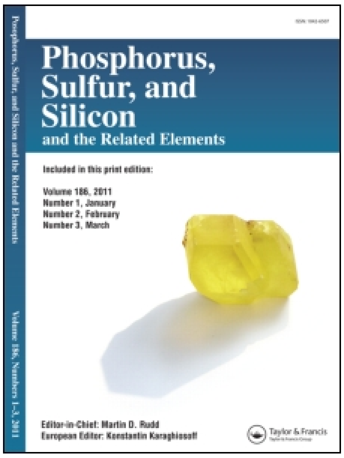

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DIASTEREOSELECTIVE OXIDATION OF 2,3-EPOXY ALCOHOL-DERIVED THIIRANES, AND ^{1}H NMR ANALYSIS OF THE CORRESPONDING THIIRANE S-OXIDES

Paul R. Carlier[a]; Guilan Liu[a]; H. Y. Peter Lam[b]
[a] Department of Chemistry, Hong Kon University of Science and Technology Clear Water Bay, Kowloon, Hong Kong [b] Department of Biochemistry, Hong Kong University of Science and Technology, Kowloon, Hong Kong

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DIASTEREOSELECTIVE OXIDATION OF 2,3-EPOXY ALCOHOL-DERIVED THIIRANES, AND ^{1}H NMR ANALYSIS OF THE CORRESPONDING THIIRANE *S*-OXIDES

PAUL R. CARLIER[a]*, GUILAN LIU[a] and H. Y. PETER LAM[b]

[a]*Department of Chemistry, Hong Kong University of Science and Technology Clear Water Bay, Kowloon, Hong Kong.* [b]*Department of Biochemistry, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong*

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Anti-thiirane *S*-oxides derived from *cis*-2,3-epoxyhexan-1-ol are prepared to serve as transition state analogs for alkene epoxidation and singlet oxygenation. The β-hydroxyl directing effect commonly exploited in sulfide oxidations is found to be completely ineffective in directing oxidation of *cis*-epoxy alcohol-derived thiiranes; steric factors alone appear to determine the anti:syn selectivity. Detailed ^{1}H NMR analysis was performed on both the stable *anti*- and the unstable *syn*-thiirane *S*-oxides. The thiirane *S*-oxide ring protons are found to possess unusually large vicinal coupling constants (approx. 11 Hz) and their chemical shifts are quite sensitive to the anisotropy of the SO moiety.

Since their first confirmed report in 1965[1], thiirane *S*-oxides have been the subject of considerable study.[2-4] Of most relevance to the current work is the observation by Kondo[5] and Baldwin[6] that a facile thermal cycloelimination pathway exists for thiirane *S*-oxides bearing a β-hydrogen proximal to the sulfoxide oxygen. Correspondingly, thiirane S-oxides derived from *trans*-1,2- or 1,1-dialkyl substituted thiiranes cannot generally be isolated, whereas the *"anti"* thiirane *S*-oxides derived from monoalkyl or *cis*-1,2-dialkyl substituted thiiranes are easily prepared. Our efforts in this area were motivated by the structural resemblance of thiirane *S*-oxides to both the perepoxide intermediate implicated in singlet oxidation of alkenes[7], and the classical Bartlett[8] transition state model for alkene epoxidation (Scheme 1).

As a first step towards developing antibody-catalyzed singlet oxygenation and epoxidation reactions, we undertook the synthesis of stable *anti*-thiirane *S*-oxides which bear appropriate functionalization to facilitate protein conjugation. This

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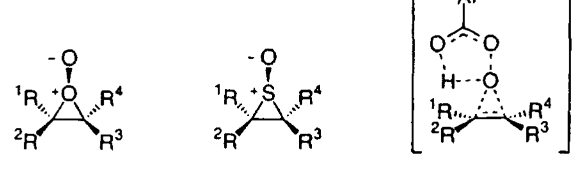
* Corresponding author.

