Favorskii Rearrangement and Carbon–Carbon Bond-Cleavage of α-Chloro-α-sulfonyl Ketones: A Synthesis of Carboxylic Acids and Their Derivatives from Aldehydes and Ketones

Tsuyoshi SATOH, Kazuko OGURO, Jun-ichi SHISHIKURA, Naomi KANETAKA, Reiko OKADA, and Koji YAMAKAWA*

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162

(Received March 15, 1993)

A method for synthesizing carboxylic acids and their derivatives from aldehydes and ketones via α-chloro-α-sulfonyl ketones is described. Acyclic α-chloro-α-sulfonyl ketones were synthesized from aldehydes and 1-chloroalkyl *p*-tolyl sulfoxides with carbon–carbon coupling in good overall yields. Cyclic α-chloro-α-sulfonyl ketones were synthesized from cyclic ketones in three steps in high overall yields. The Favorskii rearrangement of both acyclic- and cyclic α-chloro-α-sulfonyl ketones with sodium hydride in the presence of amine gave β-sulfonyl amides with skeletal rearrangement in good to excellent yield. Amides and α,β-unsaturated amides were synthesized from the β-sulfonyl amides. Treatment of the cyclic α-chloro-α-sulfonyl ketones with alkoxides and hydroxide gave carboxylic esters and acids with cleavage of the ring in good to excellent yields.

Carboxylic acids and their derivatives are one of the most fundamental compounds in organic chemistry.[1] Innumerable studies on the preparation and chemistry of carboxylic acids and their derivatives have already been reported; however, in view of the importance of these compounds in organic chemistry, new synthetic methods are still eagerly sought.

The Favorskii rearrangement[2] of α-halo ketones is a well-known method for preparation of carboxylic acids and their derivatives from ketones with a skeletal rearrangement. When hydroxide or alkoxides are used as bases, the rearrangement gives carboxylic acids and esters usually in good yields. However, the rearrangement with amines is less common and the yields were reported to be low to moderate.[2]

Recently, we reported some new synthetic methods by the use of aryl 1-haloalkyl sulfoxides as carbon homologating agents.[3] In continuation of our studies on the use of organosulfur compounds having a halogen at α-position in organic synthesis, here we describe in detail a method for synthesizing carboxylic acids and their derivatives from aldehydes and ketones via α-chloro-α-sulfonyl ketones (**2** and **4**; Scheme 1).[4]

Results and Discussion

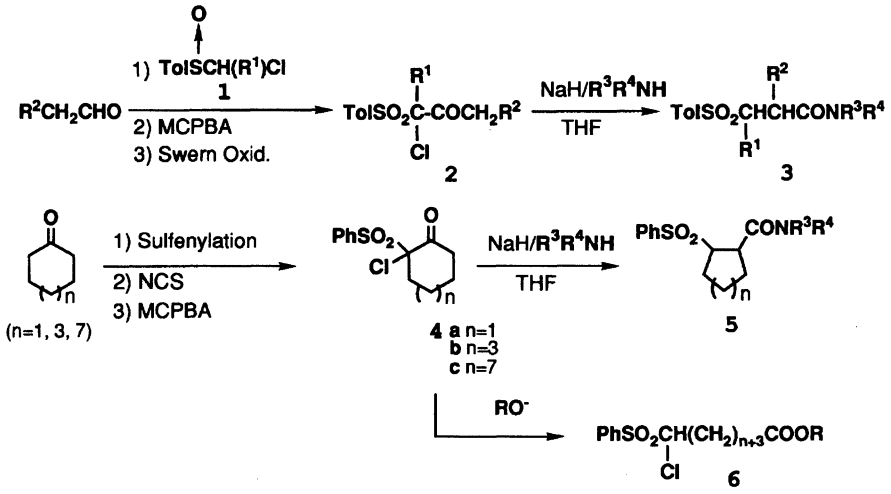
Favorskii Rearrangement of α-Chloro-α-sulfonyl Ketones with Amines. In previous studies, we developed a new method for synthesizing α-halo ketones from aldehydes via α-halo-α-sulfinyl ketones.[5] We planned the Favorskii rearrangement of the α-halo-α-sulfinyl ketones to develop a new synthetic method for α,β-unsaturated carboxylic acids and their derivatives. However, treatment of α-halo-α-sulfinyl ketones with bases only gave a complex mixture. One of the main reasons for the result was thought to be the unstable nature of the α-halo-α-sulfinyl ketones. We thereupon turned our attention to the Favorskii rearrangement of α-halo-α-sulfonyl ketones, which are much more stable than α-halo-α-sulfinyl ketones.

