Novel Synthesis of γ-Lactones Starting from β,γ-Unsaturated Carboxylic Esters

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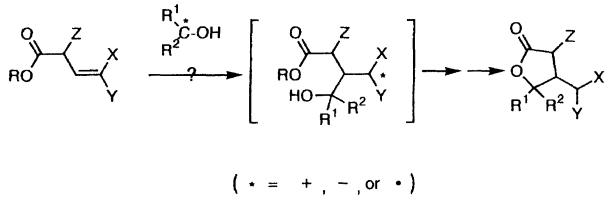
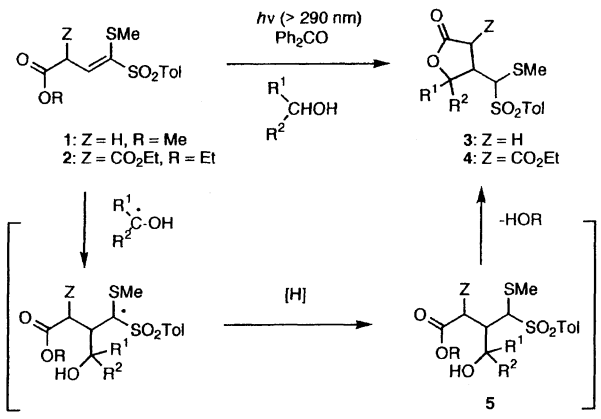
A novel synthetic route to highly substituted γ-lactones was achieved by an intermolecular radical addition to 4-(methylthio)-4-(*p*-tolylsulfonyl)-3-butenoic ester (**1**) and its 2-(ethoxycarbonyl) derivative (**2**), which were easily prepared from (methylthio)methyl *p*-tolyl sulfone. Upon the irradiation of a solution of **1** and benzophenone in an alcohol (R^1R^2CHOH), the 1-hydroxyalkyl radical ($R^1R^2\dot{C}$–OH) was generated and added regiospecifically to the 3-position of **1** to form an adduct that led to a γ-lactone by spontaneous intramolecular condensation. Similarly, **2** reacted with the alcohol to give α-(ethoxycarbonyl)-γ-lactones. The alcohol, which is a high boiling liquid or solid, can be employed in the form of a solution (10 molar amounts in acetonitrile) without greatly lowering the reaction efficiency.

Substituted γ-lactones are versatile precursors for preparing many kinds of organic molecules.[1] In addition, they are frequently found in a large variety of natural products, and their α-methylene derivatives are currently receiving considerable attention due to their potent biological activities.[2] Thus, many methods have been developed for constructing the γ-lactones skeleton. During our survey of these methods, no literature was found on a synthetic route of Scheme 1, starting from β,γ-unsaturated carboxylic esters, which requires the addition of the 1-hydroxyalkyl moiety.[3] In order to accomplish this synthetic route, there are two problems to be solved: (i) What kind of 1-hydroxyalkyl moiety is used? (ii) How is its regiospecific attack on the β-position attained? In this manuscript, we wish to describe the realization of this novel route by a radical reaction, i.e., the addition of a neutral 1-hydroxyalkyl radical ($R^1R^2\dot{C}$–OH) to β,γ-unsaturated carboxylic esters (**1**) that have methylthio and *p*-tolysulfonyl groups at the γ-position. As is well known,[4] the 2-(methylthio)-2-(*p*-tolylsulfonyl)ethenyl group of **1** has such a high acceptability for the 1-hydroxyalkyl radicals as to accomplish the regiospecificity and efficiency of the radical attack. Since the 1-hydroxyalkyl radical can approach the sterically hindered position in analogy with the usual radical reactions, we applied the present method to a synthetic route leading an α-(ethoxycarbonyl) derivative (**2**) of **1** to an α-(ethoxycarbonyl)-γ-lactone (**4**) (Scheme 2). The lactone (**4**) seems to be a synthetic precursor of the α-methylene-γ-lactone (vide infra). It should be noted that the present route contributes to the preparation of various γ-lactones because the dithioacetal *S*,*S*-dioxide functionality can be transformed optionally to such useful functionalities as acyl, formyl, (methylthio)carbonyl, and alkoxycarbonyl groups.[5]



Scheme 1.



Scheme 2.

Results and Discussion

Formation of α-Unsubstituted γ-Lactones (3). The 1-hydroxyalkyl radical ($R^1R^2\dot{C}$–OH) was generated by the α-hydrogen abstraction of an alcohol (R^1R^2CHOH) with excited benzophenone (triplet) in the same way as described in our previous papers.[4a,4d] Thus, a solution of **1** (1.00 mmol) and benzophenone (1.0 molar amount to **1**) in 2-propanol (70 ml) was irradiated with a 100-W high-pressure Hg arc lamp (Pyrex filter) for 4 h. Evaporation and column chromatography on silica gel gave a γ-lactone (**3a** in Table 1) in 77% yield, which consisted of two diastereomers in the ratio of 70 : 30. The IR spectrum of **3a** showed no absorption in the region of HO stretching, but a strong absorption appeared at 1765 cm^{-1} and 1780 (shoulder) cm^{-1}, indicating the presence of a γ-lactone ring. The ^1H NMR and elemental analysis of **3a** were in complete coincidence with those of the give structure. The formation of **3a** is rationalized in terms of the addition of the 1-hydroxy-1-methylethyl radical to **1** to afford an adduct (**5a**; $R^1=R^2=Me$) and subsequent intramolecular lactonization (Scheme 2).

When methanol, ethanol, and 2-methyl-1-propanol were employed instead of 2-propanol, the corresponding γ-lactones (**3b**—**d**) were obtained in high yields, as summarized in Table 1. The stereochemical relationship between the β- and γ-positions in **3c** and **3d** was determined after conversion to the (*p*-tolylsulfonyl)methyl derivatives (**6c** and **6d**, respectively) by reductive desulfurization with Raney-Ni (W2). In the ^1H NMR spectrum, the major isomers of **6c** and **6d** exhibited large differential NOE (Fig. 1)[6] between Hβ and Hγ, showing the stereochemistry of the major isomers to be cis and the trans : cis ratio of **6c** and **6d** to be 36 : 64 and 35 : 65, respectively.

The starting material, methyl 4-(methylthio)-4-(*p*-tolylsulfonyl)-3-butenoate (**1**), was prepared by a successive treatment of methyl acrylate with a lithio derivative of (methylthio)methyl *p*-tolyl sulfone (**7**) to afford a Michael-type adduct (**8**),[7] chlorination of **8** with SO_2Cl_2, and dehydrochlorination of the chlorinated product (**9**) in refluxing toluene (Scheme 3).

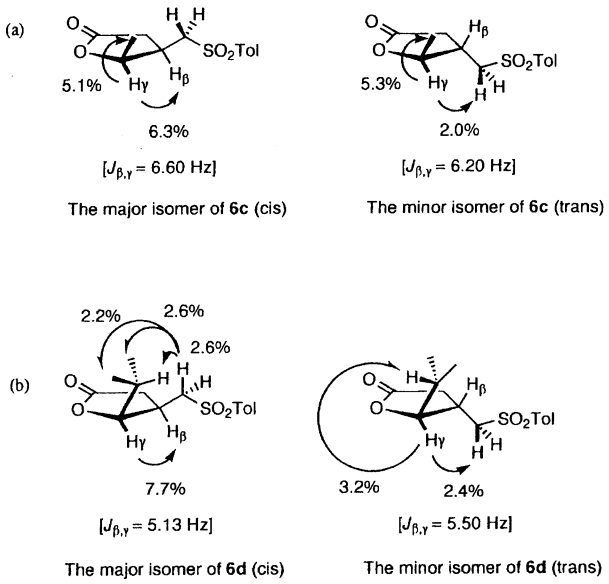
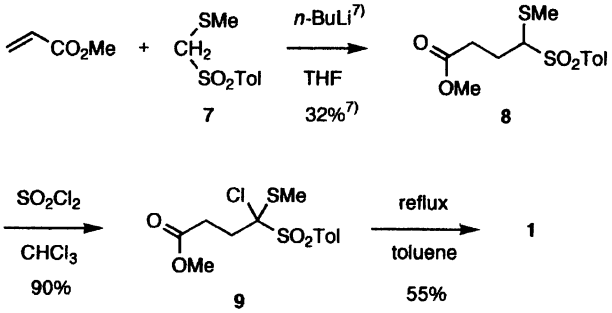
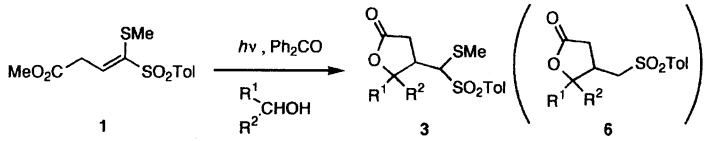


Fig. 1. The differential NOE. (a) **6c**. (b) **6d**.



Scheme 3.

Table 1. Formation of γ-Lactones (**3**) from **1**[a]



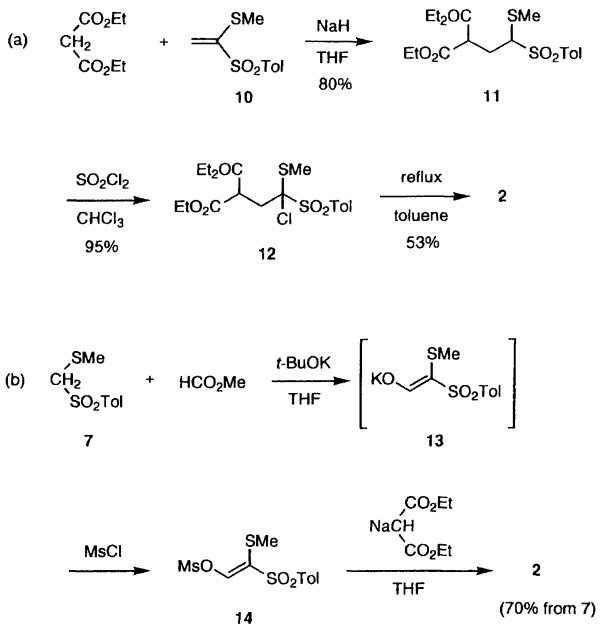
Entry	Alcohol	γ-Lactones (**3**)	R^1	R^2	Yield/%	Diastereomeric ratio
1	$(CH_3)_2CHOH$	**3a**	Me	Me	77	70 : 30
2	CH_3OH	**3b**	H	H	86	54 : 46
3	CH_3CH_2OH	**3c**	Me	H	79	38 : 24 : 22 : 16[b]
4	$(CH_3)_2CHCH_2OH$	**3d**	*i*-Pr	H	81	35 : 26 : 23 : 16[c]

a) A solution of **1** (0.57—1.00 mmol) and benzophenone (1.0 mol. amt. to **1**) in an alcohol (70 ml) was irradiated with a 100-W high-pressure Hg arc lamp. b) Reduction with Raney-Ni afforded **6c** (trans : cis=36 : 64) in 86% yield. c) Reduction with Raney-Ni afforded **6d** (trans : cis=35 : 65) in 93% yield.