Scheme 1



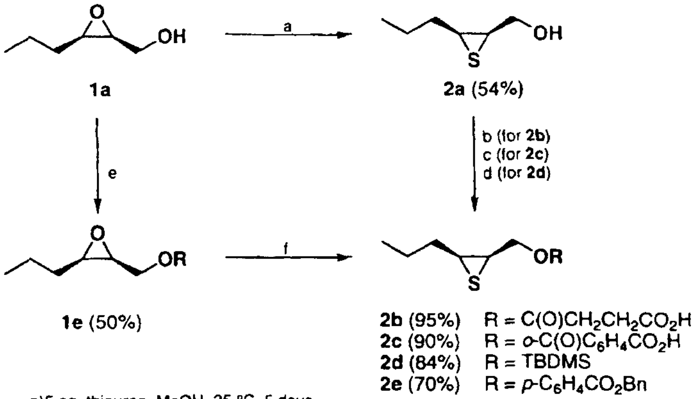
perepoxide intermediate

thiirane *S*-oxide

"Bartlett" epoxidation transition state model

report describes the synthesis of novel functionalized thiiranes **2a-e**, an *in situ* low temperature ^{1}H NMR study of the diastereoselectivity of their oxidation to thiirane *S*-oxides **3a-e**, and a detailed ^{1}H NMR analysis of both the stable *anti*- and unstable *syn*-diastereomers of **3a-e**. Most noteworthy are the observations that 1)the often exploited *syn*-directing effect of a β-hydroxyl group in sulfide oxidations is ineffective in directing oxidation of thiirane **2a**, and 2)the ring protons (H_c, H_d) of both *anti*-and *syn*-**3a-e** exhibit unusually high vicinal coupling constants J_{cd} and the anticipated (but normally absent) effect of the SO group anisotropy on chemical shift.

To allow introduction of a thiirane group and eventual preparation of covalent protein conjugates, we selected epoxy alcohol **1a** as our starting point (Scheme 2).



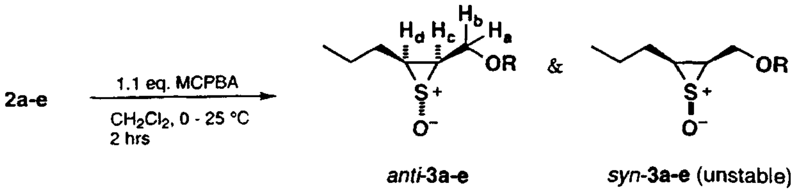
a)5 eq. thiourea, MeOH, 25 °C, 5 days.
b)1.5 eq. succinic anhydride, cat. DMAP, 1.1 eq. Et_3N, CH_2Cl_2, 25 °C, 3 h.
c)1.5 eq. phthalic anhydride, cat. DMAP, 1.4 eq. Et_3N, CH_2Cl_2, 25 °C, 6 h.
d)1.1 eq. TBDMSCl, 1.2 eq. Et_3N, CH_2Cl_2, 0 -> 25 °C, 2 h.
e)1.05 eq. TsCl, 1.2 eq. Et_3N, CH_2Cl_2, 12 hrs (74%);
1.1 eq. NaH, 1.0 eq. *p*-(BnO_2C)-C_6H_4OH, DMF, 0 -> 25 °C, 2 h (67%).
f)2 eq. KSCN, 2:1 *t*-BuOH:H_2O, 50 °C, 12 h.

SCHEME 2

Treatment of **1a** with thiourea in methanol[9] provided the corresponding thiirane **2a** in 54% yield.[10] Further functionalization of thiirane **2a** to derivatives

2b-e was carried out in two ways. Acylation or silylation of the primary hydroxyl occurred in excellent yield to provide functionalized thiiranes **2b-d.** Electrophilic activation of the primary hydroxyl of **2a** was attempted, but the corresponding tosylate could not be isolated; thus the tosylate of epoxy alcohol **1a** was prepared. Displacement of the tosylate by a substituted phenolate occurred in moderate yield to afford epoxy ether **1e**, which was then converted to thiirane **2e** by treatment with KSCN in aqueous *t*-butanol. Oxidation of thiiranes **2a-e** to the corresponding thiirane *S*-oxides *anti*-**3a-e** was carried out in CH_2Cl_2 at 0 °C with 1.1 equivalent of MCPBA. Pure samples of *anti*-**3a-e** were obtained by chromatography. In the case of *anti*-**3a**, removal of the *meta*-chlorobenzoic acid byproduct *in situ* by treatment with gaseous NH_3 and filtration[5] was required to obtain an acceptable yield of the thiirane *S*-oxide (Table I).

TABLE I Oxidation of thiiranes **2** to the diastereometic thiirane S-oxides **3**



Thiirane	R	initial anti:syn[a]	Isolated yield of *anti*-**3**
2a	H	1.5:1	37
2b	$CO(CH_2)_2CO_2H$	4:1	70
2c	*o*-$C(O)C_6H_4CO_2H$	6:1	45
2d	TBDMS	7.5:1	50
		10:1[b]	
2e	*p*-$C_6H_4CO_2Bn$	3.5:1	64

[a] Diastereomer ratio measured by ^1H NMR analysis (300 MHz) of *in situ* oxidation at –20°C in $DCDl_3$.
[b] Oxidation performed at –78°C in CD_2Cl_2, NMR analysis at –20°C.

