Diastereoselectivity in the Preparation of 4-Phenylthio-4-butanolide Derivatives by the Use of the Pummerer Rearrangement

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Diastereoselectivity in the preparation of 4-phenylthio-4-butanolide derivatives by the Pummerer rearrangement of 4-phenylsulfinylbutanoic acid derivatives was clarified. The reaction of 3-alkyl-4-phenylsulfinylbutanoic acid with acetic anhydride resulted in the predominant formation of *trans*-3-alkyl-4-phenylthio-4-butanolide. Lactonization of 2,3-dialkyl-4-phenylsulfinylbutanoic acid gave (2*RS*,3*RS*, 4*SR*)-2,3-dialkyl-4-phenylthio-4-butanolide predominantly.

The lactone ring system is a common structure in a wide variety of natural products, and a number of methods[1] are available for its construction. For example, Marino et al.[2] reported that the enantioselective preparation of 4-arylthio-4-butanolides from the chiral 1-alkenyl aryl sulfoxides and dichloroketene. Previously, we also reported[3] the synthetic route of the 4-phenylthio-4-butanolides by the Pummerer rearrangement.

We report herein the trans diastereoselectivity in the preparation of 3-alkyl or 2,3-dialkyl-4-phenylthio-4-butanolides by the Pummerer rearrangement of 4-phenylsulfinylbutanoic acids.

Results and Discussion

Preparation of 4-Phenylsulfinylbutanoic Acids. 3-Alkyl-4-phenylsulfinylbutanoic acids (**1**) were prepared by two methods shown in Scheme 1. Method A contains the Michael addition of phenylthiomethyllithium to diethyl alkylidenemalonates (**2**) (Scheme 1). Phenylthiomethyllithium, which was prepared from phenylthiomethane and butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane (Dabco), reacted with **2** at −78 °C in THF to give diethyl[1-(phenylthiomethyl)]alkylmalonates (**3**) in about 60—80% yield. The purification of **3** was very difficult due to the concomitant by-products. Further, an attempt to purify of 3-alkyl-4-phenylthiobutanoic acids (**4**), which were produced by the hydrolysis and decarboxylation of **3**, also did not give good results. Therefore, method B for the preparation of **1** was examined (Scheme 1).

The addition reaction of a mixture of geometric isomers of 1-phenylsulfinyl-1-alkenes (**5**) with the lithium enolate of ethyl acetate resulted in the formation of ethyl 3-alkyl-4-phenylsulfinylbutanoates (**6a—d**) in good yields. Hydrolysis of **6** witb 10% sodium hydroxide solution gave the desired 3-alkyl-4-phenylsulfinylbutanoic acids (**1a—d**) in good yields (see Table 1). Although compounds **1a—d** were a mixture of diastereomeric isomers, these mixtures were used in the next cyclization reactions.

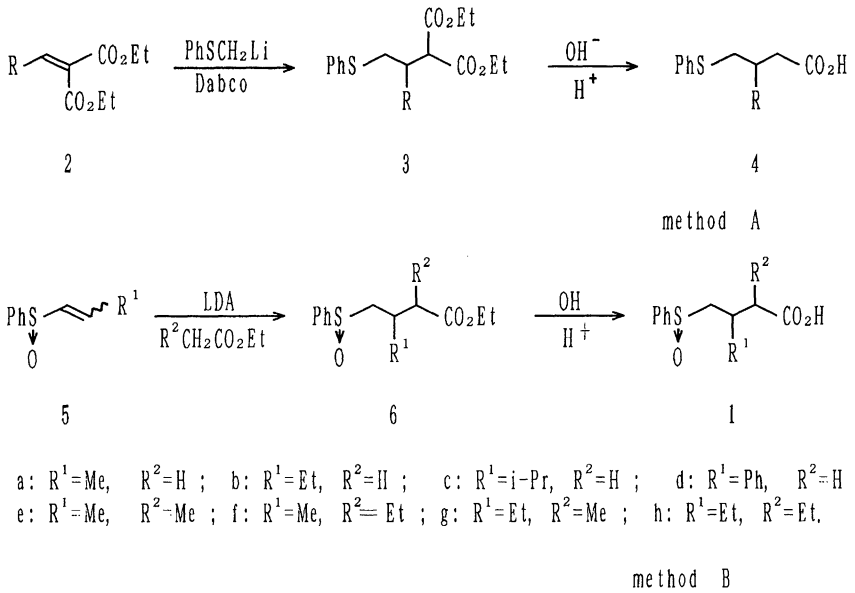
Ethyl 2,3-dialkyl-4-phenylsulfinylbutanotes (**6a—h**) were prepared by the addition reactions of the lithium enolate of ethyl propanoate or ethyl butanoate to geometircally pure (*E*)-**5** or (*Z*)-**5**. The reactions were carried out by a similar procedure with the preparation of **6a—d** and the results are summarized in Table 1. Hydrolysis of **6e—h** with 10% sodium hydroxide solution gave the corresponding 2,3-dialkyl-4-phenylsulfinylbutanoic acids (**1e—h**) in good yields (See Table 1). The compounds **1e—h** and **6e—h** were shown to be the mixture of four diastereomeric isomers from the study on the relationship between the C-2 and C-3 alkyl groups of **6e—h**, but the ratio of the four isomers would not been determined. The study on the relationship between C-2 and C-3 alkyl groups will be described later in this paper.

Table 1. Preparation of Ethyl 4-Phenylsulfinylbutanoates (**6**) and 4-Phenylsulfinylbutanoic Acids (**1**)

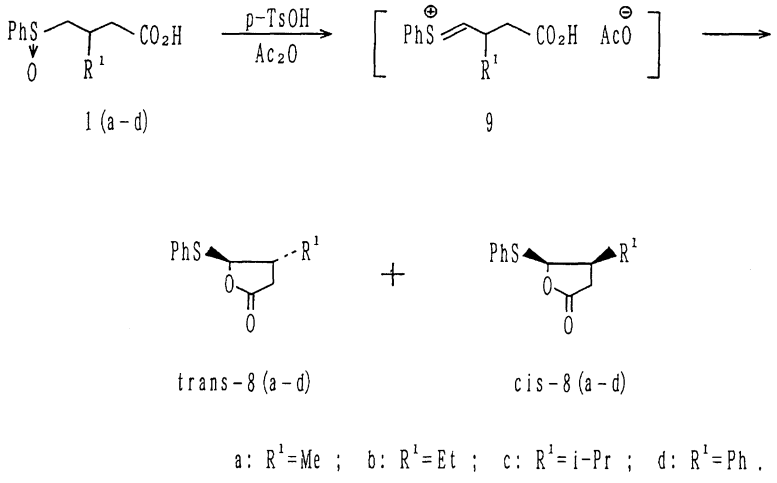
Geometry of the starting alkene **5**	Compounds	**6**(%)	**1**(%)
Mixture	**a**	56	77
Mixture	**b**	46	92
Mixture	**c**	47	60
Mixture	**d**	48	78
E	**e**	48	65
E	**f**	58	87
E	**g**	56	64
E	**h**	53	81
Z	**e**	64	80
Z	**f**	69	61
Z	**g**	53	78
Z	**h**	44	87

Synthesis and Diastereoselectivity of 4-Phenylthio-4-butanolides. When 3-methyl-4-phenylsulfinylbutanoic acid (**1a**) was allowed to react with acetic anhydride in the presence of a catalytic amount of *p*-toluenesulfonic acid in refluxing toluene, 3-methyl-4-phenylthio-4-butanolide (**8a**) was obtained as a mixture of diasteromeric isomers in 43% yield (Scheme 2). The ratio of the diastereomeric isomers was 87 : 13 as determined high performance liquid chromatography (HPLC). In a similar procedure, cyclization of **1b—d** by the Pummerer rearrangement gave the diastereomeric mixture of **8b—d** in good yields. The yields and results of HPLC analyses are summarized in the Table 2.