Formation of α-(Ethoxycarbonyl)-Substituted γ-Lactones (4). α-Methylene-γ-lactones are frequently derived from the ester and potassium salt of the corresponding α-carboxylated γ-lactones.[8] The derivation is achieved by decarboxylative methylenation via the Mannich reaction.[8c,8e,8h,8i] Therefore α-(ethoxycarbonyl)-substituted γ-lactones (**4**) were thought to be useful precursors for the synthesis of α-methylene-γ-lactones; we investigated the route starting from an α-(ethoxycarbonyl)-substituted β,γ-unsaturated carboxylic ester (**2**). The starting material (**2**) was obtained by a Michael addition of diethyl malonate to 1-(methylthio)-1-(*p*-tolylsulfonyl)ethane (**10**)[9] using NaH as a base in THF, chlorination of the thus obtained adduct (**11**) with SO_2Cl_2, and subsequent dehydrochlorination. We also developed a convenient preparative method of **2**: Treatment of **7** with methyl formate and potassium *t*-butoxide in THF formed an enolate (**13**).[10] Without purification, **13** was mesylated with methanesulfonyl chloride (MsCl) in THF to give **14** as a colorless solid. The addition of a THF solution of **14** to a solution of diethyl sodiomalonate produced **2** in an overall yield of 70% from **7**, as shown in Scheme 4.

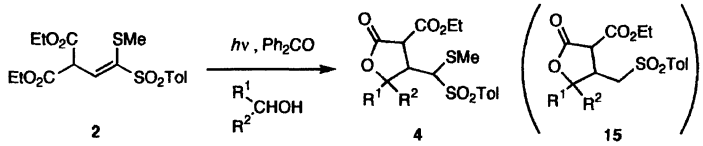
Due to the sterically crowded β-position of **2**, we had wondered if the radical addition occurs efficiently or not. However, we were surprised that the addition of the 1-hydroxyalkyl radical ($R^1R^2\dot{C}$–OH) to **2** proceeded with almost the same efficiency as that to **1**. Under similar conditions to those mentioned in the reaction of **1**, the 1-hydroxyalkyl radicals added to **2** and the corresponding α-(ethoxycarbonyl)-γ-lactones (**4**) were produced in high yields. Table 2 summarizes the results. In the case of R^1=R^2, the addition products (**4a** and **4b**) were subjected to reductive desulfurization wit Raney Ni to give β-[(*p*-tolylsulfonyl)methyl] derivatives (**15a** and **15b**). The trans : cis ratios of **15a** and **15b** were determined by ^{1}H NMR to be 87 : 13. The structure of the major isomer of **15a** was confirmed by X-ray crystallography.[11] Figure 2 exhibits an ORTEP view and the crystallographic data, are listed in Table 3.

The radical additions to **2** mentioned so far were performed by using the alcohol as a solvent. When the alcohol was a high boiling-point liquid or solid, some difficulties were encountered in carrying out the reaction and the workup. Here, it is worth noting that, when the alcohol is diluted with an inert solvent, the efficiency remains so high as to put the reaction to practical use. Thus, irradiation of a solution of **2** and 1-butanol (10 molar amounts to **2**) in acetonitrile or benzene gave the desired **4d** in 53 or 56% yield, respectively. In a simi-



Scheme 4.

Table 2. Formation of γ-Lactones (**4**) from **2**



Entry	Alcohol	γ-Lactones (**4**)	R^1	R^2	Yield/%	Diastereomeric ratio
1	$(CH_3)_2CHOH$	**4a**	Me	Me	77	47 : 33 : 16 : 4[a]
2	CH_3OH	**4b**	H	H	87	61 : 34 : 5 : <1[b]
3	CH_3CH_2OH	**4c**	Me	H	91	25 : 24 : 22 : 11 : 8 : 3 : 3 : 3
4	$CH_3(CH_2)_3OH$	**4d**	*n*-Pr	H	81[c]	23 : 17 : 16 : 13 : 11 : 10 : 6 : 4
5	$CH_3(CH_2)_5OH$[d]	**4e**	*n*-Pen	H	49	26 : 21 : 12 : 12 : 9 : 8 : 7 : 5
6	$CH_3(CH_2)_{13}OH$[d]	**4f**	*n*-$C_{13}H_{27}$	H	47	26 : 22 : 21 : 17 : 14[e]

a) Reduction with Raney-Ni afforded **15a** (trans : cis=87 : 13) in 60% yield. b) Reduction with Raney-Ni afforded **15b** (trans : cis=87 : 13) in 67% yield. c) Irradiation of a solution of **2** and 1-butanol (10 mol. amt. to **2**) in CH_3CN or benzene afforded **4d** in 53% or 56% yield, respectively. d) Irradiation of a solution of **2** and an alcohol (10 mol. amt.) in CH_3CN. e) The other minor isomers could not be observed in ^{1}H NMR spectrum of **4f**.

Table 3. Crystallographic Data of the Major Isomer of **15a** (trans)

	trans-**15a**
Chemical formula	$(C_{17}H_{22}O_6S)_2 \cdot (C_6H_{14})_{0.5}$
Formula weight	751.94
Crystal system	Triclinic
Space group	*P*-1 (No. 2)
a/Å	10.934(4)
b/Å	12.092(3)
c/Å	15.804(4)
α/°	10.934(4)
β/°	12.092(3)
γ/°	15.804(4)
V/Å^3	2004(1)
Z	2
D_{calcd}/g cm^{-3}	1.250
Diffractometer	Mac Sicence MXC18
Radiation	Mo $K\alpha$ (λ=0.71073 Å)
Monochrometer	Graphite
T/K	223
Computer program; Structure solution	Crystan GM;[a] *Sir* 92[b]
No. of measured reflections	4837
No. of unique reflections	4488
No. of observations[c]	2542
No. of variables	574
Refinement	Full-matrix
Absorption correction	refdelf
R; R_w	0.0875; 0.0753

a) See Ref. 12. b)Direct method, see Ref. 13. c) $I>3.00\ \sigma\ (I)$.

lar reaction of **2** in acetonitrile involving 1-hexanol (10 molar amounts to **2**) or solid 1-tetradecanol (10 molar amounts to **2**), the corresponding **4** were afforded in 49 and 47 % yields, respectively (Table 2; Entries 5 and 6).

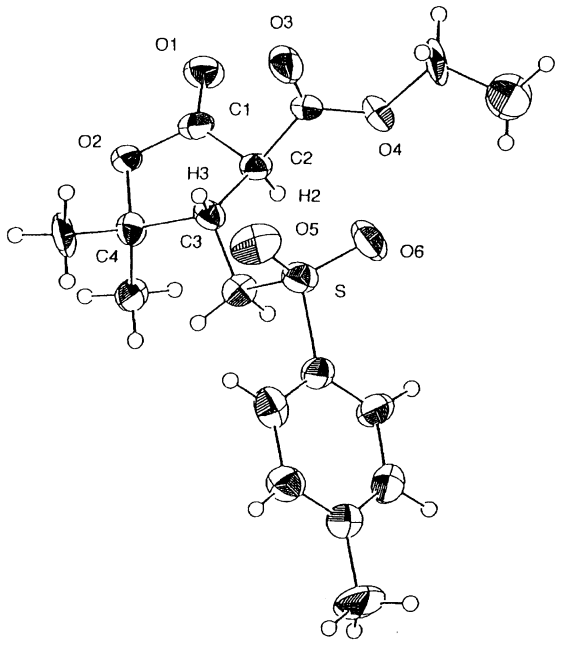
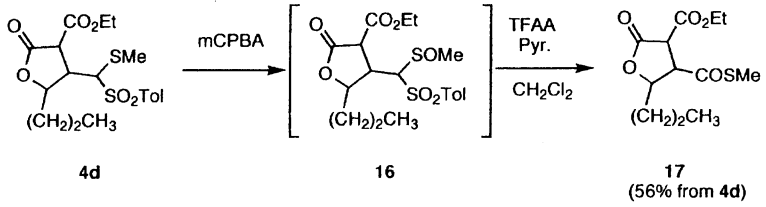


Fig. 2. ORTEP drawing of X-ray structure of the major isomer of **15a**. One molecule of **15a** was shown in the diagram for clarity.

Finally, we describe the transformation of the dithioacetal *S*, *S*-dioxide functionality into a (methylthio)carbonyl group. Upon the oxidation of **4d** (a mixture of eight diastereomers) with mCPBA to give an *S*, *S*, *S'*-trioxide (**16**) and a subsequent Pummerers's rearrangement with TFAA-pyridine, the desired thiol ester (**17**) was obtained in a 56% overall yield from **4d** (Scheme 5). It should be noted that the thiol ester (**17**) consisted mainly of two diastereomers (*tt*-**17**:*tc*-**17**= 55:45). Their stereochemical structures were established by both NOE experimental and the coupling constants in ^{1}H NMR, which are summarized in Fig. 3. From these facts, it is apparent that isomerization occurred during the present transformation to decrease the number of formed diastereomers to be two.

Conclusion

We have developed a novel synthetic route to γ-lactones based on the intermolecular additions of 1-hydroxyalkyl radicals to 4-(methylthio)-4-(*p*-tolylsulfonyl)-3-butenoic ester (**1**) and its 2-(ethoxycarbonyl) derivative (**2**), which were easily prepared from (methylthio)methyl *p*-tolyl sulfone (**7**). The present radical addition proceeded smoothly under mild conditions to afford highly substituted γ-lactones (**3** and **4**) that might be synthetic precursors for various types of γ-lactones, including α-methylene-γ-lactones.



4d 16 17 (56% from 4d)

Scheme 5.

