% yield. ^{19}F NMR spectroscopy showed one peak, (δ = −170 ppm; trifluoroacetic acid as internal standard) indicating a pure product.

1-(1,3-Dithian-2-yl)-3-fluoro-2-propanol (3): 2-(1,3-Dithian-2-ylmethyl)oxirane (**1**) (0.86 g, 4.89 mmol) and $TBAH_2F_3$ (147 mg, 0.49 mmol) were heated to 120 °C in the presence of KHF_2 (0.76 g, 9.77 mmol) with stirring. The reaction mixture was stirred at 120 °C overnight. CH_2Cl_2 (50 mL) was added and the mixture filtered followed by evaporation of the solvent. The crude product was purified by column chromatography (CH_2Cl_2/acetone, 9:1) to give **3** in 67% yield. ^{1}H{^{19}F} NMR: δ = 1.91 (m, 3 H, 1-H and 5′-H), 2.13 (m, 1 H, 5′-H), 2.89 (m, 4 H, 4′-H_2 and 6′-H_2), 4.20 (m, 1 H, 2-H), 4.27 (dd, ^3J = 5.1, 9.3 Hz, 1 H, 2′-H), 4.33 and 4.43 (2 × dd, ^2J = 9.54, ^3J = 6.09 and 3.45 Hz, 2 H, 3-H_2) ppm. ^{13}C NMR: δ = 25.8, 29.9, 30.2, 37.5, 43.4, 67.3 (d, $^3J_{C,F}$ = 19.4 Hz), and 86.5 (d, $^1J_{C,F}$ = 171 Hz) ppm. GC/MS (EI): m/z = 196 [$M^{\cdot+}$], 179, 159, 145, 133, 119.

Preparative Kinetic Resolution of 3: Racemic **3** (820 mg, 4.1 mmol) was esterified using the same procedure as for **2** to give (*S*)-**3** in 37% yield and (*R*)-**8** (380 mg, 39% yield). Physical properties for (*S*)-**3** are identical with those of *rac*-**3**. $[\alpha]_D^{20}$ = +4.56 (c = 0.97, $CHCl_3$), +5.76 (c = 0.86, EtOH).

(*R*)-1-(1,3-Dithian-2-yl)-3-fluoro-2-propyl Acetate [(*R*)-8]: ^{1}H{^{19}F} NMR: δ = 2.08 (m, 4 H, 1-H_2 and 5′-H_2), 2.15 (s, 3 H, Ac-H_3), 2.89 (m, 4 H, 4′-H_2 and 6′-H_2), 4.30 (m, 1 H, 2′-H), 4.45 (d, ^3J = 5.5 Hz, 2 H, 3-H_2), 5.13 (m, 1 H, 2-H) ppm. $[\alpha]_D^{20}$ = +4.8 (c = 1.1, EtOH)

2-(Chloromethyl)-2-(1,3-dithian-2-yl)oxirane (6): 1,3-Dithiane (1.0 g, 8.3 mmol) was dissolved in dry THF (50 mL) and cooled to −20 °C under N_2. *n*-Butyllithium (1.6 M in hexane, 8.00 mL) was added over a period of 50 min and the mixture was stirred at −25 °C for 2.5 h. The mixture was then cooled to −78 °C, DMPU (1.13 mL, 8.3 mmol) was added over a period of 5 min and stirring was continued for 1 h. 1,3-Dichloro-2-propanone (1.06 g, 8.3 mmol in 30 mL dry THF) was then added dropwise and stirring continued at −78 °C overnight. The reaction mixture was hydrolyzed by pouring it into water (100 mL), and the THF was removed in vacuo. CH_2Cl_2 (30 mL) was added and the solution was washed with base (NaOH, 1%, 25 mL). The combined organic phases were washed with water (50 mL), dried with $MgSO_4$, filtered and the solvents evaporated. The crude product was subject to column chromatography (cyclohexane/acetone, 14:1) to give **6** in 20% yield. ^{1}H-^{1}H- and ^{1}H-^{13}C-correlated 2D NMR spectroscopy was used to assign the ^{1}H and ^{13}C NMR spectra. ^{1}H NMR: δ = 1.94 (m, 1 H, 5′-H), 2.08 (m, 1 H, 5′-H), 2.78 (m, 2 H, 4′-H and 6′-H), 2.85 (d, ^2J = 5.0 Hz, 1 H, 1-H), 3.02 (m, 2 H, 4′ + 6′-H), 3.28 (dd, ^2J = 5.0, ^4J = 1.0 Hz, 1 H, 1-H), 3.69 (d, ^2J = 12.0 Hz, 1 H, ClMe),

3.98 (dd, ^2J = 12.0, ^4J = 1.0 Hz, 1 H, ClMe) and 4.46 (s, 1 H, 2′-H) ppm. ^{13}C NMR: δ = 25.8, 29.0, 29.4, 45.8, 46.3, 51.6, 61.8 ppm. GC/MS (EI): *m*/*z* =210 [M$^{\cdot+}$], 175, 145,119.