^1H NMR observation of the oxidation in situ at -20 °C in $CDCl_3$or CD_2Cl_2 demonstrated that in each case both *anti*- and *syn*- diastereomers are formed. The *syn*-diastereomers are long-lived at -20 °C, allowing determination of the anti:syn selectivity of the oxidation reaction. In each case the *anti*-diastereomer predominates, with selectivity ranging from a minimum of 1.5:1 for **2a,** to a maximum of 10:1 for **2d** (Table 1). The absence of *syn*-selectivity in the oxidation of **2a** is suprising, given the well-documented *syn*-directing effect of β-hydroxy groups in sulfide oxidation.[11,12] Apparently the unfavorable steric interaction with the *n*-propyl group suffered in approach syn to the hydroxymethyl group overwhelms the normal kinetic advantage of directed oxidation. Thiiranes **2b** and **2c** also feature groups that could donate a hydrogen bond to the incoming peracid, thereby potentially directing formation of the *syn*-thiirane *S*-oxide. However in these cases the succinoyl and phthaloyl groups appear to function only as blocking groups, favoring *anti*-attack. The highest diastereoselectivity is observed with TBDMS protected **2d** (anti:syn = 10:1 at -78 °C), and thus in summary the *anti*-selectivity of the oxidation reaction appears to be correlated to the size of the oxygen substituent (R). Warming the NMR sample to room temperature resulted in complete decomposition of the *syn*-diastereomer within 30 to 60 minutes, leaving the *anti*-diastereomer unchanged. Neither the unstable sulfenic acids derived from the *syn*-**3a-e** nor their thiosulfinate condensation products, could be unambigously identified in the ^{1}H NMR spectra.

In addition to using the criterion of thermal stability, it is also possible to assign the relative stereochemistry of thiirane *S*-oxides **3a-e** based on the anisotropy of the SO moiety. Kondo[5] noted that β-hydrogens syn- to the sulfoxide oxygen (such as those present in *syn*-**3**) are shifted downfield, whereas β-hydrogens anti- to the sulfoxide oxygen undergo little change or are shifted upfield relative to the starting thiirane. As expected, in *anti*-**3a-e,** the β-hydrogens H_a and H_b generally undergo an upfield shift, and in the *syn*-diastereomers these protons undergo a downfield shift, although the size of the shift is variable (Table II).

TABLE II Selected ^{1}H chemical shift data for thiiranes **2** and thiiranes *S*-oxides **3**[a]

Cpd	H_a	Δ	H_b	Δ	H_c	Δ	H_d	Δ
2a	3.90	-	3.82	-	3.22	-	3.04	-
anti-**3a**	3.87	-0.03	3.60	-0.22	3.50	0.28	3.32	0.28
syn-**3a**	4.11	0.21	4.03	0.21	2.70	-0.52	2.38	-0.66
2b	4.46	-	4.16	-	3.19	-	3.01	-
anti-**3b**	4.19	-0.27	4.14	-0.02	3.47	0.28	3.31	0.30
syn-**3b**	4.64	0.18	4.31	0.15	2.57	-0.62	2.36	-0.65
2c	4.72	-	4.34	-	3.33	-	3.05	-
anti-**3c**	4.46	-0.26	4.26	-0.08	3.65	0.32	3.38	0.33
syn-**3c**	4.90	0.18	4.46	0.12	2.76	-0.57	2.44	-0.61
2d	4.00	-	3.61	-	3.10	-	2.99	-
anti-**3d**	3.81	-0.19[b]	3.81	0.20[b]	3.38	0.28	3.26	0.27
syn-**3d**	3.97	-0.03[b]	3.97	0.30[b]	2.46	-0.64	2.28	-0.71
2e	4.40	-	4.02	-	3.33	-	3.08	-
anti-**3e**	4.24	-0.16	4.01	-0.01	3.62	0.29	3.39	0.31
syn-**3e**	4.37	-0.03[b]	4.37	0.35[b]	2.73	-0.60	2.43	-0.65

[a] NMR data were determined in $CDCl_3$ at room temperature for **2a-e**, and *in situ* at -20 °C for *anti*- and *syn*-**3a-e**.

[b] H_a and H_b are accidentally equivalent.

Moreover, deviations from this trend are seen in cases where H_a and H_b become accidentally equivalent upon oxidation of **2** to **3**. Suprisingly, Kondo did not observe any effect of the SO group anisotropy on the chemical shift of the ring protons in the thiirane *S*-oxides he studied. In compounds **3a-e,** however, the effect of the SO group anisotropy on the ring protons is clearly seen. Protons H_c and H_d of *anti*-**3a-e** undergo a consistent 0.3 ppm downfield shift relative to **2a-e**; in the corresponding *syn*-diastereomers these protons undergo a consistent 0.6 ppm upfield shift (Table 2). Thus in the present case, the effect of the SO anisotropy on the α-protons is larger and more consistent than that on the β-protons. Finally, in our detailed analysis of the ^{1}H NMR spectra of *anti*and *syn*-**3a-e,**we noted that the vicinal coupling constant of H_c and H_d (J_{cd}) was unusually large (Table III):