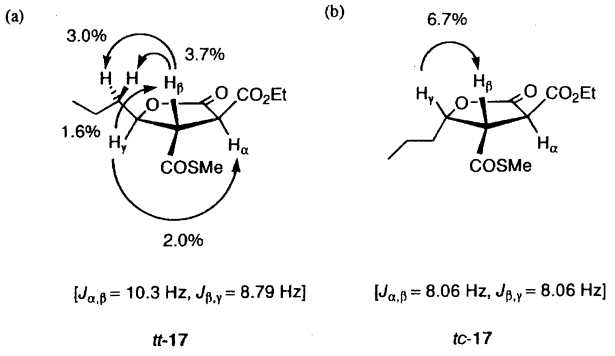


Fig. 3. The differential NOE. (a) *tt*-**17**. (b) *tc*-**17**.

Experimental

General Procedures. The melting points were determined on a hot-stage microscope apparatus (Yanagimoto) and are uncorrected. Infrared spectra were determined with a JASCO A-200, and the data are presented in cm^{-1} for important diagnostic absorptions. ^1H NMR spectra were obtained on JEOL JNM-FX 270 (270 MHz), JEOL JNM-GSX 400 (400 MHz), and JEOL JNM-GSX 500 (500 MHz) spectrometers. The chemical shifts are reported in ppm down field from tetramethylsilane as the internal standard (δ scale). Microanalytical data were provided by the Analysis Center of Chiba University. The materials employed herein were obtained from commercial suppliers (Aldrich Chemical Co., Tokyo Kasei Chemical Industry Co., Wako Pure Chemical Co., Kanto Chemical Co., and Nacalai Tesque, Inc.). THF was dried over metallic Na using the ketyl radical of benzophenone as an indicator. Other solvents were used after being purified by distillation and being dried over molecular sieves (3—4 Å). (Methylthio)methyl *p*-tolyl sulfone (**7**) was supplied from Nissan Chemical Industry Co.

Photochemical Addition of 2-Propanol to Methyl 4-(Methylthio)-4-(*p*-tolylsulfonyl)-3-butenoate (1). A Typical Procedure. A solution of **1** (182 mg, 0.61 mmol) and benzophenone (105 mg, 0.57 mmol) in 2-propanol (70 ml) was irradiated with a 100-W high-pressure Hg arc lamp (Sigemi Standard) with a water-cooled Pyrex jacket under bubbling N_2 for 2 h. Evaporation of the solvent followed by chromatography on silica gel (eluent: hexane–ethyl acetate, 3:1) gave a diastereomeric mixture (A:B=70:30) of 4-methyl-3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-pentanolide (**3a**) (153 mg, 77% yield) as colorless crystals: IR (KBr) 1780(shoulder), 1765, 1296, 1258, 1202, 1122 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ=7.86 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 3.74 (d, 1H, J=1.32 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.01 (ddd, 1H, J=1.32, 7.81 and 8.80 Hz, C*H*CH$_2$CO$_2$), 2.49 (s, 3H, ArCH$_3$), 2.40 (dd, 1H, J=7.81 and 13.3 Hz, CH$_2$CO$_2$), 2.33 (dd, 1H, J=8.80 and 13.3 Hz, CH$_2$CO$_2$), 2.18 (s, 3H, SCH$_3$), 1.47 (s, 3H, (CH$_3$)$_2$C), 1.44 (s, 3H, (CH$_3$)$_2$C); ^1H NMR of isomer B: δ=7.85 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 3.62 (d, 1H, J=11.5 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.01 (ddd, 1H, J=3.33, 11.0, and 11.5 Hz, C*H*CH$_2$CO$_2$), 2.94 (dd, 1H, J=11.0 and 18.1 Hz, CH$_2$CO$_2$), 2.59 (dd, 1H, J=3.33 and 18.1 Hz, CH$_2$CO$_2$), 2.49 (s, 3H, ArCH$_3$), 2.07 (s, 3H, SCH$_3$), 1.59 (s, 3H, (CH$_3$)$_2$C), 1.41 (s, 3H, (CH$_3$)$_2$C). Recrystallization from hexane–$CHCl_3$ afforded colorless crystals (mp 150.0—152.0 °C) which were subjected to elemental analysis. Found: C, 54.91; H, 6.20%. Calcd for $C_{15}H_{20}O_4S_2$: C, 54.85; H, 6.14%.

Similar irradiation of a solution of **1** (317 mg, 1.06 mmol) and benzophenone (192 mg, 1.06 mmol) in methanol (70 ml) for 2 h afforded a diastereomeric mixture (A:B=54:46) of 3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-butanolide (**3b**) (273 mg, 86% yield) as colorless crystals: IR (KBr) 1778, 1768(shoulder), 1283, 1178, 1135, 1080, 1042 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ=7.84 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 4.45 (dd, 1H, J=8.24 and 9.89 Hz, CH$_2$OCO), 4.11 (dd, 1H, J=8.57 and 10.2 Hz, CH$_2$OCO), 3.75 (d, 1H, J=6.26 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.36—3.16 (m, 1H, C*H*CH$_2$CO$_2$), 2.58 (dd, 1H, J=8.90 and 17.8 Hz, CH$_2$CO$_2$), 2.49 (s, 3H, ArCH$_3$), 2.46 (dd, 1H, J=9.89 and 18.1 Hz, CH$_2$CO$_2$), 2.15 (s, 3H, SCH$_3$); ^1H NMR of isomer B: δ=7.84 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 4.65 (dd, 1H, J=8.24 and 9.55 Hz, CH$_2$OCO), 4.33 (dd, 1H, J=8.24 and 9.56 Hz, CH$_2$OCO), 3.73 (d, 1H, J=6.59 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.36—3.16 (m, 1H, C*H*CH$_2$CO$_2$), 2.81 (dd, 1H, J=8.57 and 17.8 Hz, CH$_2$CO$_2$), 2.72 (dd, 1H, J=9.56 and 17.8 Hz, CH$_2$CO$_2$), 2.49 (s, 3H, ArCH$_3$), 2.08 (s, 3H, SCH$_3$). Recrystallization from hexane–CH_2Cl_2 afforded colorless crystals (mp 148.0—159.5 °C) which were subjected to an elemental analysis. Found: C, 51.70; H, 5.36%. Calcd for $C_{13}H_{16}O_4S_2$: C, 51.98; H, 5.37%.

In a similar manner, a solution of **1** (172 mg, 0.57 mmol) and benzophenone (211.6 mg, 1.16 mmol) in ethanol (70 ml) for 3 h was irradiated and a diastereomeric mixture (A:B:C:D=38:24:22:16) of 3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-pentanolide (**3c**) (142 mg, 79% yield) was given as colorless crystals: Mp 136.0—142.0 °C (hexane–$CHCl_3$); IR (KBr) 2860, 1775, 1760(shoulder), 1280, 1174, 1140, 1120 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ=7.84 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 4.99 (quintet, 1H, J=6.60 Hz, C*H*OCO), 3.79 (d, 1H, J=6.59 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.29 (*tt*-like, 1H, J=6.59 and 8.24 Hz, C*H*CH$_2$CO$_2$), 2.92—2.30 (m, 2H, CH$_2$CO$_2$), 2.49 (s, 3H, ArCH$_3$), 2.20 (s, 3H, SCH$_3$), 1.50 (d, 3H, J=6.60 Hz, CH$_3$CHOCO); ^1H NMR of isomer B: δ=7.86 (d, 2H, J=8.24 Hz, Ar*H*), 4.82

(quintet, 1H, J=6.59 Hz, C*H*OCO), 3.60 (d, 1H, J=10.6 Hz, C*H*(SCH$_3$)SO$_2$Tol), 2.89—2.75 (m, 3H, C*H*CH$_2$CO$_2$), 2.49 (s, 3H, ArC*H*$_3$), 2.14 (s, 3H, SC*H*$_3$), 1.35 (d, 3H, J=6.80 Hz, C*H*$_3$CHOCO); ^{1}H NMR of isomer C: δ=4.74 (dq, 1H, J=3.96 and 6.27 Hz, C*H*OCO), 3.65 (d, 1H, J=4.29 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.04—2.90 (m, 1H, C*H*CH$_2$CO$_2$), 2.74—2.37 (m, 2H, C*H*$_2$CO$_2$), 2.05 (s, 3H, SC*H*$_3$), 1.47 (d, 3H, J=6.27 Hz, C*H*$_3$CHOCO); ^{1}H NMR of isomer D: δ=4.61 (dq, 1H, J=3.10 and 6.57 Hz, C*H*OCO), 3.70 (d, 1H, J=1.64 Hz, C*H*(SCH$_3$)SO$_2$Tol), 2.92—2.30 (m, 2H, C*H*$_2$CO$_2$), 2.12 (s, 3H, SC*H*$_3$), 1.45 (d, 3H, J=6.27 Hz, C*H*$_3$CHOCO). The diastereomeric mixture was subjected to elemental analysis. Found: C, 53.27; H, 5.72%. Calcd for $C_{14}H_{18}O_4S_2$: C, 53.48; H, 5.77%.