3-Chloro-1-(1,3-dithian-2-yl)-2-propanone (4): Dry CH_2Cl_2 (40 mL) was cooled to −60 °C under N_2. DMSO (400 μL, 5.64 mmol) was added and the mixture stirred for 5 min, followed by dropwise addition of oxalyl chloride (337 μL, 2.59 mmol). After an additional 5 min of stirring, **2** [0.5 g, 2.35 mmol, dissolved in CH_2Cl_2 (5 mL)] was added over a period of 10 min. Stirring was continued for 1 h, Et_3N (1.65 mL, 11.75 mmol) was added, and stirring was continued at −60 °C for 18 h. The reaction mixture was then washed with HCl (4 × 50 mL, 0.5%), H_2O (2 × 50 mL), dried with $MgSO_4$ and the solvents were evaporated to give **4** in 70% yield. ^{1}H NMR: δ = 1.90 (m, 1 H, 5′-H), 2.10 (m, 1 H, 5′-H), 2.90 (m, 4 H, 4′-H_2 and 6′-H_2), 3.04 (d, ^3J = 7.0 Hz, 2 H, 1-H_2), 4.14 (s, 2 H, 3-H_2), 4.49 (t, ^3J = 7.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR: δ = 25.1, 29.9, 40.8, 45.0, 48.6, 209.0 ppm. GC/MS (EI): *m*/*z* = 210 [M$^{\cdot+}$], 175, 133, 119.

1-(1,3-Dithian-2-yl)-3-fluoro-2-propanone (5): The fluoro alcohol **3** (1.06 g, 5.4 mmol) was oxidized using the same procedure as for **4** to give **5** in 31% yield after purification by column chromatography (CH_2Cl_2/Et_2O, 9:1). ^{1}H NMR: δ = 1.90 (m, 1 H, 5′-H), 2.11 (m, 1 H, 5′-H), 2.90 (m, 4 H, 4′-H_2 and 6′-H_2), 3.05 (dd, ^3J = 7.0 Hz and ^4J_F = 2.5 Hz, 2 H, 1-H), 4.52 (t, ^3J = 7.0 Hz, 1 H, 2′-H), 4.85 (d, ^2J = 48 Hz, 2 H, 3-H_2) ppm. ^{13}C NMR: δ = 25.7, 30.0, 40.25, 44.5, 85.8 (d, $^1J_{C,F}$ = 186 Hz), 203.0 (d, $^3J_{C,F}$ = 20.5 Hz) ppm. GC/MS (EI): *m*/*z* = 194 [M$^{\cdot+}$], 161, 133, 119.

(*S*)-2-(1,3-Dithian-2-ylmethyl)oxirane [(*S*)-1]: (*S*)-**3** (0.56 g) was dissolved in CH_2Cl_2 (15 mL) and K_2CO_3 (0.5 g) was added with stirring. The formation of (*S*)-**1** was monitored by TLC and, following completion of the reaction, the solution was filtered through a pad of silica gel. Evaporation of the solvent gave the enantiopure epoxide (*S*)-**1** in 81% yield; physical properties as for *rac*-**1**. $[\alpha]_D^{20}$ = −11.48 (*c* = 1.2, $CHCl_3$).

(*R*)-2-(1,3-Dithian-2-ylmethyl)oxirane [(*R*)-1]: (*R*)-**7** (0.41 g) was dissolved in CH_2Cl_2 (15 mL) and K_2CO_3 (0.5 g) was added with stirring. The hydrolysis of (*R*)-**7** and formation of (*R*)-**1** were monitored by TLC. After completion of the reaction, the solution was filtered through a pad of silica gel and the solvent evaporated to give the enantiopure epoxide (*R*)-**1** in 66% yield; physical properties as for *rac*-**1**. $[\alpha]_D^{20}$ = +12.10 (*c* = 1.2, $CHCl_3$).

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