The diastereomeric structures of the two isomers were



Scheme 1.



Scheme 2.

determined by the ^{1}H NMR study of ASIS effect. S. Warren et al.[4] reported that the protons at the opposite side of large groups in *cis*-4-methyl-3-phenylthio-4-butanolides (**10**) were more highly solvated than those at the same side and showed large chemical shift differences ($\Delta\delta$) upon changing the solvent from chloroform-*d* to benzene-d_6. On the other hand, the protons of *trans*-**10** showed almost constant $\Delta\delta$ values. The value $\Delta\delta$ of the major isomer of **8a** was almost constant as shown in Table 3. Meanwhile, the C-3 proton and one of the C-2 protons of the minor isomer of **8a** showed large $\Delta\delta$ value (See Table 3). From these results, the major and minor isomers of **8a** were assigned as *trans* and *cis*-isomers, respectively.

To detect the stability of **8** under these cyclization conditions, the isolated *trans* or *cis* product of **8a** was refluxed in toluene with acetic anhydride and a catalytic amount of *p*-toluenesulfonic acid. The HPLC analysis of the reaction mixtures showed that both of the isomers of **8a** gave the same results containing the formation of *trans* and *cis* isomers of **8a** in the ratio of 93 : 7 (Scheme 3). These facts indicated that the thermodynamically more stable isomer was formed predominantly after formation of the butanolide structure by the equilibrium between the two isomers under the acidic reaction conditions.

The ^{1}H NMR studies of **8a**—**d** revealed significant features on the chemical shift of the C-4 proton (See Table 4). As shown in Table 4, the chemical shift of the C-4 proton in *trans*-**8a** appeared at an upper field than that of *cis*-**8a**. The ^{1}H NMR studies of **8b**—**d** also showed a similar pattern, that is, the C-4 proton of the major isomer appeared at an upper field than that of the minor isomer. From these results, it was concluded that the major products of **8b**—**d** are *trans*-isomers and the minor products are *cis*-isomers.

Next, the cyclizations of **1e**—**h** were performed by the similar procedure with the preparation of **8a** to give

Table 2. Preparation of 4-Phenylthio-4-butanolides (**8**)

	R^1	R^2	Starting alkene	**5**	**8**(%)	Major (trans)	:	Minor (cis)	**8-I** (2*RS*,3*RS*,4*SR*)	:	**8-II** (2*RS*,3*SR*, 4*RS*)	:	**8-III** (2*RS*,3*SR*,4*SR*)	:	**8-IV** (2*RS*,3*RS*,4*RS*)
a	Me	H	Mixture		43	87	:	13							
b	Et	H	Mixture		64	87	:	13							
c	*i*-Pr	H	Mixture		68	98	:	2							
d	Ph	H	Mixture		34	100	:	0							
e	Me	Me	*E*		64				61	:	32	:	7	:	0
f	Me	Et	*E*		63				47	:	22	:	21	:	10
g	Et	Me	*E*		57				70	:	20	:	10	:	0
h	Et	Et	*E*		60				70	:	20	:	10	:	0
e	Me	Me	*Z*		58				53	:	36	:	11	:	0
f	Me	Et	*Z*		62				46	:	17	:	26	:	11
g	Et	Me	*Z*		51				54	:	44	:	2	:	0
h	Et	Et	*Z*		63				66	:	26	:	8	:	0

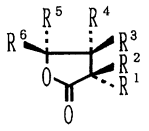
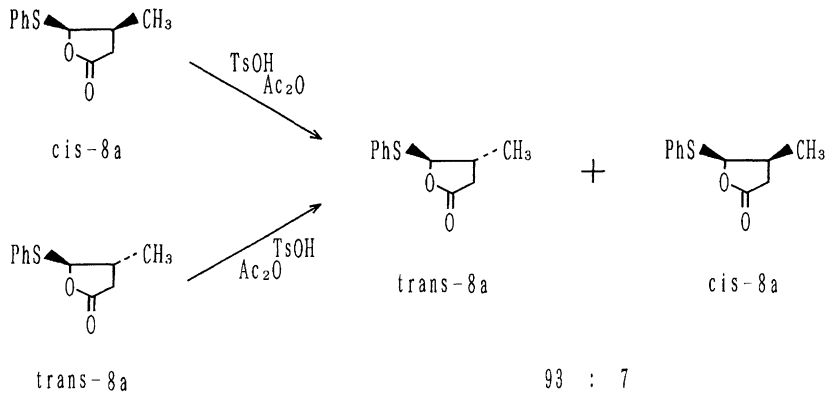


Table 3. Solvent Shift Values ($\Delta\delta$) for the Lactones (**8** and **10**)

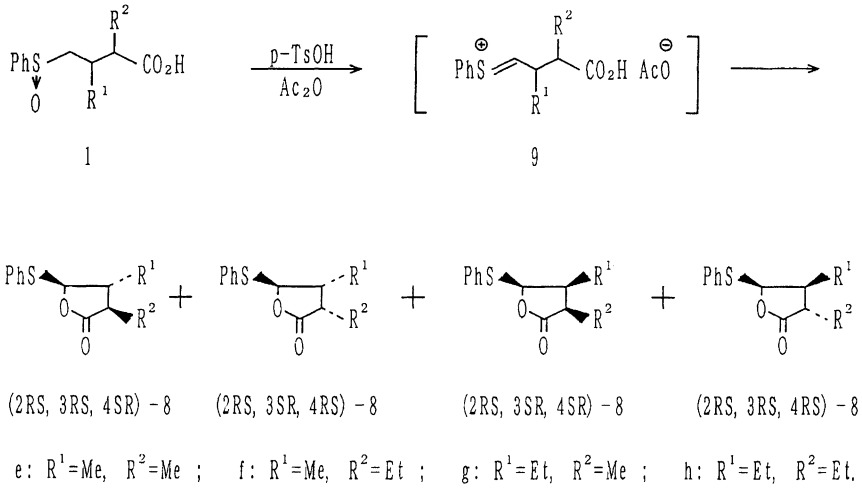
Compound	R^1	R^2	R^3	R^4	R^5	R^6	$\Delta\delta(=\delta_{CDCl_3}-\delta_{C_6D_6})$ R^1	R^2	R^3	R^4	R^5	R^6
8a(*trans*)	H	H	H	CH_3	H	PhS	0.90	0.81	0.80	0.69	0.85	—
8a(*cis*)	H	H	CH_3	H	H	PhS	0.92	0.65	0.66	1.15	0.75	—
8e	H	CH_3	H	CH_3	H	PhS	0.58	0.51	0.71	0.73	0.46	—
8e	CH_3	H	H	CH_3	H	PhS	0.68	0.80	0.50	0.89	0.67	—
8e	H	CH_3	CH_3	H	H	PhS	0.99	0.43	0.50	0.89	0.67	—
10(*trans*)[a]	H	H	PhS	H	CH_3	H	0.44	0.31	—	0.48	0.40	0.37
10(*cis*)[a]	H	H	PhS	H	H	CH_3	0.61	0.32	—	0.73	0.68	0.36

a) Ref. 4.