Similarly, a solution of **1** (240 mg, 0.80 mmol) and benzophenone (146 mg, 0.80 mmol) in 2-methyl-1-propanol (70 ml) was irradiated for 2 h to afford a diastereomeric mixture (A : B : C: D=35 : 26 : 23 : 16) of 5-methyl-3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-hexanolide (**3d**) (223 mg, 81% yield) as a colorless viscous oil: IR (neat) 2970, 1785, 1300, 1143, 1083, 1038 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) of isomer A: δ=7.82 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 4.57 (dd, 1H, J=2.97 and 3.96 Hz, C*H*OCO), 3.61 (d, 1H, J=4.28 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.30—3.20 (m, 1H, C*H*CH$_2$CO$_2$), 2.90 (dd, 1H, J=10.2 and 18.1 Hz, C*H*$_2$CO$_2$), 2.52 (dd, 1H, J=3.29 and 18.1 Hz, C*H*$_2$CO$_2$), 2.48 (s, 3H, ArC*H*$_3$), 2.10—1.90 (m, 1H, (CH$_3$)$_2$C*H*), 1.82 (s, 3H, SC*H*$_3$), 1.04 (d, 3H, J=6.92 Hz, (C*H*$_3$)$_2$CH), 0.94 (d, 3H, J=6.93 Hz, (C*H*$_3$)$_2$CH); ^{1}H NMR of isomer B: δ=7.85 (d, 2H, J=8.24 Hz, Ar*H*), 7.39 (d, 2H, J=7.91 Hz, Ar*H*), 4.12 (dd, 1H, J=5.93 and 9.45 Hz, C*H*OCO), 3.86 (d, 1H, J=1.98 Hz, C*H*(SCH$_3$)SO$_2$Tol), 3.50—3.40 (m, 1H, C*H*CH$_2$CO$_2$), 2.60—2.20 (m, 2H, C*H*$_2$CO$_2$), 2.48 (s, 3H, ArC*H*$_3$), 2.15 (s, 3H, SC*H*$_3$), 2.00—1.80 (m, 1H, (CH$_3$)$_2$C*H*), 1.14 (d, 3H, J=6.60 Hz, (C*H*$_3$)$_2$CH), 0.98 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH); ^{1}H NMR of isomer C: δ=7.86 (d, 2H, J=8.24 Hz, Ar*H*), 4.22 (*t*-like, 1H, J=5.93 Hz, C*H*OCO), 3.67 (d, 1H, J=2.63 Hz, C*H*(SCH$_3$)SO$_2$Tol), 2.90—2.80 (m, 1H, C*H*CH$_2$CO$_2$), 2.60—2.20 (m, 2H, C*H*$_2$CO$_2$), 2.48 (s, 3H, ArC*H*$_3$), 2.13 (s, 3H, SC*H*$_3$) 2.00—1.80 (m, 1H, (CH$_3$)$_2$C*H*), 1.09 (d, 3H, J=6.92 Hz, (C*H*$_3$)$_2$CH), 0.98 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH); ^{1}H NMR of isomer D: δ=4.55 (*d*-like, 1H, J=5.93 Hz, C*H*OCO), 3.69 (d, 1H, J=3.30 Hz, C*H*(SCH$_3$)-SO$_2$)Tol), 3.21—3.10 (m, 1H, C*H*CH$_2$CO$_2$), 2.60—2.20 (m, 2H, C*H*$_2$CO$_2$), 2.48 (s, 3H, ArC*H*$_3$), 2.14 (s, 3H, SC*H*$_3$), 2.00—1.80 (m, 1H, (CH$_3$)$_2$C*H*), 0.98 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH), 0.965 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH). The diastereomeric mixture was subjected to elemental analysis. Found: C, 55.92; H, 6.36%. Calcd for $C_{16}H_{22}O_4S_2$: C, 56.11; H, 6.47%.

Desulfurization of 3c by Raney-Ni (W2). To a solution of **3c** (20.1 mg, 0.64 mmol) in ethanol (1.5 ml) was added Raney-Ni (W2) (1.0 cm^3); the mixture was stirred at room temperature for 1 h. After insoluble solid was filtered off through Celite, the filtrate was concentrated in vacuo and purified by column chromatography on silica gel (eluent: ethyl acetate) to afford a diastereomeric mixture (trans : cis=36 : 64) of 3-[(*p*-tolylsulfonyl)methyl]-4-pentanolide (**6c**) (14.7 mg, 86% yield) as colorless solid. These diastereomers were separated by a recycling preparative HPLC equipped with D-SIL-5-06-B YMC-packed column (ϕ 60×250 mm)(eluent: hexane–ethyl acetate, 3 : 2; flow rate: 9.00 ml min^{-1}).

***cis*-6c (A More Polar Isomer):** Colorless crystals; mp 109.5—111.0 °C (hexane–CH$_2$Cl$_2$); IR (KBr) 1776, 1758, 1593, 1302, 1175, 1130 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ=7.80 (d, 2H, J=8.43 Hz, Ar*H*), 7.41 (d, 2H, J=8.06 Hz, Ar*H*), 4.82 (quintet, 1H, J=6.59 Hz, C*H*OCO), 3.25—3.20 (m, 1H, C*H*$_2$SO$_2$Tol), 3.18—3.04 (m, 2H, C*H*C*H*$_2$SO$_2$Tol), 2.67 (dd, 1H, J=7.70 and 17.6 Hz, C*H*$_2$O), 2.53 (dd, 1H, J=8.98 and 17.6 Hz, C*H*$_2$CO), 2.48 (s, 3H, ArC*H*$_3$), 1.29 (d, 3H, J=6.59 Hz, C*H*$_3$CHO); The observed differential NOE: C4-*H* to C3-*H*, 6.3%; C4-*H* to 5-C*H*$_3$, 5.1%; C4-*H* to TolSO$_2$C*H*$_2$(a), 1.2%; C2-*H*(a) to C3-H, 4.7%; C2-*H*(b) to C3-*H*, 1.9%. Found: C, 58.48%; H, 5.98%. Calcd for $C_{13}H_{16}O_4S$: C, 58.19; H, 6.01%.

***trans*-6c (A Less Polar Isomer):** Colorless crystals; mp 114.5—115.5 °C (hexane–CH$_2$Cl$_2$); IR (KBr) 1775(shoulder), 1763, 1290, 1180, 1150, 1038 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ=7.79 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.88 Hz, Ar*H*), 4.35 (quintet, 1H, J=6.23 Hz, C*H*OCO), 3.24 (dd, 1H, J=4.76 and 13.9 Hz, C*H*$_2$SO$_2$Tol), 3.10 (dd, 1H, J=8.98 and 13.9 Hz, C*H*$_2$SO$_2$Tol), 2.84 (dd, 1H, J=8.61 and 17.8 Hz, C*H*$_2$CO$_2$), 2.65—2.60 (m, 1H, C*H*CH$_2$SO$_2$Tol), 2.48 (s, 3H, ArC*H*$_3$), 2.40 (dd, 1H, J=8.61 and 17.8 Hz, C*H*$_2$CO$_2$), 1.43 (d, 3H, J=6.23 Hz, C*H*$_3$CHOCO); The observed differential NOE: C4-*H* to 5-C*H*$_3$, 5.3%; C4-*H* to TolSO$_2$C*H*$_2$(a), 2.0%. Found: C, 57.86; H, 5.92%. Calcd for $C_{13}H_{16}O_4S$: C, 58.19; H, 6.01%.

Similar reductive desulfurization of **3d** (489 mg, 1.43 mmol) afforded a diastereomeric mixture (trans : cis=35 : 65) of **6d** (396 mg, 93% yield) as colorless crystals. These isomers were separated by a recycling preparative HPLC (column: D-SIL-5-06-B YMC; eluent: hexane–ethyl acetate, 2 : 1).

***cis*-6d (A More Polar Isomer):** Colorless crystals; mp 116.0—118.0 °C (hexane–CH$_2$Cl$_2$); IR (KBr) 1771, 1755, 1290, 1180, 1140, 984 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ=7.79 (d, 2H, J=8.06 Hz, Ar*H*), 7.40 (d, 2H, J=8.06 Hz, Ar*H*), 4.07 (dd, 1H, J=5.13 and 9.15 Hz, C*H*OCO), 3.19 (*d*-like, 1H, J=13.2 Hz, C*H*$_2$SO$_2$Tol), 3.10—3.00 (m, 1H, C*H*CH$_2$CO$_2$Et), 2.99 (*d*-like, 1H, J=13.2 Hz, C*H*$_2$SO$_2$Tol), 2.84 (dd, 1H, J=2.56 and 17.6 Hz, C*H*$_2$CO$_2$), 2.71 (dd, 1H, J=7.33 and 17.9 Hz, C*H*$_2$CO$_2$), 2.47 (s, 3H, ArC*H*$_3$), 1.77—1.72 (m, 1H, (CH$_3$)$_2$C*H*), 1.05 (d, 3H, J=6.60 Hz, (C*H*$_3$)$_2$CH), 0.86 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH); the observed differential NOE: C4-*H* to C3-*H*, 7.7%; C4-*H* to C5-*H*, 2.6%; C4-*H* to 6-C*H*$_3$(a), 2.6%; C4-*H* to 6-C*H*$_3$(b), 2.2%; TolSO$_2$C*H*$_2$(c) to C5-*H*, 1.9%; TolSO$_2$C*H*$_2$(c) to C3-*H*, 4.0%; TolSO$_2$C*H*$_2$(c) to C4-*H*, 2.6%. Found: C, 60.76; H, 6.74%. Calcd for $C_{15}H_{20}O_4S$: C, 60.79%; H, 6.80%.

***trans*-6d (A Less Polar Isomer):** Colorless crystals; mp 109.0—109.5 °C (hexane–CH$_2$Cl$_2$); IR (KBr) 1769, 1762, 1595, 1290, 1169, 1140 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ=7.79 (d, 2H, J=8.10 Hz, Ar*H*), 7.40 (d, 2H, J=8.06 Hz, Ar*H*), 4.06 (*t*-like, 1H, J=5.50 Hz, C*H*OCO), 3.24 (dd, 1H, J=4.40 and 13.9 Hz, C*H*$_2$SO$_2$Tol), 3.12 (dd, 1H, J=8.79 and 13.9 Hz, C*H*$_2$SO$_2$Tol), 2.85—2.79 (m, 1H, C*H*CH$_2$CO$_2$), 2.83 (dd, 1H, J=11.1 and 21.3 Hz, C*H*$_2$CO$_2$), 2.48 (s, 3H, ArC*H*$_3$), 2.42 (dd, 1H, J=10.6 and 21.3 Hz, C*H*$_2$CO$_2$), 1.90—1.85 (m, 1H, (CH$_3$)$_2$C*H*), 0.99 (d, 3H, J=6.96 Hz, (C*H*$_3$)$_2$CH), 0.95 (d, 3H, J=6.59 Hz, (C*H*$_3$)$_2$CH); the observed differential NOE: C4-*H* to C5-*H*, 3.2%; C4-*H* to 6-C*H*$_3$(a), 1.8%; C4-*H* to 6-C*H*$_3$(b), 1.4%; TolSO$_2$C*H*$_2$(c) to

C2-*H*(d), 3.6%; C4-*H* to $TolSO_2CH_2$(c), 2.4%. Found: C, 60.58; H, 6.60%. Calcd for $C_{15}H_{20}O_4S$: C, 60.79; H, 6.80%.