TABLE III Selected proton coupling constants for epoxides **1**, thiirane **2**, and thiiranes *S*-oxides **3**[a]

Compound	J_{ab}	J_{ac}	J_{bc}	J_{cd}
1a	12.2	3.9	7.1	4.0
1e	10.5	4.2	6.2	4.5
2a	11.7	6.4	6.4	6.6
2b	11.7	6.1	8.0	6.4
2c	11.7	6.0	8.1	6.5
2d	11.0	5.3	8.2	6.8
2e	10.2	5.4	8.4	obsc.[b]
anti-**3a**	12.5	5.6	8.6	10.7
syn-**3a**	13.7	3.4	9.3	11.7
anti-**3b**	acc. eq[c]	7.5	7.5	10.8
syn-**3b**	12.8	3.8	9.2	11.6
anti-**3c**	obsc.[b]	7.7	7.7	10.6
syn-**3c**	12.5	3.5	10.5	11.1
anti-**3d**	11.8	6.4	6.4	11.0
syn-**3d**	nd[d]	nd[d]	nd[d]	nd[d]
anti-**3e**	11.0	7.1	7.7	10.3
syn-**3e**	11.6	7.9	4.2	11.5

[a] Coupling constants were determined in $CDCl_3$ at room temperature for **1a,e** and **2a-e**; measurements for *anti*- and *syn*-**3a-e** were carried out *in situ* at −20°C.

[b] Obscured

[c] H_a and H_b are accidentally equivalent.

[d] Not determined due to poor resolution.

The values of J_{cd} for epoxides **1** (4-4.5 Hz) and thiiranes **2** (6-7 Hz) match the literature precedent[13] and the qualitative expection that a decrease in substituent electronegativity will lead to an increase in J_{cd}.[14] The increase in J_{cd} to approximately 11 Hz upon oxidation of **2** to **3** is therefore unexpected on the basis of substituent electronegativity, but precedent is found in the work of Ohtsuru *et al.*,[15] who reported similar vicinal coupling constants for the thiirane *S*-oxides derived from ethylene and propylene. Based on our study we can can state that this unusually high vicinal coupling constant appears to be a general characteristic of both *anti*- and *syn*-thiirane *S*-oxides.[16]

EXPERIMENTAL SECTION

General :

All reactions were performed in oven-dried glassware under a nitrogen atmosphere. THF and Et_2O were distilled from Na/benzophenone immediately prior to use. DMF and DMSO were dried by treatment with 4 Å molecular sieves. Unless noted otherwise, NMR spectra were measured in $CDCl_3$ at 300 MHz (^1H) and at 75 MHz (^{13}C). Elemental analysis was performed at the Shanghai Institute of Organic Chemistry (Chinese Academy of Sciences, P. R. C.). *cis*-2,3-Epoxyhexan-1-ol **1a** was prepared by MCPBA oxidation of the commerically available *cis*-2-hexen-1-ol. Benzyl *p*-hydroxybenzoate was prepared from benzyl alcohol and *p*-hydroxybenzoic acid. *In situ* NMR investigation of the oxidation of thiiranes **2a-e** was performed at a substrate concentration of 0.04 M, with 1.0 equivalents added MCPBA, in $CDCl_3$ at -20°C, except where otherwise noted. Note that the chemical shift values reported in Table 2 for *anti*-**3a-e** in the *in situ* oxidation experiments differ slightly from those listed below for the pure compounds.

cis-1-(4'-carbobenzyloxy)phenoxymethyl-2-propyloxirane (1e)

Preparation of tosylate of cis-2,3-epoxyhexan-1-ol: a 250 mL round-bottomed flask charged with epoxy alcohol **1a** (3.5 g, 30 mmol), 4-dimethylaminopyridine (186 mg, 1.5 mmol) triethylamine (6.2 mL, 45 mmol), magnetic stirring bar and CH_2Cl_2 (60 mL) was cooled to -20 °C. A solution of *p*-toluenesulfonyl chloride (6.3g, 31.5 mmol) in 40 mL CH_2Cl_2 was added and the reaction was kept at -25 °C for 15 hours. Aqueous workup, followed by concentration *in vacuo* afforded 4.8 g of the tosylate as a colorless oil (R_f = 0.43, 20% ethyl acetate/hexane), which was used without further purification.

Reaction of tosylate with the phenolate: a 100 mL round-bottomed flask charged with NaH (60% oil dispersion, 800 mg, 20 mmol), DMSO (15 mL) and DMF (10 mL), and a magnetic stirring bar. After cooling to 0 °C, a solution of benzyl *p*-hydroxybenzoate (3.42 g, 15 mmol) in 20 mL DMF. was added; 30 minutes later a solution of the tosylate (2.7 g, 10 mmol) in 20 mL DMF was added. After 30 minutes the reaction was allowed to warm to room temperature and stirred until TLC indicated complete consumption of the tosylate (15 hours). After addition of Et_2O (50 mL), aqueous workup, and chromatography (25% ethyl acetate/hexane), **1e** was obtained as white crystals (2.2g, 50% from **1a**, $R_f = 0.53$).