Scheme 3.

the diastereomeric mixtures of 2,3-dialkyl-4-phenylthio-4-butanolides (**8e**—**h**) in good yields (Scheme 4). The HPLC analyses of these products showed three peaks (the three peaks are indicated as follows: first peak; **8-I**, second peak; **8-II**, third peak; **8-III**), except in the case of **8f** whose HPLC analysis showed four peaks. The ratios of these peaks revealed that the cyclization reactions of **1e**—**h** which were prepared from (*E*)-**5** gave higher diastereoselectivity than that of **1e**—**h** which were from (*Z*)-**5**. For example, the cyclization reaction of **1g** which was prepared from (*E*)-**5** gave three isomers, **8g-I**, **8g-II**, and **8g-III**, in the ratio of 70 : 20 : 10. One the other hand, the cyclization reaction of **1g** which was prepared from (*Z*)-**5** gave **8g-I**, **8g-II**, and **8g-III** in the



Scheme 4.

Table 4. Chemical Shifts and Coupling Constants of the C-4 Protons of **8a—d**

	R^2	Major isomer (*trans*)		Minor isomer (*cis*)	
		δ	J/Hz	δ	J/Hz
8a	Me	5.34	5.9	5.85	5.9
8b	Et	5.39	5.4	5.81	6.0
8c	*i*-Pr	5.47	6.0	5.76	8.0
8d	Ph	5.47	7.0	—	—

ratio of 54 : 44 : 2 (See Table 2).

The configurations of these isomers were established by the following procedure. It was found that the lithium enolate of *trans* **8a** with methyl iodide resulted in the formation of two products, **8e-I** and **8e-II**, in the ratio of 38 : 62.

From this result, it was clarified that the relationship of the C-3 methyl group and the phenylthio group of **8e-I** and **8e-II** has *trans* configuration, and **8e-III** has *cis* configuration. Further, the NOE analyses of these isomers showed that the irradiation of C-2 proton of **8e-I** enhanced the C-4 proton, indicating that the phenylthio group of **8e-I** is in the *cis* position to the C-2 methyl group. Therefore, **8e-I** and **8e-II** are assigned to be (2*RS*, 3*RS*,4*SR*)-**8e** and (2*RS*, 3*SR*, 4*RS*)-**8e**, respectively (Scheme 5). Further, the ASIS analysis of three isomers of **8e** by the use of $\Delta\delta$ are summarized in Table 3. From this pattern, **8e-III** could be (2*RS*, 3*SR*, 4*SR*)-**8e**.

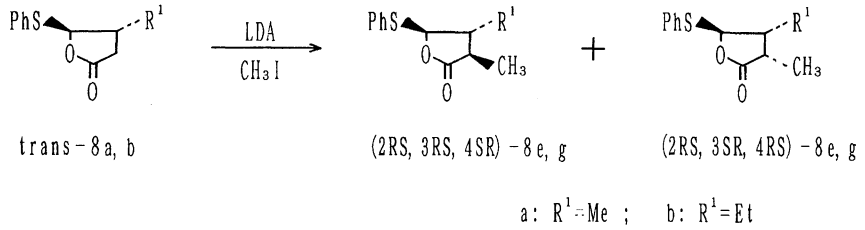
The chemical shift and coupling constant of the C-4 proton in **8e** showed a significant feature: (1) C-4 proton in (2*RS*, 3*SR*, 4*RS*)-**8e** showed the resonance at the highest field and the largest coupling constant. (2) Chemical shift of (2*RS*, 3*SR*, 4*SR*)-**8e** revealed the lowest-field resonance. (3) The coupling constant of (2*RS*, 3*RS*, 4*SR*)-**8e** was the smallest. From these features, the configurations of **8f—h** were assigned (See Table 5). In conclusion, the cyclization reactions of **1e—h** gave (2*RS*, 3*RS*, 4*SR*)-**8e—h** predominantly especially in the case of the cyclization reaction of **1e—h** starting from (*E*)-**5**. It is interesting that the isomeric ratio of **8e—h** which was prepared from (*E*)-**5** is different from that of **8e—h** which was prepared from (*Z*)-**5**. This result means that the ratios of the diastereomeric isomers of **1e—h** or **6e—h** depend on the geometry of **5**. As mentioned before, we could not clarify the ratio of diastereomeric isomers of **1e—h** or **6e—h**. Therefore, the attempt of the determination of the relationship between the C-2 and C-3 alkyl groups of **6** was performed with the corresponding sulfones (**11**) which were produced by oxidation of **6** with *m*-chloroperbenzoic acid (Scheme 6 and Table 6).

Unfortunately, the separations of the two isomers of **11** were unsuccessful, but the ^{1}H NMR spectra of C-4 protons of two isomers showed different chemical shifts. From the peak ratio of these protons, the ratios of the major and minor isomers of **11** which was prepared from (*E*)-**5** or (*Z*)-**5** were about 90 : 10 or 65 : 35. The relationship of two alkyl groups at C-2 and C-3 in **1e—h** would remain during the cyclization reaction. Thus, (2*RS*, 3*RS*)-**1e—h** gave the 2,3-*trans* isomer of **8** and (2*RS*, 3*SR*)-**1e—h** gave the 2,3-*cis* isomer of **8** (Scheme 7). However, the proportion of the 2,3-*trans* isomer in **8** was a little lower than that in **11**. It would be concluded that isomerization of the (2*RS*, 3*RS*)-isomer of **1** to the (2*RS*, 3*SR*)-isomer occurred to some extent during the cyclization reactions.

Experimental

IR spectra were determined with a Hitachi 15 Infracord spectrophotometer. ^{1}H NMR spectra were recorded on G. E. OMEGA-300 NB instruments. Mass spectra were measured on a Shimadzu GCMS-QP 1000EX spectrometer. Elemental analyses were made with a Yanaco CHN-CORDER MT-5.

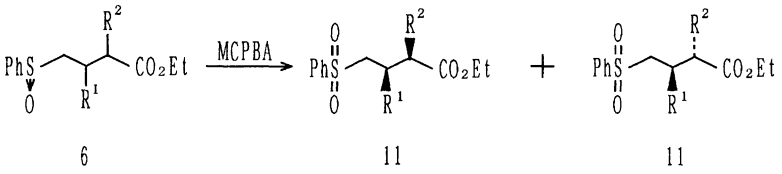
Preparation of Ethyl 3-Methyl-4-phenylsulfinylbutanoate (6a). To a solution of lithium diisopropyl-



Scheme 5.

Table 5. Chemical Shifts and Coupling Constants of the C-4 Protons of **8e—h**

	R^1	R^2	(2*RS*,3*RS*,4*SR*)-**8**		(2*RS*,3*SR*,4*RS*)-**8**		(2*RS*,3*SR*,4*SR*)-**8**		(2*RS*,3*RS*,4*RS*)-**8**	
			δ	J/Hz	δ	J/Hz	δ	J/Hz	δ	J/Hz
8e	Me	Me	5.39	4.2	5.21	9.6	5.71	5.4	—	—
8f	Me	Et	5.39	2.7	5.17	8.7	5.65	5.1	5.80	6.9
8g	Et	Me	5.47	4.5	5.27	8.1	5.80	8.1	—	—
8h	Et	Et	5.52	3.6	5.33	7.5	5.81	6.9	—	—



Scheme 6.