Preparation of Methyl 4-(Methylthio)-4-(*p*-tolylsulfonyl)-3-butenoate (1). To a solution of methyl 4-(methylthio)-4-(*p*-tolylsulfonyl)butenoate (**8**)[7] (1.01 g, 3.34 mmol) in $CHCl_3$ (17 ml), was dropwise added sulfuryl chloride (0.30 ml, 3.73 mmol) at 0 °C; then the mixture was stirred at the same temperature for 3 h. After evaporation of solvent, the residue was diluted with CH_2Cl_2 (10 ml), the organic layer was washed with brine (10 ml), dried ($MgSO_4$), and concentrated in vacuo. Purification by column chromatography on silica gel (hexane–ethyl acetate, 4:1) afford methyl 4-chloro-4-(methylthio)-4-(*p*-tolylsulfonyl)butanoate (**9**) (1.01 g, 90% yield) as a colorless oil: IR (neat) 1708, 1596, 1436, 1326, 1304, 1146 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ=7.88 (d, 2H, J=8.24 Hz, Ar*H*), 7.37 (d, 2H, J=7.91 Hz, Ar*H*), 3.68 (s, 3H, CO_2CH_3), 2.78—2.49 (m, 4H, $(CH_2)_2$), 2.47 (s, 3H, $ArCH_3$), 2.46 (s, 3H, SCH_3). Found: C, 46.34; H, 5.28%. Calcd for $C_{13}H_{17}ClO_4S_2$: C, 46.35; H, 5.09%.

A solution of **9** (375 mg, 1.11 mmol) in toluene (5.5 ml) was refluxed under an N_2 atmosphere for 42 h. The reaction mixture was washed with brine, dried ($MgSO_4$), and concentrated to give a dark-brown oil (361 mg), which was purified by column chromatography on silica gel (hexane–ethyl acetate, 5:1) to afford **1** (182 mg, 55% yield) as a colorless oil, which was shown by ^1H NMR to consist of two geometric isomers (E:Z=79:21): IR (neat) 1740, 1724, 1314, 1282, 1144, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of (*E*)-**1**: δ=7.82 (d, 2H, J=8.57 Hz, Ar*H*), 7.64 (t, 1H, J=7.25 Hz, C*H*=C), 7.33 (d, 2H, J=7.91 Hz, Ar*H*), 3.74 (s, 3H, CO_2CH_3), 3.56 (d, 2H, J=7.25 Hz, CH_2C=C), 2.44 (s, 3H, $ArCH_3$), 2.28 (S, 3H, SCH_3); ^1H NMR of (*Z*)-**1**: δ=7.87 (d, 2H, J=8.56 Hz, Ar*H*), 7.33 (d, 2H, J=7.91 Hz, Ar*H*), 6.60 (t, 1H, J=7.25 Hz, C*H*=C), 3.89 (d, 2H, J=7.25 Hz, CH_2CH=C), 3.72 (s, 3H, CO_2CH_3), 2.45 (s, 3H, $ArCH_3$), 2.33 (s, 3H, SCH_3). Found: C, 51.71; H, 5.33%. Calcd for $C_{13}H_{16}O_4S_2$: C, 51.98; H, 5.37%.

1-(Methylthio)-1-(*p*-tolylsulfonyl)ethane (10). To a solution of **7** (10.0 g, 46.2 mmol) in DMF (70 ml), was added NaH (2.23 g, 55.8 mmol; dispersed in an oil) at 0 °C; the mixture was stirred at room temperature for 1 h. The reaction mixture was added to a DMF solution of methyl iodide (11.0 ml, 184 mmol in 40 ml) at room temperature and the resulting mixture was further stirred for 2 h. After the addition of water (150 ml), the mixture was extracted with diisopropyl ether (150 ml×4). The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a yellow oil (10.6 g). The oil was again dissolved in methanol and then concd HCl (2 ml) was added. The mixture was then refluxed for 12 h to decompose the formed dimethyl derivative of **1**. After evaporation, the residue was diluted with CH_2Cl_2 (150 ml), washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford crude 1-(methylthio)-1-(*p*-tolylsulfonyl)ethane as a yellow oil (10.1 g). To a solution of the crude 1-(methylthio)-1-(*p*-tolylsulfonyl)ethane (10.1 g) in $CHCl_3$ (80 ml) was dropwise added sulfuryl chloride (6.0 ml) at 0 °C and the mixture was stirred at 0 °C for 2 h. After evaporation, the residue was diluted with CH_2Cl_2 (100 ml), washed with a saturated aqueous solution of $Na_2S_2O_3$ (100 ml), dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography on silica gel (benzene as an eluent) afforded 1-chloro-1-(methylthio)-1-(*p*-tolylsulfonyl)ethane (6.18 g, 51% yield) as a colorless oil: IR (neat) 1598, 1327, 1153, 820 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ=7.92 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.91 Hz, Ar*H*), 2.484 (s, 3H, $ArCH_3$), 2.482 (s, 3H, SCH_3), 2.01 (s, 3H, CH_3). Found: C, 45.57; H, 4.95%. Calcd for $C_{10}H_{13}ClO_2S_2$: C, 45.36; H, 4.95%.

A solution of 1-chloro-1-(methylthio)-1-(*p*-tolylsulfonyl)-ethane (5.77 g, 21.8 mmol) in toluene (110 ml) was refluxed under an N_2 atmosphere for 6 d. The resulting mixture was washed with brine, dried ($MgSO_4$), concentrated in vacuo, and purified by recrystallization from benzene–hexane to afford **10** (3.78 g, 76% yield) as colorless crystals: Mp 85.5—86.0 °C (ethanol); IR (KBr) 1593, 1307, 1155, 899, 812 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ=7.84 (d, 2H, J=8.24 Hz, Ar*H*), 7.33 (d, 2H, J=7.91 Hz, Ar*H*), 6.56 (d, 1H, J=18.2 Hz, CH_2=C), 5.69 (d, 1H, J=1.82 Hz, CH_2=C), 2.24 (s, 3H, $ArCH_3$), 2.29 (s, 3H, SCH_3). Found: C, 52.61; 5.28%. Calcd for $C_{10}H_{12}O_2S_2$: C, 52.61; H, 5.30%.

Preparation of Ethyl 2-(Ethoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)-3-butenoate (2). Route (a). To a solution of NaH (406 mg, 16.9 mmol; dispersed in an oil) in THF (13.0 ml), was dropwise added diethyl malonate (2.0 ml, 13.2 mmol) and then the mixture was stirred at room temperature for 30 min. A THF solution of **10** (2.67 g, 11.7 mmol in 10.0 ml) was dropwise, and the mixture was stirred for 2 h. After the addition of water (20 ml) and subsequent extraction with diisopropyl ether (40 ml×5), the combined extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a yellow oil (4.02 g), with was purified by column chromatography on silica gel (hexane–ethyl acetate, 4:1) to afford ethyl 2-(ethoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)butanoate (**11**; 3.66 g, 80% yield) as a colorless oil: IR (neat) 1732, 1370, 1302, 1146, 1084, 1024 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ=7.83 (d, 2H, J=8.24 Hz, Ar*H*), 7.37 (d, 2H, J=7.91 Hz, Ar*H*), 4.23—4.00 (2×q, 4H, $CO_2CH_2CH_3$), 3.90 (dd, 1H, J=3.63 and 11.9 Hz, $CH(SCH_3)SO_2Tol$ or $CHCO_2Et$), 3.79 (dd, 1H, J=4.61 and 10.2 Hz, $CH(SCH_3)SO_2Tol$ or $CHCO_2Et$), 2.71 (ddd, 1H, J=3.96, 10.2 and 14.2 Hz, CH_2CHCO_2Et), 2.46 (s, 3H, $ArCH_3$), 2.24 (s, 3H, SCH_3), 2.08 (ddd, 1H, J=4.61, 11.5 and 14.5 Hz, CH_2CHCO_2Et), 1.26 (t, 3H, J=7.09 Hz, $CO_2CH_2CH_3$), 1.25 (t, 3H, J=7.09 Hz, $CO_2CH_2CH_3$). Found: C, 52.47; H, 6.21%. Calcd for $C_{17}H_{24}O_6S_2$: C, 52.56; H, 6.23%.

To a solution of **11** (3.71 g, 9.55 mmol) in $CHCl_3$ (48 ml), was added dropwise sulfuryl chloride (0.84 ml, 10.5 mmol) at 0 °C; the mixture was then stirred at the same temperature for 1 h. After evaporation in vacuo, the residue was dissolved in CH_2Cl_2 (30 ml). The resulting solution was washed with brine, dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography on silica gel (hexane–ethyl acetate, 4:1) to give ethyl 4-chloro-2-(ethoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)butanoate (**12**; 3.90 g, 95% yield) as a colorless oil: IR (neat) 1756, 1736, 1328, 1268, 1146, 646 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ=7.89 (d, 2H, J=8.24 Hz, Ar*H*), 7.38 (d, 2H, J=8.24 Hz, Ar*H*), 4.18 (2×q, 4H, J=7.25 Hz, $CO_2CH_2CH_3$), 3.86 (*t*-like, 1H, J=5.60 Hz, $CHCO_2Et$), 3.02 (dd, 1H, J=5.61 and 15.2 Hz, CH_2CHCO_2Et), 2.86 (dd, 1H, J=5.43 and 15.3 Hz, CH_2CHCO_2Et), 2.47 (s, 3H, $ArCH_3$), 2.46 (s, 3H, SCH_3), 1.261 (t, 3H, J=7.25 Hz, OCH_2CH_3), 1.256 (t, 3H, J=7.25

Hz, OCH_2CH_3). Found: C, 48.43; H, 5.49%. Calcd for $C_{17}H_{23}ClO_6S_2$: C, 48.28; H, 5.48%.

A solution of **12** (1.23 g, 2.91 mmol) in toluene (6.0 ml) was refluxed under bubbling N_2 for 41 h. The reaction mixture was washed with brine, dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography on silica gel (hexane–ethyl acetate, 2 : 1) to give **2** (203 mg, 53% yield) as a mixture of two geometrical isomers (E : Z = 52 : 48): A colorless oil; IR (neat) 1724, 1322, 1266, 1236, 1150, 1084 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of (*E*)-**2**: δ = 7.82 (d, 2H, J = 8.24 Hz, Ar*H*), 7.65 (d, 1H, J = 9.56 Hz, C*H*=C), 7.33 (d, 2H, J = 8.24 Hz, Ar*H*), 4.85 (d, 1H, J = 9.89 Hz, C*H*CH=C), 4.29—4.09 (2×q, 4H, J = 7.25 Hz, OCH_2CH_3), 2.44 (s, 3H, $ArCH_3$), 2.34 (s, 3H, SCH_3), 1.27 (2×t, 6H, J = 7.25 Hz, OCH_2CH_3); ^1H NMR of (*Z*)-**2**: δ = 7.77 (d, 2H, J = 8.24 Hz, Ar*H*), 7.35 (d, 2H, J = 8.24 Hz, Ar*H*), 6.78 (d, 1H, J = 11.2 Hz, C*H*=C), 5.22 (d, 2H, J = 10.9 Hz, C*H*CH=CH), 4.29—4.09 (2×q, 4H, J = 7.25 Hz, OCH_2CH_3), 2.46 (s, 3H, $ArCH_3$), 2.38 (s, 3H, SCH_3), 1.25 (2×t, 6H, J = 7.25 Hz, OCH_2CH_3). Found: C, 52.96; H, 5.70%. Calcd for $C_{17}H_{22}O_6S_2$: C, 52.83; H, 5.74%.