^{1}H NMR: δ 0.999 (t, *J* = 6.9 Hz, 3H), 1.50-1.60 (m, 4H), 3.100 (m, 1H), 3.333 (ddd, *J* = 6.2, 4.5, 4.2 Hz, 1H), 4.093, (dd, *J* = 10.5, 6.2 Hz, 1H), 4.205 (dd, *J* = 10.5, 4.2 Hz, 1H), 5.339 (s, 2H), 6.951 (d, *J* = 8.5 Hz, 2H), 7.355 (m, 5H), 8.039 (d, *J* = 8.5 Hz, 2H);

^{13}C NMR: δ 13.89, 19.91, 30.05, 54.14, 56.32, 66.39, 66.57, 114.19, 122.99, 128.06, 128.11, 128.53, 131.75, 136.22, 162.31, 166.02;

IR (NaCl): 3034, 2960, 2874, 1708, 1606, 1510, 1456, 1376, 1316, 1254, 1172, 1102, 1020, 918, 852, 770, 696 cm^{-1};

MS(EI^+): 326 (m);

mp: 70.5-72.4 °C.

cis-1-hydroxymethyl-2-propylthiirane (2a)

A 25 mL flask charged with **1a** (581 mg, 5 mmol), methanol (6 mL), and thiourea (1.9 g, 25 mmol) was allowed to stir for 5 days at room temperature. The solvent was removed *in vacuo* and replaced with Et_2O (25 mL). Aqueous workup, followed by flash chromatography (20% ethyl acetate/hexane) afforded **2a** as a colorless oil (305 mg, 54%, R_f= 0.53 in 30% ethyl acetate/hexane).

^{1}H NMR ($CDCl_3 + D_2O$): δ 0.994 (t, *J* = 7.2 Hz, 3H), 1.55 (m, 3H), 1.88 (m, 1H), 3.04 (m, 1H), 3.216 (ddd, *J* = 6.4, 6.4, 6.4 Hz, 1H), 3.800 (dd, *J* = 11.7, 6.4 Hz, 1H), 3.890 (dd, *J* = 11.7, 6.4 Hz, 1H);

^{13}CNMR: δ 13.75, 22.89, 32.54, 41.30, 41.38, 62.45;

IR (NaCl): 3360 br, 2958, 1464, 1380, 1034, 894, 746 cm^{-1};

MS(EI^+): 132 (m);

mp: liquid.

cis-1-(succinoxymethyl)-2-propylthiirane (2b)

A 25 mL flask was charged with **2a** (150 mg, 1.13 mmol), succinic anhydride (169 mg, 1.69 mmol), 4-dimethylaminopyridine (911 mg, 0.09 mmol), triethylamine (125 mg, 1.24 mmol) and 5 mL CH_2Cl_2. TLC indicated complete consumption of **2a** after 2 hours. Addition of Et_2O (20 mL), washing with 1N HCl (2 x 5 mL), drying (Na_2SO_4), and concentration in *vacuo* afforded **2b** as a white semi-solid (248 mg, 95%, $R_f = 0.65$ in 80% ethyl acetate/hexane).

^{1}H NMR: δ 0.992 (t, $J = 7.2$ Hz, 3H), 1.44 - 1.61 (m, 3H), 1.85 - 1.87 (m, 1 H), 2.65 - 2.73 (m, 4 H), 3.01 (m, 1H), 3.187 (ddd, $J = 8.0, 6.5, 6.1$ Hz, 1H), 4.158 (dd, $J = 11.7, 8.0$ Hz), 4.460 (dd, $J = 11.7, 6.1$ Hz, 1H);

^{13}C NMR: δ 13.68, 22.77, 28.75, 28.86, 32.46, 35.68, 40.53, 64.83, 171.65, 177.90;

IR (NaCl): 3350-2700 br, 2934, 1736, 1420, 1366, 1166, 998, 840, 804, cm^{-1};

MS (EI$^+$): 232 (m);

Analysis: Calcd for $C_{10}H_{16}O_4S$: %C, 51.71; %H, 6.94. Found: %C, 51.59; %H, 7.06; mp: semi-solid.

cis-1-(*o*-phthaloxymethyl)-2-propylthiirane (2c)