Table 6. Isomer Ratios of Ethyl 4-Phenylsulfonylbutanoates **11** and **8**

Starting alkene	Compound	Isomer ratio in **11** (2*RS*,3*RS*) : (2*RS*,3*SR*)		Isomer ratio in **8** 2,3-*trans* : 2,3-*cis*	
(*E*)-**5**	**e**	90	10	61	39
(*E*)-**5**	**g**	90	10	70	30
(*E*)-**5**	**h**	92	8	70	30
(*Z*)-**5**	**e**	61	39	53	47
(*Z*)-**5**	**g**	73	27	54	46
(*Z*)-**5**	**h**	68	32	66	34

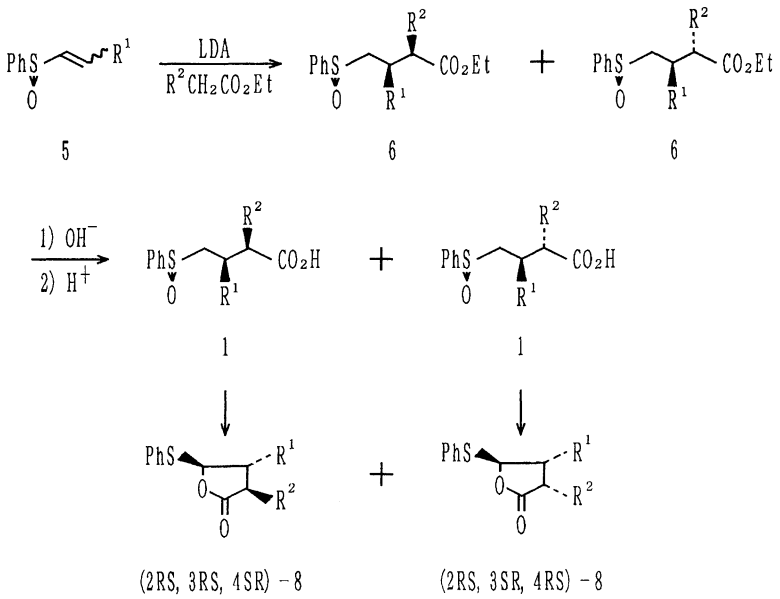
amide (LDA) in 20 cm^3 of THF, prepared from diisopropylamine (1.98 g, 18.9 mmol) and butyllithium (18.9 mmol), a solution of ethyl acetate (1.66 g, 18.9 mmol) in 10 cm^3 of THF was added at −78 °C under nitrogen with stirring. The reaction mixture was stirred for 1 h, then 1-phenylsulfinyl-1-propene (**5a**) (3.14 g, 18.9 mmol) in 10 cm^3 of THF was added to the mixture. The reaction mixture was stirred at −78 °C for 3 h and was then allowed to warm to 0 °C. Then, the reaction mixture was quenched with 10% hydrochloric acid. The whole was extracted with chloroform and the chloroform layer was washed with saturated sodium chloride solution. The chloroform layer was dried over magnesium sulfate and then the solvent was evaporated under reduced pressure to give the residue, which was purified with silica-gel column chromatography. From the eluate with benzene–ether (1:1), **6a** was obtained as an oil, 2.69 g (56%). IR (NaCl) 1730 (C=O), 1210, 1040 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, d, J=7.0 Hz), 1.24 (3H, t, J=8.0 Hz), 1.56—3.00 (5H, m), 4.12 (2H, q, J=8.0 Hz), 7.36—7.93 (5H, m); MS m/z 209 (M^+ − EtO). Found: C, 61.38; H, 7.15%. Calcd for $C_{13}H_{18}O_3S$: C, 61.41; H, 7.09%.

Similarly, ethyl 3-(phenylsulfinylmethyl)pentanoate (**6b**), ethyl 4-methyl-3-(phenylsulfinylmethyl)pentanoate (**6c**), and ethyl 3-phenyl-4-phenylsulfinylbutanoate (**6d**) were prepared from the corresponding 1-phenylsulfinyl-1-alkene and ethyl acetate. Yields, spectral and analytical data of **6b**, **6c**, and **6d** are as follows:

6b: Yield 46%, oil. IR (NaCl) 1740 (C=O), 1210 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, t, J=7.0 Hz), 1.22 (3H, t, J=7.0 Hz), 1.32—1.65 (3H, m), 2.30—2.90 (4H, m), 4.12 (2H, q, J=7.0 Hz), 7.27—7.71 (5H, m); MS m/z 223 (M^+ − EtO). Found: C, 62.86; H, 7.71%. Calcd for $C_{14}H_{20}O_3S$: C, 62.69; H, 7.46%.

6c: Yield 47%, oil. IR (NaCl) 1740 (C=O), 1090, 1040 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=0.82 (6H, d, J=7.0 Hz), 1.16 (3H, t, J=7.0 Hz), 1.63—2.11 (1H, m), 2.14—2.90 (5H, m), 4.11 (2H, q, J=7.0 Hz), 7.26—8.05 (5H, m); MS m/z 237 (M^+ − EtO). Found: C, 63.98; H, 8.06%. Calcd for $C_{15}H_{22}O_3S$: C, 63.80; H, 7.80%.

6d: Yield 48%, mp 85.4—90.7 °C (from petroleum



Scheme 7.

ether–benzene). IR (KBr) 1740 (C=O), 1040 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=1.05 (3H, t, J=7.0 Hz), 2.69—3.71 (5H, m), 3.95 (2H, q, J=7.0 Hz), 6.96—7.87 (10H, m); MS m/z 271 (M^+−EtO). Found: C, 68.33; H, 6.37%. Calcd for $C_{18}H_{20}O_3S$: C, 68.22; H, 6.56%.

Preparation of ethyl 2, 3- dimethyl- 4- phenylsulfinylbutanoate (**6e**), ethyl 2-ethyl-3-methyl-4-phenylsulfinylbutanoate (**6f**), ethyl 2-methyl-3-(phenylsulfinylmethyl)pentanoate (**6g**), and ethyl 2-ethyl-3-(phenylsulfinylmethyl)pentanoate (**6h**) were prepared by the similar procedure to the preparation of **6a** from the geometrically pure 1-phenylsulfinyl-1-propene or 1-phenylsulfinyl-1-butene with ethyl propanoate or ethyl butanoate. The yields, spectral and analytical data of **6e**, **6f**, **6g**, and **6h**, which were prepared from the (*E*)-alkene are as follows:

6e: Yield 48%, oil. IR (NaCl) 1730 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=1.13 (3H, d, J=6.6 Hz), 1.20 (3H, d, J=6.3 Hz), 1.22 (3H, t, J=6.9 Hz), 2.38—2.58 (3H, m), 2.94 (1H, dd, J=2.7, 12.9 Hz), 4.10 (2H, q, J=6.9 Hz), 7.45—7.66 (5H, m); MS m/z 223 (M^+−EtO). Found: C, 62.64; H, 7.68%. Calcd for $C_{14}H_{20}O_3S$: C, 62.66; H, 7.51%.

6f: Yield 58%, oil. IR (NaCl) 1745 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.85 (3H, t, J=7.0 Hz), 1.18 (3H, d, J=6.0 Hz), 1.19 (3H, t, J=7.0 Hz), 2.05—3.07 (6H, m), 4.08 (2H, q, J=7.0 Hz), 7.40—7.98 (5H, m); MS m/z 237 (M^+−EtO). Found: C, 63.83; H, 8.15%. Calcd for $C_{15}H_{22}O_3S$: C, 63.80; H, 7.85%.