Route (b). To a suspension of **7** (2.00 g, 9.25 mmol) and potassium *t*-butoxide (2.07 g, 18.5 mmol) in THF (20 ml), was added a THF solution of methyl formate (1.14 ml, 18.5 mmol in 5.0 ml); the mixture was stirred at room temperature for 10 min and then refluxed for 30 min. After being cooled to room temperature, the precipitated potassium enolate of 2-(methylthio)-2-(*p*-tolylsulfonyl)ethanal (**13**; 2.17 g, 83% yield) was isolated by filtration, washed with THF, and dried in vacuo. Its ^1H NMR (d_6-DMSO) and IR spectra agreed with those reported in literature.[10] To a THF solution of MsCl (0.86 ml, 15.8 mmol in 15 ml) was added, **13** (1.50 g, 5.26 mmol) at −20 °C and then the resulting mixture was stirred for 30 min at the same temperature. A saturated aqueous solution of K_2CO_3 was added, and the resulting suspension was stirred for 30 min at room temperature. After extraction with CH_2Cl_2 (30 ml×3), the combined extracts were dried (Na_2SO_4) and evaporated in vacuo to give 2-[(methylsulfonyl)oxy]-1-(methylthio)-1-(*p*-tolylsulfonyl)ethane (**14**; 1.42 g, 84% yield) as colorless crystals: Mp 74.5—75.5 °C (diisoropyl ether–benzene); IR (KBr) 1610, 1372, 1148, 1103, 1088, 792 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ = 8.31 (s, 1H, C*H*=C), 7.84 (d, 2H, J = 8.57 Hz, Ar*H*), 7.36 (d, 2H, J = 7.91 Hz, Ar*H*), 3.26 (s, 3H, OSO_2CH_3), 2.45 (s, 3H, $ArCH_3$), 2.21 (s, 3H, SCH_3). Found: C, 41.07; H, 4.21%. Calcd for $C_{11}H_{14}O_5S_3$: C, 40.98; H, 4.38%.

To a suspension of NaH (307 mg, 7.68 mmol; dispersed in an oil) in THF (20 ml), was added diethyl malonate (0.97 mg, 6.40 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. Then, a THF solution of **14** (1.32 g, 4.09 mmol in 10 ml) was dropwise added at 0 °C over 5 min and the mixture was stirred for 1 h. After the reaction was quenched with a saturated aqueous NH_4Cl (5.0 ml), the usual workup (extraction with CH_2Cl_2, being dried, and concentration) followed by column chromatography on silica gel (hexane–ethyl acetate, 6 : 1 to 3 : 1) gave **2** (1.58 g, 80% yield) as a mixture of two geometrical isomers (E : Z = 52 : 48).

2-(Ethoxycarbonyl)-4-methyl-3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-pentanolide (4a). A Typical Procedure. A solution of **2** (386 mg, 1.00 mmol) and benzophenone (182 mg, 1.00 mmol) in 2-propanol (70 ml) was irradiated with a 100-W high-pressure Hg arc lamp under bubbling N_2 for 2.5 h. Evaporation of the solvent and subsequent chromatography on silica gel (eluent: hexane–ethyl acetate, 5 : 1 and 1 : 1) afforded a diastereomeric mixture (A : B : C : D = 47 : 33 : 16 : 4) of **4a** (316 mg, 77% yield) as colorless crystals: IR (KBr) 1766, 1730, 1372, 1302, 1142, 1084 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ = 7.87 (d, 2H, J = 8.24 Hz, Ar*H*), 7.40 (d, 2H, J = 7.91 Hz, Ar*H*), 4.28 (q, 2H, J = 6.92 Hz, OCH_2CH_3), 3.78 (d, 1H, J = 8.24 Hz, C*H*CO_2Et), 3.70 (d, 1H, J = 1.65 Hz, C*H*(SCH_3)SO_2Tol), 3.43 (dd, J = 1.65 and 8.24 Hz, C*H*CHCO_2Et), 2.48 (s, 3H, $ArCH_3$), 2.24 (s, 3H, SCH_3), 1.47 (s, 3H, $C(CH_3)_2$), 1.34 (t, 3H, J = 7.09 Hz, OCH_2CH_3), 1.27 (s, 3H, $C(CH_3)_2$); ^1H NMR of isomer B: δ = 7.83 (d, 2H, J = 8.24 Hz, Ar*H*), 7.37 (d, 2H, J = 7.91 Hz, Ar*H*), 4.33 (q, 2H, J = 7.25 Hz, OCH_2CH_3), 3.20—3.18 (m, 1H, C*H*CO_2Et), 3.74 (d, 1H, J = 1.65 Hz, C*H*(SCH_3)SO_2Tol), 3.43 (*d*-like, 1H, J = 11.2 Hz, C*H*CHCO_2Et), 2.48 (s, 3H, $ArCH_3$), 2.18 (s, 3H, SCH_3), 1.67 (s, 3H, $(CH_3)_2C$), 1.44 (t, 3H, J = 7.25 Hz, OCH_2CH_3), 1.29 (s, 3H, $(CH_3)_2C$); ^1H NMR of isomer C: δ = 3.74 (d, 1H, J = 8.24 Hz, C*H*CO_2Et), 2.07 (s, 3H, SCH_3), 1.49 (s, 3H, $(SH_3)_2C$), 1.36 (t, 3H, J = 7.09 Hz, OCH_2CH_3), 1.26 (s, 3H, $(CH_3)_2C$); ^1H NMR of isomer D: δ = 1.81 (s, 3H, SCH_3), 1.78 (s, 3H, $(CH_3)_2C$), 1.47 (s, 3H, $(CH_3)_2C$). Recrystallization from hexane–$CHCl_3$ afforded colorless crystals: Mp 166.4—167.5 °C. Found: C, 53.76; H, 5.92%. Calcd for $C_{18}H_{24}O_6S_2$: C, 53.98; H, 6.04%.

To a solution of **4a** (70 mg, 0.18 mmol) in ethanol (2.0 ml) and ethyl acetate (2.0 ml), was added Raney-Ni (W2) (2.0 cm^3) and stirred for 2 h at room temperature. After any insoluble solid was filtered off and washed with ethanol, the filtrate and the washing were combined, concentrated in vacuo, and purified by column chromatography on silica gel (eluted: ethyl acetate) to afford 2-(ethoxycarbonyl)-4-methyl-3-[(*p*-tolylsulfonyl)methyl]-4-pentanolide (**15a**) (51.4 mg, 60% yield) as a diastereomeric mixture (trans : cis = 87 : 13): Colorless crystals; IR (KBr) 1762, 1723, 1374, 1310, 1189, 1140 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$), of *trans*-**15a**: δ = 7.81 (d, 2H, J = 8.24 Hz, Ar*H*), 7.40 (d, 2H, J = 8.24 Hz, Ar*H*), 4.32 (q, 2H, J = 7.25 Hz, OCH_2CH_3), 3.64 (ddd, 1H, J = 3.36, 6.60, and 10.6 Hz, C*H*CHCO_2Et), 3.30—3.10 (m, 3H, CH_2SO_2Tol and CHC*H*CO_2Et), 2.47 (s, 3H, $ArCH_3$), 1.46 (s, 3H, $(CH_3)_2C$), 1.36 (t, 3H, J = 7.25 Hz, OCH_2CH_3), 1.29 (s, 3H, $(CH_3)_2C$); two singlets at δ = 1.48 and 1.43 were assigned to methyl protons at the C-4 position of *cis*-**15a**. Recrystallization from hexane–CH_2Cl_2 afforded colorless crystals: Mp 76.0—78.0 °C. Found: C, 57.51; H, 6.25%. Calcd for $C_{17}H_{22}O_6S$: C, 57.61; H, 6.26%.

Similarly a solution of **2** (386.4 mg, 1.00 mmol) and benzophenone (182 mg, 1.00 mmol) in methanol (70 ml) was irradiated for 1.5 h to give 2-(ethoxycarbonyl)-3-[(methylthio)*p*-tolylsulfonyl)methyl]-4-butanolide (**4b**) (324 mg, 87% yield) as a diastereomeric mixture (A : B : C : D = 61 : 34 : 5 : <1): Colorless crystals; IR (KBr) 1770, 1725, 1295, 1240, 1140, 1084 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ = 7.78 (d, 2H, J = 8.56 Hz, Ar*H*), 7.42 (d, 2H, J = 8.24 Hz, Ar*H*), 4.53 (dd, 1H, J = 7.91 and 10.22 Hz, CH_2OCO), 4.27 (q, 2H, J = 7.25 Hz, OCH_2CH_3), 4.12 (dd, 1H, J = 9.56 and 10.22 Hz, CH_2OCO), 3.88 (d, 1H, J = 2.97 Hz, C*H*(SCH_3)SO_2Tol or C*H*CO_2Et), 3.86 (d, 1H, J = 3.30 Hz, C*H*(SCH_3)SO_2Tol or C*H*CO_2Et), 3.80—3.72 (m, 1H,

CHCHCO$_2$Et), 2.49 (s, 3H, ArCH$_3$), 2.07 (s, 3H, SCH$_3$), 1.30 (t, 3H, J=7.25 Hz, OCH$_2$CH$_3$); ^{1}H NMR of isomer B: δ=7.84 (d, 2H, J=8.57 Hz, ArH), 7.40 (d, 2H, J=7.91 Hz, ArH), 4.73 (dd, 1H, J=7.53 and 9.55 Hz, CH$_2$OCO), 4.38 (dd, 1H, J=7.25 and 9.55 Hz, CH$_2$OCO), 4.27 (q, 2H, J=7.25 Hz, OCH$_2$CH$_3$), 3.79—3.72 (m, 1H, CHCHCO$_2$Et), 3.68 (d, 1H, J=7.26 Hz, CHCO$_2$Et), 3.65 (diffused s, 1H, CH(SCH$_3$)SO$_2$Tol), 2.49 (s, 3H, ArCH$_3$), 2.17 (s, 3H, SCH$_3$), 1.30 (t, 3H, J=7.25 Hz, OCH$_2$CH$_3$); ^{1}H NMR of isomer C: δ=2.11 (s, 3H, SCH$_3$), 1.34 (t, 3H, J=7.25 Hz, OCH$_2$CH$_3$). Recrystallization from hexane–CH$_2$Cl$_2$ gave colorless crystals: Mp 156.0—159.0 °C. Found: C, 51.40; H, 5.38%. Calcd for C$_{16}$H$_{20}$O$_6$S$_2$: C, 51.60; H, 5.41%.