A 25 mL flask charged with **2a** (150 mg, 1.14 mmol), phthalic anhydride (252 mg, 1.71 mmol), 4-dimethylaminopyridine (15 mg, 0.12 mmol), triethylamine (168 mg, 1.6 mmol) and 10 mL CH_2Cl_2 was stirred at room temperature until TLC indicated complete consumption of **2a** (6 hours). Replacement of the solvent with Et_2O, aqueous workup, and flash chromatography (90% ethyl acetate/hexane) afforded **2c** as a white solid (285 mg, 90%, $R_f = 0.62$)

^{1}H NMR: δ 0.969 (t, $J = 7.2$, 3H), 1.52 (m, 3H), 1.94 (m, 1H), 3.050 (m, 1H), 3.326 (dd, $J = 8.1, 6.5, 6.1$ Hz, 1H), 4.355 (dd, J=11.7,8.1 Hz, 1H), 4.716 (dd, J=11.7, 6.1 Hz, 1H), 7.5 - 7.7 (m, 3H), 7.955 (d, $J = 9.0$ Hz, 1H);

^{13}C NMR: δ 13.74, 22.85, 32.49, 35.53, 40.79, 65.80, 128.76, 129.71, 129.99, 130.99, 132.42, 133.17, 167.66, 172.35;

IR (NaCl): 3250 - 2300 br, 2960, 1738, 1694, 1578, 1492, 1422, 1286, 1256, 1118, 1034, 776, 746 cm^{-1};

MS (CI$^+$(NH_3)): 298 (m+NH_4);

Analysis: Calcd for $C_{14}H_{16}O_4S$: %C, 59.96; %H, 5.71. Found: %C, 60.01; %H, 5.93. mp: 52.5-54.1 °C.

cis-1-*t*-butyldimethylsilyloxymethyl-2-propylthiirane (2d)

A 50 mL flask charged with **2a** (463 mg, 3.5 mmol), 4-dimethylaminopyridine (43 mg, 0.35 mmol), triethylamine (531 mg, 5.3 mmol) and 25 mL CH_2Cl_2 was cooled to 0°C. *t*-Butyldimethylsilylchloride (623 mg, 4.2 mmol) was added as a solution in CH_2Cl_2 (5 ml); after 30 minutes the reaction was warmed to room temperature, and after 90 minutes TLC indicated complete consumption of **2a**.

Aqueous workup followed by column chromatography (10% ethyl acetate/hexane) yielded **2d** as a colorless oil (725 mg, 84%, R_f= 0.83).

^{1}H NMR: δ 0.077 (s, 3H), 0.091 (s, 3H), 0.908 (s, 9H), 0.985 (t, *J* = 7.2 Hz, 3H), 1.45 (m, 1H), 1.55 (m, 2H), 1.85 (m, 1H), 2.99 (ddd, *J* = 8.3, 6.8, 5.3 Hz, 1H), 3.10 (ddd, *J* = 8.2, 6.8, 5.3 Hz, 1H), 3.61 (dd, *J* = 11.0, 8.2 Hz, 1H), 4.00 (dd, *J* = 11.0, 5.3 Hz, 1H);

^{13}C NMR: δ -5.35, -5.19, 13.78, 18.27, 22.77, 25.85, 32.49, 39.77, 41.19, 63.63;

IR (NaCl): 2958, 2858, 1470, 1464, 1380, 1362, 1256, 1084, 838, 776 cm^{-1};

MS(CI$^+$(NH$_3$)): 247 (m+1), 264 (m+NH4);

mp: liquid.

cis-1-(4'-carbobenzyloxy)phenoxymethyl-2-propylthiirane (2e)

A 50 mL flask charged with **1e** (1.63 g, 5.0 mmol), KSCN (1.72 g, 17.4 mmol) and 30 mL of 2:1 *t*BuOH:H_2O was stirred at 50 °C for 24 hours. Addition of Et_2O (50 mL), aqueous workup, and flash chromatography (20% ethyl acetate/hexane) yielded **2e** as a pale yellow liquid (1.19 g, 70%, R_f = 0.63).

^{1}H NMR: δ 0.975 (t, *J* = 7.2, 3H), 1.47-1.65 (m, 3H), 1.904 (m, 1H), 3.081 (m, 1H), 3.326 (m, 1H), 4.017 (dd, *J* = 10.2, 8.4 Hz, 1H), 4.399 (dd, *J* = 10.2, 5.4 Hz, 1H), 5.336 (s, 2H), 6.927 (d, *J* = 8.7 Hz, 2H), 7.229 (m, 5H), 8.036 (d, *J* = 9.0 Hz, 2H);

^{13}C NMR: δ 13.73, 22.72, 32.41, 35.94, 40.71, 66.38, 68.29, 114.09, 122.93, 128.05, 128.10, 128.51, 131.77, 136.20, 162.18, 165.98;

IR (NaCl): 3032, 2958, 2872, 1716, 1606, 1510, 1456, 1420, 1376, 1312, 1250, 1168, 1102, 1028, 1004, 912, 846, 768, 696 cm^{-1};