6g: Yield 56%, oil. IR (NaCl) 1730 (C=O); 1180, 1030 cm^{-1} (–O–); ^{1}H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7.0 Hz), 0.96 (3H, d, J=8.0 Hz), 1.22 (3H, t, J=7.0 Hz), 1.40—1.80 (2H, m), 2.09—2.44 (1H, m), 2.63 (2H, d, J=8.0 Hz), 2.79 (1H, dq, J=4.0 Hz), 4.10 (2H, q, J=7.0 Hz), 7.31—7.73 (5H, m); MS m/z 237 (M^+−EtO). Found: C, 63.60; H, 7.88%. Calcd for $C_{15}H_{22}O_3S$: C, 63.83; H, 7.80%.

6h: Yield 53%, oil. IR (NaCl) 1740 (C=O), 1170, 1030 cm^{-1} (–O–); ^{1}H NMR ($CDCl_3$) δ=0.84 (3H, t, J=7.0 Hz), 0.94 (3H, t, J=7.0 Hz), 1.22 (3H, t, J=7.0 Hz), 1.36—1.78 (4H, m), 2.04—2.68 (2H, m), 2.42 (1H, dd, J=9.0, 13.0 Hz), 3.00 (1H, dd, J=5.0, 13.0 Hz), 4.11 (2H, q, J=7.0 Hz), 7.44—7.73 (5H, m); MS m/z 251 (M^+−EtO). Found: C, 64.67; H, 8.45%. Calcd for $C_{16}H_{24}O_3S$: C, 64.86; H, 8.11%.

The yields, spectral and analytical data **6e**, **6f**, **6g**, and **6h**, which were prepared from the (*Z*)-alkene are as follows:

6e: Yield 64%, oil. IR (NaCl) 1735 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=1.10 (3H, d, J=6.9 Hz), 1.12 (3H, d, J=7.2 Hz), 1.22 (3H, t, J=6.9 Hz), 2.25—2.44 (2H, m), 2.71—2.80 (1H, m), 2.94 (1H, dd, J=7.2, 13.2 Hz), 4.10 (2H, q, J=6.9 Hz), 7.45—7.66 (5H, m); MS m/z 223 (M^+−EtO).

6f: Yield 69%, oil. IR (NaCl) 1735 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7.0 Hz), 1.05 (3H, d, J=7.0 Hz), 1.22 (3H, t, J=8.0 Hz), 2.11—2.65 (4H, m), 2.82 (2H, qu), 4.12 (2H, q, J=8.0 Hz), 7.37—7.78 (5H, m); MS m/z 266 (M^+−O).

6g: Yield 53%, oil. IR (NaCl): 1730 (C=O), 1180, 1030 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7.0 Hz), 1.18 (3H, d, J=8.0 Hz), 1.20 (3H, t, J=7.0 Hz), 1.33—1.58 (2H, m), 1.96—2.36 (1H, m), 2.80 (2H, d, J=8.0 Hz), 2.56—3.04 (1H, m), 4.07 (2H, q, J=7.0 Hz), 7.42—7.73 (5H, m); MS m/z 237 (M^+−EtO). Found: C, 63.59; H, 8.08%. Calcd for $C_{15}H_{22}O_3S$: C, 63.83; H, 7.80%.

6h: Yield 44%, oil. IR (NaCl) 1740 (C=O), 1190, 1040 cm^{-1} (–SO–); ^{1}H NMR ($CDCl_3$) δ=0.89 (6H, t, J=7.0 Hz), 1.22 (3H, t, J=7.0 Hz), 1.33—1.78 (4H, m), 2.00—2.22 (1H, m), 2.66 (1H, dd, J=5.0, 8.0 Hz), 2.68—2.84 (1H, m), 2.87 (1H, dd, J=5.0, 8.0 Hz), 4.09 (2H, q, J=7.0 Hz), 7.44—7.67 (5H, m); MS m/z 251 (M^+−EtO). Found: C, 64.70; H, 8.30%. Calcd for $C_{16}H_{24}O_3S$: C, 64.86; H, 8.11%.

Preparation of 3-Methyl-4-phenylsulfinylbutanoic Acid (1a). To a solution of **6a** (3.81 g, 15.0 mmol) in 30 cm^3 ethanol, 30 cm^3 of 10% aqueous sodium hydroxide solution was added with stirring. The reaction mixture was stirred at room temperature for 4 h, then the mixture was evaporated under the reduced pressure to give the residue. The residue was acidified with 10% hydrochloric acid and was extracted with chloroform. The chloroform layer was washed once with saturated sodium chloride solution and

was dried over magnesium sulfate. After removal of the solvent, the residue was chromatographed on silica gel. From the eluate with benzene–acetone (10 : 1), **1a** was obtained as an oil, 2.61 g (77%). The **1a** was used for the next reaction without further purification. IR (NaCl) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.08, 1.15 (3H, d, J=7.0 Hz), 2.07—3.38 (5H, m), 7.18—8.22 (5H, m), 9.5 (1H, brs); MS m/z 210 (M^+-O).

Similarly, another butanoic acid derivatives (**1b—h**) were obtained by the hydrolysis of corresponding **6**. The yields and spectral data are as follows:

3-(Phenylsulfinylmethyl)pentanoic Acid (1b): Yield 92%, oil. IR (NaCl) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.92 (3H, t, J=7.0 Hz), 1.40—1.73 (2H, m), 2.33—3.18 (5H, m), 7.40—7.71 (5H, m), 10.5 (1H, brs); MS m/z 224 (M^+-O).

4-Methyl-3-(phenylsulfinylmethyl)pentanoic Acid (1c): Yield 60%, oil. IR (NaCl) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.88 (6H, d, J=7.0 Hz), 1.56—3.31 (6H, m), 7.38—7.98 (5H, m), 9.5 (1H, brs); MS m/z 238 (M^+-O).

3-Phenyl-4-phenylsulfinylbutanoic Acid (1d): Yield 78%, mp 83.8—87.9 °C (from petroleum ether). IR (KBr) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=2.52—3.77 (5H, m), 7.13—7.76 (10H, m); MS m/z 162 (M^+-PhSO).

2,3-Dimethyl-4-phenylsulfinylbutanoic Acid (1e) (starting alkene (*E*)-5): Yield 65%, oil. IR (NaCl) 3500—2500 (CO_2H), 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.13 (3H, d, J=6.0 Hz), 1.19 (3H, d, J=5.0 Hz), 2.16—3.21 (4H, m), 7.42—7.81 (5H, m), 9.1 (1H, brs); MS m/z 224 (M^+-O).

2-Ethyl-3-methyl-4-phenylsulfinylbutanoic Acid (1f) (starting alkene (*E*)-5): Yield 87%, oil. IR (NaCl) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7.5 Hz), 1.19, 1.24 (3H, d, J=6.6 Hz), 1.39—1.54 (1H, m), 1.63—1.81 (1H, m), 2.28—2.66 (3H, m), 3.01, 3.09 (1H, dd, J=3.9, 12.6 Hz), 7.24—7.68 (5H, m), 7.9 (1H, brs); MS m/z 238 (M^+-O).

2-Methyl-3-(phenylsulfinylmethyl)pentanoic Acid (1g) (starting alkene (*E*)-5): Yield 64%, oil. IR (NaCl) 3650—2300 (CO_2H), 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, J=7.0 Hz), 1.07 (3H, d, J=6.0 Hz), 1.38—1.80 (2H, m), 2.11—3.20 (4H, m), 7.44—7.78 (5H, m), 8.3 (1H, brs); MS m/z 254 (M^+).