α-Chloro-α-sulfonyl ketones **2** were easily synthesized from aldehydes and 1-chloroalkyl *p*-tolyl sulfoxides **1**. Synthesis of **2a** is described as an example (Scheme 2). 1-Chloroethyl *p*-tolyl sulfoxide was treated with lithium diisopropylamide (LDA) at −60 °C to afford the carbanion, then 3-phenylpropanal was added to the carbanion to give the adduct **7** as a mixture of two diastereomers in 93% yield.[6] The adduct was first oxidized to the corresponding sulfone and then the hydroxyl group was oxidized to ketone **2a** under Swern's conditions in 92% overall yield.

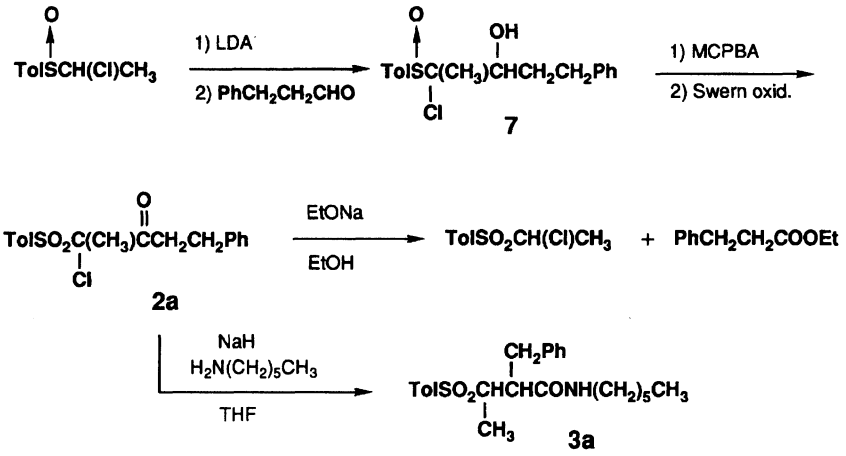
The ketone **2a** was treated with sodium ethoxide in ethanol at room temperature. Unfortunately, this reaction gave not the desired Favorskii rearrangement product but 1-chloroethyl *p*-tolyl sulfone (93%) and ethyl 3-phenylpropionate (75%). Obviously, the carbon–carbon bond between carbonyl carbon and the carbon bearing the sulfonyl group was cleaved by the attack of ethoxide to carbonyl carbon.[7] Next, **2a** was treated with 1.2 equivalents of sodium hydride and hexylamine in THF at room temperature for 4 h. Clean reaction took place and the desired Favorskii rearrangement product **3a** was obtained in 71% yield. Interestingly, although **3a** has two chiral centers, only a single product was obtained. Unfortunately, the stereochemistry of **3a** has not yet been determined (except **3m**, all the products **3** obtained in this study are single isomer). It is interesting to note that treatment of **2a** with sodium hydride in THF without amine gave a complex mixture within a few hours.

Representative examples of the synthesis of β-sulfonyl amides **3** from α-chloro-α-sulfonyl ketones **2** are summarized in Table 1. The characteristics of this reaction are as follows. a) The yields of the amides **3** are uniformly good to excellent. b) Generally speaking, the yields and the reaction time are not affected by the kinds of amines used in this study. c) When R^1 is sterically hindered, much longer reaction time was required.

Next, the Favorskii rearrangement of cyclic α-chloro-



Scheme 1.



Scheme 2.