MS(EI$^+$): 342 (m);

mp: liquid.

anti, cis-1-hydroxymethyl-2-propylthiirane S-oxide (*anti-3a*)

A 100 mL flask charged with **2a** (397 mg, 3 mmol) and 20 mL CH_2Cl_2 was cooled to 0 °C; a solution of MCPBA (55%, 94 mg, 3.0 mmol) in CH_2Cl_2 was then added over 15 minutes. TLC indicated complete reaction after 90 minutes, after which NH_3 (gas) was allowed to impinge on the surface of the reaction. After 30 seconds precipation of the ammonium salt of *m*-chlorobenzoic acid appeared to cease, after which the gas flow was stopped and the reaction quickly filtered, collecting the filtrate in an ice-bath cooled flask. The solution was treated with NH_3(g) and filtered one more time, again maintaining the solution at

0°C. The filtrate was concentrated *in vacuo* and immediately chromatographed (70% ethyl acetate/hexane), affording *anti*-**3a** as a colorless oil (165 mg, 39%, $R_f = 0.30$).

^{1}H NMR: δ 1.027 (t, J = 7.3 Hz, 3H), 1.35 (m, 1H), 1.50 (m, 1H), 1.62 (m, 2H), 3.161 (ddd, J = 10.9, 9.7, 5.8 Hz, 1H), 3.345 (ddd, J = 10.9, 8.3, 5.8 Hz, 1H), 3.551 (dd, J = 12.7, 8.3 Hz, 1H), 3.776 (dd, J=12.7, 5.8 Hz, 1H);

^{13}C NMR: δ 13.58, 22.15, 26.76, 56.21, 56.95, 57.78;

IR (NaCl): 3376 (br, s), 2960, 2932, 2874, 1466, 1056, 990 cm^{-1};

MS ($CI^+(NH_3)$): 149(m+1), 166 (m+NH_4);

mp: liquid.

Analysis: Calcd for $C_6H_{12}O_2S$: %C, 48.62; %H, 8.16. Found: %C, 48.32; %H, 8.47.

cis-1-(succinoxymethyl)-2-propylthiirane S-oxide (*anti*-3b)

A 25 mL flask charged with **2b** (100 mg, 0.43 mmol) and 6 mL CH_2Cl_2 was cooled to 0 °C. A solution of MCPBA (55%, 135 mg, 0.43 mmol) in 4 mL CH_2Cl_2 was added over 15 minutes. After 90 minutes TLC indicated complete consumption of **2b**. The solvent was removed *in vacuo*, 10 mL H_2O was added, and the mixture stirred vigorously for 30 minutes, and filtered, The precipitate (largely *m*-chlorobenzoic acid) was washed (2 x 5 mL H_2O), and the combined aqueous phases were extracted with CH_2Cl_2 (5 x 10 mL). The organic extract was dried (Na_2SO_4) and concentrated *in vacuo* to afford *anti*-**3b** as a white solid (89 mg, 83%, R_f = 0.32 in 80% ethyl acetate/hexane). ^{1}H NMR: δ 1.036 (t, J =7.5 Hz, 3H), 1.31 (m, 1H), 1.51 (m, 1H), 1.64 (m, 2H), 2.69 (m, 4H), 3.214 (ddd, J = 10.8, 9.9, 5.7 Hz, 1H), 3.376 (ddd, J = 10.8, 7.5, 7.5 Hz, 1H), 4.160 (d, J = 7.5 Hz, 2H); ^{13}C NMR: δ 13.55, 22.02, 26.76, 28.78, 28.81, 52.92, 55.56, 58.58, 171.74, 176.63; IR (NaCl): 3500-2500 br, 2962, 1724, 1426, 1324, 1266, 1162, 1034, 990, 820 cm^{-1}; MS ($CI^+(NH_3)$): 249 (m+1);

mp: 27.5-28.2 °C

Analysis: Calcd for $C_{10}H_{16}O_5S \bullet 0.5\ H_2O$: %C, 46.68; %H, 6.66. Found: %C, 46.80; %H, 6.35.

anti, cis-1-(*o*-phtaloxymethyl)-2-propylthiirane *S*-oxide (*anti*-3c)