2-Ethyl-3-(phenylsulfinylmethyl)pentanoic Acid (1h) (starting alkene (*E*)-5): Yield 82%, oil. IR (NaCl) 3650—2300 (CO_2H), 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, J=9.9 Hz), 0.95 (3H, t, J=7.5 Hz), 1.39—1.73 (4H, m), 2.26—2.61 (2H, m), 2.65 (1H, dd, J=8.4, 13.5 Hz), 3.18 (1H, dd, J=5.7, 13.5 Hz), 7.49—7.55 (3H, m), 7.63—7.69 (2H, m), 9.8 (1H, brs); MS m/z 252 (M^+-O).

1e (starting alkene (*Z*)-5): Yield 80%, oil. IR (NaCl) 3500—2500 (CO_2H), 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.07 (3H, d, J=6.0 Hz), 1.15 (3H, d, J=8.0 Hz), 2.12—3.26 (4H, m), 7.38—7.76 (5H, m), 9.4 (1H, brs); MS m/z 224 (M^+-O).

1f (starting alkene (Z)-5): Yield 61%, oil. IR (NaCl) 3500—2500 (CO_2H), 1735 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.92 (3H, t, J=7.0 Hz), 1.07 (3H, d, J=7.0 Hz), 2.07—2.76 (4H, m), 2.92 (2H, qu), 7.44—7.95 (5H, m), 10.0 (1H, brs); MS m/z 238 (M^+-O).

1g (starting alkene (*Z*)-5): Yield 78%, oil. IR (NaCl) 3500—2500 (CO_2H), 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7.0 Hz), 1.14 (3H, d, J=8.0 Hz), 1.40—1.68 (2H, m), 2.00—2.31 (1H, m), 2.73—3.07 (1H, m), 2.93 (2H, d, J=6.0 Hz), 7.44—7.67 (5H, m); MS m/z 254 (M^+).

1h (starting alkene (*Z*)-5): Yield 87%, oil. IR (NaCl) 3650—2300 (CO_2H), 1735 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.87 (3H, t, J=6.0 Hz), 0.91 (3H, t, J=7.0 Hz), 1.20—1.84 (4H, m), 1.96—2.20 (1H, m), 2.69 (1H, dd, J=5.0, 9.0 Hz), 2.71—2.87 (1H, m), 2.91 (1H, dd, J=3.0, 9.0 Hz), 7.42—7.76 (5H, m), 9.6 (1H, brs); MS m/z 268 (M^+).

Preparation of 3-Methyl-4-phenylthio-4-butanolide (8a). A solution of **1a** (2.26 g, 10.0 mmol), acetic anhydride (2.04 g, 20.0 mmol), and a catalytic amount of *p*-toluenesulfonic acid in 50 cm^3 of dry toluene was refluxed for 2 h. The reaction mixture was cooled to room temperature, then 50 cm^3 of bezene was added into the mixture. The mixture was washed with saturated sodium hydrogencarbonate solution. The organic layer was dried over magnesium sulfate and then the solvent was evaporated under reduced pressure to give the residue which was purified with silica gel column chromatography. From the eluate with benzene, diastereomeric mixture of **8a** was obtained as an oil, 0.89 g (43%). IR (NaCl) 1780 cm^{-1} (C=O), ^1H NMR ($CDCl_3$) δ=1.28, 1.29 (3H, d, J=6.6, 6.9 Hz), 1.71—2.82 (3H, m), 5.30, 5.81 (1H, d, J=5.9, 5.9 Hz), 7.04—7.87 (5H, m); MS m/z 208 (M^+).

The diastereomeric mixture was chromatographed on silica gel again and pure *trans*-**8a** and *cis*-**8a** were obtained from the eluate with petroleum ether–ether (6 : 1). The ratio of resulting *trans*-**8a** and *cis*-**8a** was determined with high performance liquid chromatography by the use of purified *trans*-**8a** and *cis*-**8a** as the authentic samples. The ^1H NMR spectra of purified *trans*-**8a** and *cis*-**8a** are as follows:

***trans*-8a:** ^1H NMR ($CDCl_3$) δ=1.28 (3H, d, J=6.6 Hz), 2.23 (1H, dd, J=7.8, 17.1 Hz), 2.44—2.57 (1H, m), 2.70 (1H, dd, J=8.4, 17.1 Hz), 5.34 (1H, d, J=5.9 Hz), 7.27—7.57 (5H, m).

***cis*-8a:** ^1H NMR ($CDCl_3$) δ=1.29 (3H, d, J=6.9 Hz), 2.37 (1H, dd, J=8.7, 17.1 Hz), 2.68 (1H, dd, J=8.1, 17.1 Hz), 2.88—3.03 (1H, m), 5.85 (1H, d, J=5.9 Hz), 7.18—7.57 (5H, m).

Similarly, another butanolide derivatives were prepared from the corresponding butanoic acid derivatives. The yields, spectral and analytical data of butanolide are as follows:

Diastereomeric Mixture of 3-Ethyl-4-phenylthio-4-butanolide (8b): Yield 64%. oil. IR (NaCl) 1780 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, J=7.0 Hz), 1.22—1.89 (3H, m), 2.00—2.71 (2H, m), 5.37, 5.81 (1H, d, J=5.4, 6.0 Hz), 7.24—7.40 (3H, m), 7.44—7.58 (2H, m). MS m/z 222 (M^+).

The ^1H NMR spectra of isolated *trans*-**8b**: ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, J=7.0 Hz), 1.13—1.41 (3H, m), 2.02—2.51 (1H, m), 2.04—2.66 (1H, m), 5.39 (1H, d, J=5.4 Hz), 7.24—7.40 (3H, m), 7.44—7.58 (2H, m).

Diastereomeric Mixture of 4-Phenylthio-3-isopropyl-4-butanolide (8c): Yield 63%, oil. IR (NaCl) 1780 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=0.94 (6H, d, J=7.0 Hz), 1.80 (1H, sep), 2.00—2.74 (3H, m), 5.47, 5.76 (1H, d, J=6.0, 8.0 Hz), 7.17—7.78 (5H, m); MS m/z 236 (M^+). Found: C, 66.28; H, 6.62%. Calcd for $C_{13}H_{16}O_2S$: C, 66.10; H, 6.78%.

The ^{1}H NMR spectra of isolated *trans*-**8c**: ^{1}H NMR ($CDCl_3$) δ=0.94 (6H, d, J=7.0 Hz), 1.60—1.90 (1H, m), 2.00—2.50 (1H, m), 2.32 (2H, d, J=8.0 Hz), 5.47 (1H, d, J=6.0 Hz), 7.17—7.78 (5H, m).

***trans*-3-Phenyl-4-phenylthio-4-butanolide (8d):** Yield 34%, oil. IR (NaCl) 1790 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=2.66 (1H, dd, J=9.0, 15.0 Hz), 2.66 (1H, dd, J=8.0, 15.0 Hz), 3.46 (1H, dt J=6.0, 9.0 Hz), 5.47 (1H, d, J=7.0 Hz), 7.00—7.50 (10H, m); MS m/z 270 (M^+).

Diastereomeric Mixture of 2,3-Dimethyl-4-phenylthio-4-butanolide (8e): Yield 64% (starting alkene (*E*)-**5**), 58% (starting alkene (*Z*)-**5**). IR (NaCl) 1780 cm^{-1} (C=O); MS m/z 222 (M^+). Found: C, 64.53; H, 6.49%. Calcd for $C_{12}H_{14}O_2S$: C, 64.83; H, 6.35%.