To a solution of **4b** (200 mg, 0.54 mmol) in ethanol (2.0 ml) and THF (8.0 ml) was added Raney-Ni (W2) (1.5 cm^3); the resulting suspension was stirred at room temperature for 2 h. The usual workup and subsequent column chromatography on silica gel (eluent: ethyl acetate) afforded 2-(ethoxycarbonyl)-3-[(*p*-tolylsulfonyl)methyl]-4-butanolide (**15b**) (51.4 mg, 67% yield) as mixture of two diastereomers (trasn : cis=87 : 13): A colorless oil; IR (neat) 1784, 1737, 1316, 1303, 1145, 1088 cm^{-1}; ^{1}H NMR (270 MHz, CDCl$_3$) of *trans*-**15b**: δ=7.80 (d, 2H, J=8.24 Hz, ArH), 7.40 (d, 2H, J=8.23 Hz, ArH), 4.67 (ddd, 1H, J=2.30, 5.28, and 9.88 Hz, CH$_2$OCO), 4.26 (q, 2H, J=7.25 Hz, OCH$_2$CH$_3$), 4.14 (ddd, 1H, J=1.32, 8.23, and 9.56 Hz, CH$_2$OCO), 3.60—3.40 (m, 2H, CHCHCO$_2$Et), 3.35 (ddd, 1H, J=1.64, 5.27, and 13.8 Hz, CH$_2$SO$_2$Tol), 3.21 (ddd, 1H, J=2.64, 8.24, and 13.8 Hz, CH$_2$SO$_2$Tol), 2.47 (s, 3H, ArCH$_3$), 1.30 (t, 3H, J=7.25 Hz, OCH$_2$CH$_3$); ^{1}H NMR of *cis*-**15b**: δ=7.78 (d, 2H, J=8.24 Hz, ArH), 4.56 (dd, 1H, J=7.58 and 11.7 Hz, CH$_2$OCO). The diastereomeric mixture was subjected to elemental analysis. Found: C, 54.80; H, 5.71%. Calcd for C$_{15}$H$_{18}$O$_6$S·0.03CHCl$_3$: C, 54.88; H, 5.53%.

Similarly a solution of **2** (361 mg, 0.93 mmol) and benzophenone (182 mg, 1.10 mmol) in ethanol (70 ml) was irradiated for 2.5 h to afford 2-(ethoxycarbonyl)-3-[(methylthio)(*p*-tolylsulfonyl)methyl]-4-pentanolide (**4c**) (350 mg, 91% yield) as a colorless viscous oil: A diastereomeric mixture (A : B : C : D : E : F : G : H=25 : 24 : 22 : 11 : 8 : 3 : 3 : 3); IR (neat) 1780, 1742, 1309, 1157, 1039, 760 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) of isomer A: δ=7.87 (d, 2H, J=8.43 Hz, ArH), 7.40 (d, 2H, J=8.43 Hz, ArH), 4.96 (quintet, 1H, J=6.59 Hz, CHOCH), 4.32 (q, 2H, J=7.33 Hz, OCHCH$_3$), 4.01 (d, 1H, J=12.1 Hz, CHCO$_2$Et), 3.75 (d, 1H, J=3.30 Hz, CH(SCH$_3$)SO$_2$Tol), 3.72 (*dt*-like, 1H, J=6.23 and 7.33 Hz, CHCHCO$_2$Et), 2.48 (s, 3H, ArCH$_3$), 2.02 (s, 3H, SCH$_3$), 1.41 (d, 3H, J=6.96 Hz, CH$_3$CHOCO), 1.33 (t, 3H, J=6.96 Hz, OCH$_2$CH$_3$); ^{1}H NMR of isomer B: δ=7.84 (d, 2H, J=8.43 Hz, ArH), 7.40 (d, 2H, J=8.43 Hz, ArH), 5.07 (quintet, 1H, J=6.59 Hz, CHOCO), 4.31 (q, 2H, J=7.33 Hz, OCH$_2$CH$_3$), 3.78 (d, 1H, J=6.59 Hz, CHCO$_2$Et or CH(SCH$_3$)SO$_2$Tol), 3.65 (*q*-like, 1H, J=7.33 Hz, CHCHCO$_2$Et), 3.48 (d, 1H, J=6.96 Hz, CH(SCH$_3$)-SO$_2$Tol or CHCO$_2$Et), 2.48 (s, 3H, ArCH$_3$), 2.25 (s, 3H, SCH$_3$), 1.58 (d, 3H, J=6.60 Hz, CH$_3$CHOCO), 1.32 (t, 3H, J=6.96 Hz, OCH$_2$CH$_3$); ^{1}H NMR of isomer C: δ=7.86 (d, 2H, J=8.43 Hz, ArH), 7.40 (d, 2H, J=8.43 Hz, ArH), 4.73 (quintet, 1H, J=6.60 Hz, CH$_3$CHOCO), 4.38 (q, 2H, J=7.33 Hz, OCH$_2$CH$_3$), 3.85 (d, 1H, J=6.59 Hz, CHCO$_2$Et), 3.66 (d, 1H, J=2.93 Hz, CH(SCH$_3$)SO$_2$Tol), 3.43 (m, 1H, CHCHCO$_2$Et), 2.48 (s, 3H, ArCH$_3$), 1.92 (s, 3H, SCH$_3$), 1.41 (d, 3H, J=6.96 Hz, CH$_3$CHOCO), 1.25 (t, 3H, J=7.33 Hz, OCH$_2$CH$_3$); ^{1}H NMR of isomer D: δ=4.63 (quintet, 1H, J=6.59 Hz, CHOCO), 4.19 (q, 2H, J=7.33 Hz, OCH$_2$CH$_3$), 3.77 (d, 1H, J=5.86 Hz, CHCO$_2$Et), 3.37 (*dt*-like, 1H, J=3.30 and 8.06 Hz, CHCHCO$_2$Et), 2.48 (s, 3H, ArCH$_3$), 2.14 (s, 3H, SCH$_3$), 1.52 (d, 3H, J=6.60 Hz, CH$_3$CHOCO), 1.36 (t, 3H, J=7.33 Hz, OCH$_2$CH$_3$); δ=(s, 3H, SCH$_3$): Four singlets at δ=2.19, 2.06, 1.97, and 1.87 were assigned to those of the isomers F, E, G, and H, respectively. The diastereomeric mixture was subjected to elemental analysis. Found: C, 51.81; H, 5.75%. Calcd for C$_{17}$H$_{22}$O$_6$S$_2$: C, 51.82; H, 5.62%.

Similarly irradiation of **2** (387 mg, 1.00 mmol) and benzophenone (183 mg, 1.00 mmol) in 1-butanol (70 ml) for 2 h afforded 2-(ethoxycarbonyl)-3-[(methylthio)-(*p*-tolylsulfonyl)methyl]-4-heptanolide (**4d**) (350 mg, 81% yield) as a diastereomeric mixture (A : B : C : D : E : F : G : H= 23 : 17 : 16 : 13 : 11 : 10 : 6 : 4): A colorless viscous oil; IR (neat) 2960, 1774, 1736, 1298, 1140, 1080 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) of isomer A: δ=7.84 (d, 2H, J=8.43 Hz, ArH), 7.41 (d, 2H, J=8.06 Hz, ArH), 4.80—4.72 (m, 1H, CHOCO), 4.27 (q, 2H, J=6.96 Hz, OCH$_2$CH$_3$), 4.00 (d, 1H, J=1.83 Hz, CH(SCH$_3$)SO$_2$Tol), 3.75 (d, 1H, J= 7.69 Hz, CHCO$_2$Et), 3.30—3.18 (m, 1H, CHCHCO$_2$Et), 2.48 (s, 3H, ArCH$_3$), 2.02 (s, 3H, SCH$_3$), 1.80—1.23 (m, 7H, OCH$_2$CH$_3$ and CH$_3$(CH$_2$)$_2$), 0.95 (t, 3H, J=7.33 Hz, CH$_3$(CH$_2$)$_2$); ^{1}H NMR of isomer B: δ=7.882 (d, 2H, J=8.43 ArH), 7.40 (d, 2H, J=8.06 Hz, ArH), 4.87—4.80 (m, 1H, CHOCO), 4.30 (q, 2H, J=6.96 Hz, OCH$_2$CH$_3$), 3.76 (d, 1H, J=6.23 Hz, CHCO$_2$Et or CH(SCH$_3$)SO$_2$Tol), 3.41 (d, 1H, J=5.50 Hz, CHCO$_2$Et or CH(SCH$_3$)SO$_2$Tol), 3.48 (*q*-like, 1H, J=6.23 Hz, CHCHCO$_2$Et), 2.47 (s, 3H, ArCH$_3$), 2.17 (s, 3H, SCH$_3$), 0.91 (t, 3H, J=7.33 Hz, CH$_3$CH$_2$); ^{1}H NMR of isomer C: δ=7.871 (d, 2H, J=8.43 Hz, ArH), 4.62—4.57 (m, 1H, CH$_2$CHO), 3.86 (d, 1H, J=5.13 Hz, CHCO$_2$Et or CH(SCH$_3$)SO$_2$Tol), 3.69 (d, 1H, J=9.16 Hz, CHCO$_2$Et or CH(SCH$_3$)SO$_2$Tol), 2.46 (s, 3H, ArCH$_3$), 2.26 (s, 3H, SCH$_3$), 0.94 (t, 3H, J=7.33 Hz, CH$_3$CH$_2$); ^{1}H NMR of isomer D: δ=7.878 (d, 2H, J=8.43 Hz, ArH), 4.48—4.40 (m, 1H, CHOCO), 3.62 (d, 1H, J=11.3 Hz, CHCO$_2$Et), 3.45—3.38 (m, 1H, CHCHCO$_2$Et), 1.91 (s, 3H, SCH$_3$), 1.00 (t, 3H, J=7.33 Hz, CH$_3$(CH$_2$)$_2$: δ(=s, 3H, SCH$_3$); four singlets at δ=2.33, 1.85, 1.98, and 1.69 were assigned to those of the isomers E, F, G, and H, respectively. Found: C, 54.91; H, 6.29%. Calcd for C$_{19}$H$_{26}$O$_6$S$_2$: C, 55.05; H, 6.32%.