Table 1. Synthesis of β-Sulfonyl Amides **3** via the Favorskii Rearrangement of **2**

Entry	2			R^3R^4NH		Time	3	
		R^1	R^2	R^3	R^4	h		(Yield/%)[a]
1	**2a**	CH_3	CH_2Ph	$(CH_2)_5CH_3$	H	4.0	**3a**	(71)
2	**2a**			CH_2Ph	H	3.0	**3b**	(70)
3	**2a**			C_2H_5	C_2H_5	3.0	**3c**	(84)
4	**2a**			$(CH_2)_5$		4.5	**3d**	(74)
5	**2b**	CH_3	$(CH_2)_4CH_3$	$(CH_2)_5CH_3$	H	3.0	**3e**	(75)
6	**2b**			CH_2Ph	H	2.5	**3f**	(93)
7	**2b**			C_2H_5	C_2H_5	3.5	**3g**	(67)
8	**2b**			$(CH_2)_5$		4.5	**3h**	(88)
9	**2c**	$CH(CH_3)_2$	CH_2Ph	$(CH_2)_5CH_3$	H	22.0	**3i**	(85)
10	**2c**			CH_2Ph	H	6.0	**3j**	(91)
11	**2c**			C_2H_5	C_2H_5	22.0	**3k**	(59)
12	**2c**			$(CH_2)_5$		18.0	**3l**	(79)
13	**2d**	$CH(CH_3)_2$	$(CH_2)_4CH_3$	$(CH_2)_5CH_3$	H	16.5	**3m**	(99)
14	**2d**			CH_2Ph	H	8.0	**3n**	(95)
15	**2d**			C_2H_5	C_2H_5	23.0	**3o**	(57)
16	**2d**			$(CH_2)_5$		19.0	**3p**	(59)

a) Isolated yield.

α-sulfonyl ketones with amines was investigated. The desired cyclic α-chloro-α-sulfonyl ketones **4** were easily prepared from cyclic ketones in three steps as follows (Scheme 1). Cyclic ketones were first converted to 2-phenylthio ketones by Trost's procedure.[8] The 2-phenylthio ketones were treated with *N*-chlorosuccinimide (NCS) to give 2-chloro-2-(phenylthio)cycloalkanones. As the chlorides are unstable, without further purification, they were oxidized with *m*-chloroperbenzoic acid (MCPBA) to the sulfone **4** in overall over 90% yields. The chlorination finished within 3 h when 2-(phenylthio)cyclohexanone and 2-(phenylthio)cyclooctanone were reacted with NCS. On the other hand, the chlorination of 2-(phenylthio)cyclododecanone required over 27 h for completion.

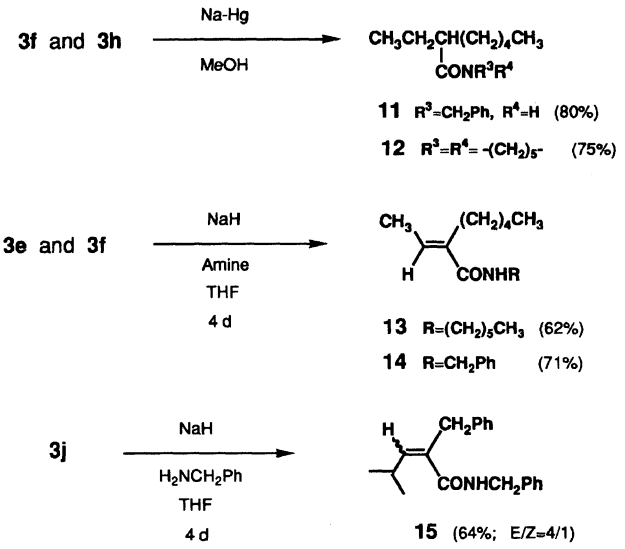
Table 2 shows the results for the Favorskii rearrangement of the cyclic α-chloro-α-sulfonyl ketones **4** with amines. Similarly as the rearrangement of acyclic ketones **2**, cyclic ketones **4** gave the ring-contracted β-sulfonyl amides **5** in good to excellent yields. The reaction of **4a** with benzylamine gave **5b** with a fair amount of the cleaved product **8** (Entry b). As the more sterically hindered primary amine (*t*-butylamine; Entry c) and secondary amine (piperidine; Entry a) did not give a cleaved product, this cleavage is shown to be dependent on the bulkiness of the amines and ring size of the α-chloro-α-sulfonyl ketones.