The ^{1}H NMR spectra of isolated (2*RS*, 3*RS*, 4*SR*)-**8e**, (2*RS*, 3*SR*, 4*RS*)-**8e**, and (2*RS*, 3*SR*, 4*SR*)-**8e** are as follows:

(2*RS*, 3*RS*, 4*SR*)-8e: Oil. ^{1}H NMR ($CDCl_3$) δ=1.13 (3H, d, J=6.9 Hz), 1.18 (3H, d, J=7.5 Hz), 2.54—2.66 (1H, m), 2.83 (1H, qu, J=7.5 Hz), 5.39 (1H, d, J=4.2 Hz), 7.31—7.36 (3H, m), 7.52—7.56 (2H, m).

(2*RS*, 3*SR*, 4*RS*)-8e: Oil. ^{1}H NMR ($CDCl_3$) δ=1.22 (3H, d, J=6.9 Hz), 1.28 (3H, d, J=6.6 Hz), 1.93—2.02 (1H, m), 2.16 (1H, oct), 5.21 (1H, d, J=9.6 Hz), 7.31—7.38 (3H, m), 7.51—7.56 (2H, m).

(2*RS*, 3*SR*, 4*SR*)-8e: Mp 71—74 °C (from petroleum ether). ^{1}H NMR ($CDCl_3$) δ=1.11 (3H, d, J=6.9 Hz), 1.24 (3H, d, J=7.2 Hz), 2.79 (1H, qu, J=7.2 Hz), 2.90 (1H, sex), 5.71 (1H, d, J=5.4 Hz), 7.29—7.36 (3H, m), 7.53—7.56 (2H, m).

Diastereomeric Mixture of 2-Ethyl-3-methyl-4-phenylthio-4-butanolide (8f): Yield 63% (starting alkene (*E*)-**5**), 62% (starting alkene (*Z*)-**5**). IR (NaCl) 1780 cm^{-1} (C=O); MS m/z 236 (M^+). Found: C, 66.44; H, 7.07%. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82%.

The ^{1}H NMR spectra of isolated (2*RS*, 3*RS*, 4*SR*)-**8f**, (2*RS*, 3*SR*, 4*RS*)-**8f**, (2*RS*, 3*SR*, 4*SR*)-**8f**, (2*RS*, 3*RS*, 4*RS*)-**8f** are as follows:

(2*RS*, 3*RS*, 4*SR*)-8f: Oil. ^{1}H NMR ($CDCl_3$) δ=1.04 (3H, t, J=7.2 Hz), 1.11 (3H, d, J=6.6 Hz), 1.49—1.53 (1H, m), 1.67—1.87 (1H, m), 2.58—2.72 (2H, m), 5.39 (1H, d, J=2.7 Hz), 7.27—7.35 (3H, m), 7.51—7.55 (2H, m).

(2*RS*, 3*SR*, 4*RS*)-8f: Oil, ^{1}H NMR ($CDCl_3$) δ=0.94 (3H, t, J=7.5 Hz), 1.27 (3H, d, J=6.6 Hz), 1.58—1.79 (2H, m), 2.05—2.16 (1H, m), 2.19 (1H, sep, J=5.7 Hz), 5.17 (1H, d, J=8.7 Hz), 7.27—7.36 (3H, m), 7.50—7.54 (2H, m).

(2*RS*, 3*SR*, 4*SR*)-8f: Oil. ^{1}H NMR ($CDCl_3$) δ=1.03 (3H, t, J=7.2 Hz), 1.07 (3H, d, J=6.9 Hz), 1.43—1.57 (1H, m), 1.87 (1H, sep, J=7.5 Hz), 2.51—2.58 (1H, m), 2.84—2.96 (1H, m), 5.65 (1H, d, J=5.1 Hz), 7.27—7.36 (3H, m), 7.50—7.54 (2H, m).

(2*RS*, 3*RS*, 4*RS*)-8f: Oil. ^{1}H NMR ($CDCl_3$) δ=1.03 (3H, t, J=7.5 Hz), 1.27 (3H, d, J=6.9 Hz), 1.67—1.87 (1H, m), 2.29—2.37 (1H, m), 2.58—2.72 (2H, m), 5.80 (1H, d, J=6.9 Hz), 7.27—7.35 (3H, m), 7.51—7.55 (2H, m).

Diastereomeric Mixture of 3-Ethyl-2-methyl-4-phenylthio-4-butanolide (8g): Yield 57% (starting alkene (*E*)-**5**), 51% (starting alkene (*Z*)-**5**). IR (NaCl) 1780 cm^{-1} (C=O); MS m/z 236 (M^+). Found: C, 65.83; H, 6.99%. Calcd for $C_{13}H_{16}O_2S$: C, 66.03; H, 6.84%.

The ^{1}H NMR spectra of isolated (2*RS*, 3*RS*, 4*SR*)-**8g**, (2*RS*, 3*SR*, 4*RS*)-**8g**, (2*RS*, 3*SR*, 4*SR*)-**8g** are as follows:

(2*RS*, 3*RS*, 4*SR*)-8g: Oil. ^{1}H NMR ($CDCl_3$) δ=0.96 (3H, t, J=7.0 Hz), 1.16 (3H, d, J=7.0 Hz), 1.36—1.69 (2H, m), 2.11—2.47 (1H, m), 2.80 (1H, sep), 5.47 (1H, d, J=4.5 Hz), 7.22—7.42 (3H, m), 7.42—7.67 (2H, m).

(2*RS*, 3*SR*, 4*RS*)-8g: Oil. ^{1}H NMR ($CDCl_3$) δ=1.00 (3H, t, J=7.0 Hz), 1.19 (3H, d, J=7.0 Hz), 1.36—2.07 (3H, m), 2.29 (1H, sep), 5.27 (1H, d, J=8.1 Hz), 7.22—7.38 (3H, m), 7.38—7.49 (2H, m).

(2*RS*, 3*SR*, 4*SR*)-8g: Oil. ^{1}H NMR ($CDCl_3$) δ=1.04 (3H, t, J=7.0 Hz), 1.31 (3H, d, J=7.0 Hz), 1.44—1.64 (3H, m), 2.71 (1H, sep), 5.83 (1H, d, J=8.1 Hz), 7.24—7.40 (3H, m), 7.47—7.60 (2H, m).

Diastereomeric Mixture of 2,3-Diethyl-4-phenylthio-4-butanolide (8h): Yield 60% (starting alkene (*E*)-**5**), 63% (starting alkene (*Z*)-**5**). IR (NaCl) 1780 cm^{-1} (C=O); MS m/z 250 (M^+). Found: C, 66.94; H, 7.48%. Calcd for $C_{14}H_{18}O_2S$: C, 67.20; H, 7.20%.

The ^{1}H NMR spectra of isolated (2*RS*, 3*RS*, 4*SR*)-**8h**, (2*RS*, 3*SR*, 4*RS*)-**8h**, (2*RS*, 3*SR*, 4*SR*)-**8h** are as follows:

(2*RS*, 3*RS*, 4*SR*)-8h: Oil. ^{1}H NMR ($CDCl_3$) δ=0.99 (3H, t, J=7.5 Hz), 1.05 (3H, t, J=7.5 Hz), 1.55 (2H, sex), 1.74 (2H, sex), 2.36—2.45 (1H, m), 2.66 (1H, q, J=7.5 Hz), 5.52 (1H, d, J=3.6 Hz), 7.32—7.37 (3H, m), 7.51—7.57 (2H, m).