A 25 mL round-bottomed flask charged with **2c** (125 mg, 0.45 mmol) and 8 mL of CH_2Cl_2 was cooled to 0 °C. A solution of MCPBA (55%, 142 mg, 0.45 mmol) in 4 mL of CH_2Cl_2 was added over 20 minutes. After an additional 40 minutes TLC indicated complete consumption of the starting material. The solvent volume was reduced by 75% *in vacuo* and the mixture filtered to remove residual *meta*-chlorobenzoic acid. The filtrate was then concentrated and chromatographed on silica gel (90% ethyl acetate/hexane) to give *anti*-**3c** as a white semi-solid (60 mg, 45%, R_f = 0.39). ^{1}H NMR: δ 1.009 (t, *J* = 7.2 Hz, 3H), 1.35 (m, 1H), 1.65 (m, 3H), 3.396 (ddd, *J* = 10.6, 10.6, 5.4 Hz, 1H), 3.640 (ddd, *J* = 10.6, 7.7, 7.7 Hz, 1H), 4.38 (m, 2H), 7.58 (m, 2H), 7.66 (m, 1H), 7.89 (m, 1H), 9.15 (br s, 1H);

^{13}C NMR: δ 13.51, 21.98, 26.73, 52.84, 55.73, 59.33, 128.52, 129.65, 131.14, 131.60, 132.09, 167.83, 169.33;

IR (NaCl); 3500 - 2500 br, 2962, 1728, 1600, 1580, 1490, 1284, 1120, 1072, 1036, 792, 744 cm^{-1}; MS (CI$^+$(NH$_3$)): 297 (m+1);

Anal.: Calcd for $C_{14}H_{16}O_5S$: %C, 56.72; %H, 5.40. Found: %C, 56.80; %H, 5.40;

mp: liquid.

anti, cis-1-t-butyldimethylsilyloxymethyl-2-propylthiirane S-oxide (*anti*-3d)

A 25 mL flask charged with **2d** (246 mg, 1.0 mmol) and 10 mL CH_2Cl_2 was cooled to 0 °C, and a solution of MCPBA (55%, 314 mg, 1.0 mmol) in 10 mL $CH_2Cl_2$was added over 30 minutes. TLC indicated complete consumption of **2d** after 2 hours. The solvent volume was reduced by 75% *in vacuo* and the mixture filtered to remove residual *meta*-chlorobenzoic acid. The filtrate was then concentrated and chromatographed on silica gel (20% ethyl acetate/hexane) to give *anti*-**3d** as a colorless oil (130 mg, 50%, R_f= 0.23).

^{1}H NMR: δ 0.085 (s, 6H), 0.895 (s, 9H), 1.025 (t, *J* = 7.2 Hz, 3H), 1.40 (m, 1H), 1.55 (m, 1H), 1.65 (m, 2H), 3.08 (ddd, *J* = 11.0, 9.2, 5.8 Hz, 1H), 3.21 (ddd, *J* = 11.0, 6.4, 6.4 Hz, 1H), 3.74 (dd, *J* = 11.8, 6.4 Hz, 1H), 3.805 (dd, *J* = 11.8, 6.4 Hz);

^{13}C NMR: δ -5.50, -5.39, 13.63, 18.13, 22.17, 25.71, 26.75, 56.11, 56.78, 57.66; IR (NaCl): 2958, 2930, 2858, 1472, 1256, 1070, 838, 778 cm^{-1};

MS(CI$^+$(NH$_3$)): 263 (m+1), 280 (m+NH$_4$);

mp: liquid

anti, cis-1-(4'-carbobenzyloxy)phenoxymethyl-2-propylthiirane S-oxide (*anti*-3e)

A 100 mL flask charged with **2e** (825 mg, 2.3 mmol) and CH_2Cl_2 (30 mL) was cooled to 0 °C. A solution of MCPBA (55%, 759 mg, 2.4 mmol) was added over 30 minutes. TLC indicated complete reaction after an additional 30 minutes.

Addition of ether, aqueous workup, and flash chromatography (50% ethyl acetate/hexane) yielded *anti-3e* as a pale yellow liquid (550 mg, 56%, $R_f = 0.31$).

^{1}H NMR: δ 1.034 (t, $J = 7.2$ Hz, 3H), 1.297 (m, 1H), 1.57-1.71 (m, 3H), 3.221 (ddd, $J = 10.3, 5.6, 5.6$ Hz, 1H), 3.442 (ddd, $J = 10.3, 7.7, 7.1$, 1H), 3.985 (dd, $J = 11.0, 7.7$ Hz, 1H), 4.239 (dd, $J = 11.0, 7.1$ Hz, 1H), 5.339 (s, 2H), 6.902 (d, $J = 7.1$ Hz, 2H), 7.339 (m, 5H), 8.042 (d, $J = 7.1$ Hz, 2H); ^{13}C NMR: δ 13.60, 22.03, 26.84, 52.84, 55.57, 62.23, 66.49, 114.08, 123.54, 128.08, 128.17, 128.54, 131.84, 136.11, 161.48, 165.85;

IR(NaCl): 2960, 1712, 1606, 1510, 1456, 1376, 1274, 1250, 1168, 1102, 1070, 1028, 848, 768, 696 cm^{-1};

MS(CI$^+$(NH$_3$)): 359(m+1);

mp: liquid.

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