The reaction of eight-membered ketone **4b** is quite sluggish compared with other ketones (Entries d—f); however, the yields were still good. Surprisingly, the reaction of **4b** with benzylamine gave α,β-unsaturated amide **9** in 92% yield (Entry e). Similar to this, the reaction of **4b** with primary amine (hexylamine) gave some amount of α,β-unsaturated amide **10** (Entry f).

The reaction of twelve-membered ketone **4c** with amines took place smoothly within 4 h to give the desired amides (**5g**—**5i**). In contrast to the other examples, **4c** gave two products, which were found to be the cis/trans-isomers as summarized in Table 2. For example, treatment of one of the isomers of **5i** with a base at room temperature gave a mixture of the isomers.

Reductive Desulfonylation and β-Elimination of the Sulfonyl Group of β-Sulfonyl Amides 3 and 5. In order to extend this procedure to a general method for the synthesis of amides and α,β-unsaturated amides, reductive desulfonylation and β-elimination of the sulfonyl group in **3** and **5** were investigated. As expected, reductive desulfonylation of the sulfonyl group of **3** was realized by known procedure.[9] For example, reductive desulfonylation of **3f** and **3h** with 6% Na–Hg in methanol at room temperature gave the amides **11** and **12**, respectively, smoothly in good yields (Scheme 3).

β-Elimination of the sulfonyl group in **3** and **5** was found to be problematical. First, **3e** was treated with various bases, such as DBU, *t*-BuOK, NaOEt, and LDA, under several conditions to give only unchanged starting



Scheme 3.

materials. One of the main reasons for this difficulty is thought to be the similarity of the acidity of the hydrogens on the carbon bearing a sulfonyl group and an amide carbonyl (pK_a about 29).[10]

Finally, treatment with sodium hydride and hexylamine (5-equivalents) in THF for a few days was found to be the conditions of choice for the elimination. Under these conditions for 4 d, **3e** gave **13** in 62% yield. Examples for the β-elimination of acyclic β-sulfonyl amides are shown in Scheme 3. In this reaction, sodium hydride without amine was also effective; however, the presence of the corresponding amine gave a much cleaner reaction and higher yields.

Strangely, this elimination totally failed with the β-sulfonyl amides (**3** and **5**) synthesized from **2** and **4** with secondary amines. For example, β-sulfonyl amides **3h** and **5g**, on treatment with 5-equivalents of sodium hydride and piperidine, gave the starting material without any detectable amount of α,β-unsaturated amides. While the exact reason for this result is still obscure, it is thought that presence of the amide hydrogen plays an essential role in this elimination.

Table 3 shows the results for β-elimination of the sulfonyl group in cyclic β-sulfonyl amide **5**. Interestingly, *N*-*t*-butylamides **5c** and **5i** required more than 4 d for the completion of the elimination.

Carbon–Carbon Bond-Cleavage of Cyclic α-Chloro-α-sulfonyl Ketones 4 Giving Carboxylic Acids and Esters. As mentioned above, carbon–carbon bond-cleavage takes place on treatment of the α-chloro-α-sulfonyl ketone **2a** with sodium ethoxide to give an ester (Scheme 2). We envisioned that this reaction could be used for formation of ω-functionalized carboxylic acids and esters from cyclic ketones.

First, **4a** was treated with 1.5-equivalents of sodium methoxide in methanol–THF at room temperature. Quite clean reaction took place within 10 min to give

Table 2. Synthesis of Cyclic β-Sulfonyl Amides **5** via the Favorskii Rearrangement of **4** with Amines