(2*RS*, 3*SR*, 4*RS*)-8h: Oil. ^{1}H NMR ($CDCl_3$) δ=0.95 (3H, t, J=7.5 Hz), 1.04 (3H, t, J=7.5 Hz), 1.63—1.75 (4H, m), 2.11 (1H, sep), 2.32 (1H, dt, J=6.8, 8.7 Hz), 5.33 (1H, d, J=7.5 Hz), 7.31—7.36 (3H, m), 7.52—7.56 (2H, m).

(2*RS*, 3*SR*, 4*SR*)-8h: Oil. ^{1}H NMR ($CDCl_3$) δ=1.05 (3H, t, J=7.5 Hz), 1.14 (3H, t, J=7.5 Hz), 1.61—1.90 (4H, m), 2.04—2.40 (1H, m), 2.85 (1H, qu), 5.81 (1H, d, J=6.9 Hz), 7.30—7.37 (3H, m), 7.53—7.57 (2H, m).

The Reaction of Lithium Enolate of *trans*-8b with Methyl Iodide. To the solution of LDA, which was prepared from diisopropylamine (0.35 g, 3.5 mmol) and butyllithium (3.5 mmol), in 20 cm^3 of THF, a solution of **8b** (0.67 g, 3.0 mmol) in 5 cm^3 of THF was added at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 1 h and then a solution of methyl iodide (0.43 g, 3.0 mmol) in 5 cm^3 of THF was added to the mixture. The mixture was stirred at the same temperature for 3 h, and then was quenched with 10% hydrochloric acid. The mixture was extracted with ether and the ethereal layer was dried over magnesium sulfate. After removal of the ether, the residue was chromatographed on silica gel to give a diastereomeric mixture of **8g** by elution with benzene, 0.52 g (73%). The ratio of (2*RS*, 3*SR*, 4*RS*)-**8g** and (2*RS*, 3*RS*, 4*SR*)-**8g** was determained with HPLC, 16:84.

Preparation of Ethyl 2,3-Dimethyl-4-phenylsulfonylbutanoate (11e). To a solution of **6a** (0.54 g, 2.0 mmol) in 50 cm^3 dichlorometane, *m*-chloroperbenzoic acid (MCPBA) (0.35 g, 2.0 mmol) was added at 0 °C and the mixture was stirred at this temperature of 1 h, and for 10 h at room temperature. The reaction mixture was filtered. The filtrate was washed with sodium hydrogencarbonate solution and was dried over magnesium sulfate. After removal of the solvent, the residue was chromatographed on silica gel. From the eluate with benzene–ether (10:1), **11e** was obtained as an oil. Yield 93% (starting from (*E*)-**5**) and 87% (starting from (*Z*)-**5**). IR (NaCl) 1740 (C=O), 1150, 1310 cm^{-1} (SO_2); MS m/z 239 (M^+ − EtO).

Major Isomer (2*RS*, 3*RS*-11e): ^{1}H NMR ($CDCl_3$)

δ=1.08 (3H, d, J=7.5 Hz), 1.13 (3H, d, J=6.9 Hz), 1.21 (3H, t, J=7.5 Hz), 2.35—2.46 (1H, m), 2.55 (1H, dq, J=4.4, 7.1 Hz), 2.97 (1H, dd, J=8.6, 14.3 Hz), 3.36 (1H, dd, J=3.6, 14.1 Hz), 4.00—4.11 (2H, m), 7.54—7.69 (3H, m), 7.90—7.94 (2H, m).

Minor Isomer (2*RS*, 3*SR*-11e): ^{1}H NMR ($CDCl_3$) δ=1.07 (3H, d, J=6.9 Hz), 1.09 (3H, d, J=6.6 Hz), 1.23 (3H, t, J=7.5 Hz), 2.35—2.46 (1H, m), 2.60 (1H, dq, J=4.4, 6.6 Hz), 2.99 (1H, dd, J=8.3, 14.3 Hz), 3.21 (1H, dd, J=4.2, 14.4 Hz), 4.00—4.11 (2H, m), 7.54—7.69 (3H, m), 7.90—7.94 (2H, m).

Similarly, ethyl 2- methyl- 3- (phenylsulfonylmethyl)-pentanoate (**11g**) and ethyl 2-ethyl-3-(phenylsulfonylmethyl)pentanoate (**11h**) were prepared by the similar procedure to **11e**. Yields, spectral and analytical data of **11g** and **11h** are as follows:

11g: Yield 87% (starting from (*E*)-**5**) and 86% (starting from (*Z*)-**5**). IR (NaCl) 1730 (C=O), 1145, 1310 cm^{-1} (SO_2); MS m/z: 253 (M^+ − EtO).

Major Isomer (2*RS*, 3*RS*-11g): ^{1}H NMR ($CDCl_3$) δ=0.85 (3H, t, J=7.4 Hz), 1.02 (3H, d, J=6.9 Hz), 1.19 (3H, t, J=7.1 Hz), 1.40—1.66 (2H, m), 2.13—2.33 (1H, m), 2.77 (1H, dq, J=3.6, 6.9 Hz), 2.95 (1H, dd, J=6.9, 14.4 Hz), 3.36 (1H, dd, J=4.4, 14.3 Hz), 3.95—4.13 (2H, m), 7.53—7.68 (3H, m), 7.88—7.93 (2H, m).

Minor Isomer (2*RS*, 3*SR*-11g): ^{1}H NMR ($CDCl_3$) δ=0.82 (3H, t, J=7.5 Hz), 1.05 (3H, d, J=7.2 Hz), 1.22 (3H, t, J=8.1 Hz), 1.40—1.66 (2H, m), 2.13—2.33 (1H, m), 2.82 (1H, dq, J=4.5, 7.1 Hz), 3.02 (1H, dd, J=6.5, 14.3 Hz), 3.22 (1H, dd, J=5.1, 14.7 Hz), 3.95—4.13 (2H, m), 7.53—7.68 (3H, m), 7.88—7.93 (2H, m).

11h: Yield 95% (starting from (*E*)-**5**) and 87% (starting from (*Z*)-**5**). IR (NaCl) 1740 (C=O), 1150, 1310 cm^{-1} (SO_2); MS m/z 267 (M^+ − EtO).

Major Isomer (2*RS*, 3*RS*-11h): ^{1}H NMR ($CDCl_3$) δ=0.85 (3H, t, J=7.4 Hz), 0.86 (3H, t, J=7.4 Hz), 1.21 (3H, t, J=7.1 Hz), 1.33—1.44 (2H, m), 1.46—1.62 (2H, m), 2.11—2.17 (1H, m), 2.52 (1H, dt, J=4.4, 10.2 Hz), 2.96 (1H, dd, J=6.6, 14.7 Hz), 3.44 (1H, dd, J=5.1, 14.4 Hz), 3.99—4.10 (2H, m), 7.54—7.65 (3H, m), 7.89—7.92 (2H, m).

Minor Isomer (2*RS*, 3*SR*-11h): ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=7.4 Hz), 0.89 (3H, t, J=7.4 Hz), 1.22 (3H, t, J=6.9 Hz), 1.33—1.44 (2H, m), 1.46—1.62 (2H, m), 2.22—2.35 (1H, m), 2.99 (1H, dd, J=8.3, 14.9 Hz), 3.35 (1H, dd, J=2.4, 15.0 Hz), 2.53—2.57 (1H, m), 3.99—4.10 (2H, m), 7.54—7.65 (3H, m), 7.89—7.92 (2H, m).

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