Photochemical Addition of 1-Butanol to 2 in Acetonitrile. A Typical Procedure. A solution of **2** (388 mg, 1.00 mmol) and 1-butanol (0.92 ml, 10.0 mmol) in acetonitrile (70 ml) was irradiated in the presence of benzophenone (364 mg, 2.00 mmol) under bubbling N$_2$ at room temperature for 4.5 h. After evaporation in vacuo, the residue was purified by column chromatography on silica gel (hexane–ethyl acetate, 4 : 1) and the recycling preparative HPLC mentioned above to afford **4d** (157 mg, 53% yield).

In a similar manner, a solution of **2** (386 mg, 1.00 mmol), benzophenone (364 mg, 2.00 mmol), and 1-butanol (0.92 ml, 10.0 mmol) in benzene (70 ml) was irradiated for 5 h to afford **4d** (222 mg, 56% yield).

A solution of **2** (387 mg, 1.00 mmol), 1-hexanol (1.26 ml, 10.0 mmol), and benzophenone (364 mg, 2.00 mmol) in acetonitrile (70 ml) was similarly irradiated for 5 h to afford 2-(ethoxycarbonyl)-3-[(methylthio)(*p*-tolylsulfonyl)methyl]-

4-nonanolide (**4e**) (218 mg, 49% yield) as a diastereomeric mixture (A : B : C : D : E : F : G : H=26 : 21 : 12 : 12 : 9 : 8 : 7 : 5): A colorless viscous oil; IR (neat) 1783, 1740, 1300, 1150, 1084, 1019 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ=7.80 (d, 2H, J=8.24 Hz, Ar*H*), 7.37 (d, 2H, J=6.93 Hz, Ar*H*), 4.40—4.10 (m, 1H, C*H*OCO), 4.25 (q, 2H, J=6.92 Hz, OCH_2CH_3), 4.01 (d, 1H, J=2.31 Hz, $CH(SCH_3)SO_2Tol$), 3.90—3.10 (m, 1H, C*H*CHCO$_2$Et), 3.69 (d, 1H, J=8.23 Hz, C*H*CO$_2$Et), 2.47 (s, 3H, ArCH_3), 1.85 (s, 3H, SCH_3), 1.90—1.23 (m, 11H, OCH_2CH_3 and $CH_3(CH_2)_4$), 0.88 (t, 3H, J=6.59 Hz, $CH_3(CH_2)_4$); ^1H NMR of isomer B: δ=7.87 (d, 2H, J=8.57 Hz, Ar*H*), 7.40 (d, 2H, J=7.25 Hz, Ar*H*), 4.26 (q, 2H, J=6.92 Hz, OCH_2CH_3), 4.00 (*s*-like, 1H, $CH(SCH_3)SO_2Tol$), 3.62 (d, 1H, J=8.24 Hz, C*H*CO$_2$Et), 2.02 (s, 3H, SCH_3); ^1H NMR of isomer C: δ=3.76 (d, 1H, J=6.59 Hz, C*H*CO$_2$Et), 2.17 (s, 3H, SCH_3); δ=(s, 3H, SCH_3); five singlets at δ=2.25, 2.21, 2.05, 1.99, and 1.91 were assigned to those of the isomers F, H, E, D, and G, respectively. Found: C, 56.99; H, 6.83%. Calcd for $C_{21}H_{30}O_6S_2$: C, 57.06; H, 6.84%.

Similarly, a solution of **2** (237 mg, 0.61 mmol), benzophenone (182 mg, 1.00 mmol), and 1-tetradecanol (2.14 g, 9.98 mmol) in acetonitrile (70 ml) was irradiated to afford 2-(ethoxycarbonyl)-3-[(methylthio)(*p*-tolylsulfonyl)-methyl]-4-heptadecanolide (**4f**) (165 mg, 47% yield) as a diastereomeric mixture (A : B : C : D : E=26 : 22 : 21 : 17 : 14): A colorless viscous oil; IR (neat) 2920, 2860, 1788, 1728, 1302, 1154 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) of isomer A: δ=7.80 (d, 2H, J=8.24 Hz, Ar*H*), 7.40 (d, 2H, J=7.90 Hz, Ar*H*), 4.25 (q, 2H, J=7.25 Hz, OCH_2CH_3), 4.38—4.10 (m, 1H, C*H*OCO), 3.69 (d, 1H, J=9.23 Hz, C*H*CO$_2$Et or $CH(SCH_3)SO_2Tol$), 3.62 (d, 1H, J=8.24 Hz, C*H*CO$_2$Et or $CH(SCH_3)SO_2Tol$), 3.30—3.10 (m, 1H, C*H*CHCO$_2$Et), 2.47 (s, 3H, ArCH_3), 1.69 (s, 3H, SCH_3), 1.80—1.20 (m, 27H, OCH_2CH_3 and $(CH_2)_{12}CH_3$), 0.88 (t, 3H, J=6.92 Hz, $(CH_2)_{12}CH_3$); ^1H NMR of isomer B: J=4.32 (q, 1H, J=7.33 Hz, OCH_2CH_3); 3.70 (d, 1H, J=9.23 Hz, C*H*CO$_2$Et or $CH(SCH_3)SO_2Tol$), 2.25 (s, 3H, SCH_3); ^1H NMR of isomer C: δ=4.73—4.69 (m, 1H, C*H*OCO), 4.30 (q, 2H, J=6.96 Hz, OCH_2CO_3), 3.98 (d, 1H, J=11.7 Hz, C*H*CO$_2$Et or $CH(SCH_3)SO_2Tol$), 3.74—3.68 (m, 1H, C*H*CHCO$_2$Et), 2.20 (s, 3H, SCH_3); ^1H NMR of isomer D: δ=4.27 (q, 2H, J=6.96 Hz, OCH_2CH_3), 1.91 (s, 3H, SCH_3); ^1H NMR of isomer E: δ=4.32 (q, 2H, J=6.96 Hz, OCH_2CH_3), 2.20 (s, 3H, SCH_3). The other isomers could not be detected by ^1H NMR spectra. Found: C, 62.80; H, 8.56%. Calcd for $C_{29}H_{46}O_6S_2$: C, 62.78; H, 8.36%.

Transformation of 4d to 2-(Ethoxycarbonyl)-3-[(methylthio)carbonyl]-4-heptanolide (17). To a solution of **4d** (1.10 g, 2.65 mmol; a diastereomeric mixture in a ratio of 23 : 17 : 16 : 13 : 11 : 10 : 6 : 4) in CH_2Cl_2 (26.5 ml) was added mCPBA (664 mg, 3.85 mmol) at 0 °C, and the resulting mixture was stirred at the same temperature for 3 h. Then, a saturated aqueous solution (20 ml) of K_2CO_3 was added, and the mixture was extracted with CH_2Cl_2 (20 ml×3). The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated in vacuo to afford a colorless viscous oil (1.07 g) that was shown by ^1H NMR to consist mainly of 2-(ethoxycarbonyl)-3-[(methylsulfinyl)(*p*-tolylsulfonyl)methyl]-4-heptanolide (**16**). This oil (380 mg) was dissolved in CH_2Cl_2 (5.0 ml) containing pyridine (0.71 ml, 8.80 mmol). After trifluoroacetic anhydride (0.56 ml, 3.52 mmol) was added at −78 °C, the resulting mixture was stirred at −20 °C for 3 h and then at room temperature for 12 h. Water (20 ml) was added and extraction with CH_2Cl_2 (20 ml×3) was carried out. The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$, water, 1 mol dm^{-3} HCl, water, and brine. The organic solution was dried ($MgSO_4$), concentrated, and purified by column chromatography on silica gel (hexane–ethyl acetate, 7 : 1) to afford **17** (146 mg, 60% yield) as a diastereomeric mixture [(2*R**,3*S**,4*R**) : (2*R**,3*S**,4*S**)=55 : 45]: A yellow oil; IR (neat) 1783, 1738, 1680, 1176, 1032, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) of (2*R**,3*S**,4*R**)-**17**: δ=4.51 (*dt*-like, 1H, J=4.40 and 8.43 Hz, C*H*OCO), 4.33 (q, 2H, J=7.14 Hz, OCH_2CH_3), 4.01 (d, 1H, J=10.3 Hz, C*H*CO$_2$Et), 3.76 (dd, 1H, J=8.79 and 10.3 Hz, C*H*COSCH$_3$), 2.388 (s, 3H, SCH_3), 1.86—1.78 (m, 1H, $CH_3CH_2CH_2$), 1.61—1.20 (m, 3H, $CH_3CH_2CH_2$), 1.34 (t, 3H, J=7.14 Hz, OCH_2CH_3), 0.94 (t, 3H, J=7.14 Hz, $CH(CH_2)_2$); The observation differential NOE: C4-*H* to C2-*H*, 2.2%; C4-*H* to C3-*H*, 1.6%; C3-*H* to C5-*H*, 3.7%; C4-*H* to C5-*H*, 3.0%; ^1H NMR of (2*R**,3*S**,4*S**)-**17**: δ=4.81 (*q*-like, 1H, J=7.70 Hz, C*H*OCO), 4.27 (q, 2H, J=7.14 Hz, OCH_2CH_3), 4.13 (*t*-like, 1H, J=8.06 Hz, C*H*COSCH$_3$), 4.02 (d, 1H, J=8.06 Hz, C*H*CO$_2$Et), 2.394 (s, 3H, SCH_3), 1.86—1.78 (m, 1H, $CH_3CH_2CH_2$), 1.61—1.20 (m, 3H, $CH_3CH_2CH_2$), 1.32 (t, 3H, J=7.14 Hz, OCH_2CH_3), 0.94 (t, 3H, J=7.14 Hz, $CH_3(CH_2)_2$); The observed differential NOE: C4-*H* to C3-*H*, 6.7%. Found: C, 52.73; H, 6.67%. Calcd for $C_{12}H_{18}O_5S$: C, 52.44; H, 6.61%.

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