Entry	4	R^3R^4NH		NaH,Amine	Time	Product
	(n)	R^3	R^4	(equiv)	h	(Yield/%)[a]
a	**4a** (1)	$(CH_2)_5$		1.3	4.5	**5a** (78)
b	**4a** (1)	CH_2Ph	H	1.3	4.5	**5b** (43) + **8** (43)
c	**4a** (1)	$(CH_3)_3C$	H	3.2	21.0	**5c** (94)
d	**4b** (3)	$(CH_2)_5$		1.5	48.0	**5d** (72)
e	**4b** (3)	CH_2Ph	H	2.0	48.0	**9** (92)
f	**4b** (3)	$(CH_2)_5CH_3$	H	2.0	48.0	**5f** (71) + **10** (24)
g	**4c** (7)	$(CH_2)_5$		1.3	4.0	**5g** (94)[b]
h	**4c** (7)	CH_2Ph	H	1.3	0.5	**5h** (59)[c]
i	**4c** (7)	$(CH_3)_3C$	H	1.3	2.0	**5i** (59)[d]

a) Isolated yield. b) Ratio of isomers (18 : 76). c) Ratio of isomers (20 : 39). d) Ratio of isomers (16 : 43).

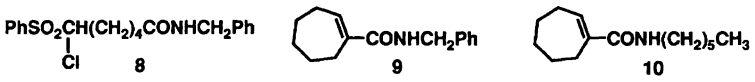
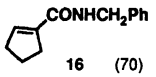
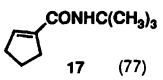
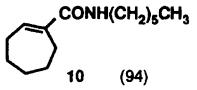
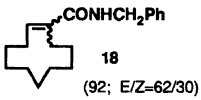
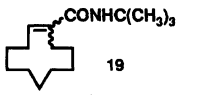
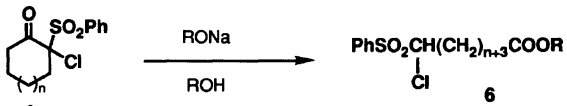


Table 3. β-Elimination of the Sulfonyl Group in Cyclic β-Sulfonyl Amides **5**

5	NaH and Amine (equiv)		Time	α,β-Unsaturated Amide (Yield/%)[a]
5b	(2)	H_2NCH_2Ph	7 h	 **16** (70)
5c	(4)	$H_2NC(CH_3)_3$	4 d	 **17** (77)
5f	(5)	$H_2N(CH_2)_5CH_3$	2 d	 **10** (94)
5h	(4)	H_2NCH_2Ph	22 h	 **18** (92; E/Z=62/30)
5i	(6)	$H_2NC(CH_3)_3$	4 d	 **19** (74; E/Z=39/35)

a) All reactions were carried out in dry THF at room temperature. Isolated yield.

Table 4. Carbon–Carbon Bond-Cleavage of Cyclic α-Chloro-α-sulfonyl Ketones **4** with Alkoxide and Hydroxide



Entry	4 / n	ROH	Time	6	(Yield/%)[a]
1	1	CH_3OH	10 min	**6a**	(99)
2	1	CH_3CH_2OH	10 min	**6b**	(85)
3	1	H_2O	10 min	**6c**	(85)
4	3	CH_3OH	21 h	**6d**	(92)
5	3	CH_3CH_2OH	5 h	**6e**	(61)[b]
6	3	H_2O	29 h	**6f**	(96)
7	7	CH_3OH	2.5 h	**6g**	(96)
8	7	H_2O	18 h	**6h**	(78)

a) Isolated yield. b) Carboxylic acid **6f** (31%) was obtained as a by-product.

methyl ester (**6a**, Table 4) in quantitative yield. Similarly, the reaction of **4a** with sodium ethoxide and hydroxide gave ethyl ester **6b** and carboxylic acid **6c**, both in 85% yield. The results are summarized in Table 4.

As shown in Table 4, the ring-cleavage of six-membered ketone **4a** proceeds quite easily (Entries 1—3). Sodium methoxide in methanol–THF is the condition of choice for obtaining esters (Entries 1, 4, and 7). Sodium ethoxide in ethanol was found to be problematical (Entries 2 and 5). Especially, the reaction of **4b** with sodium ethoxide gave the desired ester **6e** with a fair amount of carboxylic acid **6f** (Entry 5). Even when carefully dried ethanol was used, **6f** was obtained in more than 30% yield. We are not sure at present of the reason for the formation of acid **6f**.

In this paper, we reported a method for synthesizing carboxylic acids, esters, and amides from aldehydes and ketones. Because the procedure is simple and the yields are good, the presented method will prove to be valuable in the synthesis of carboxylic acids and their derivatives, especially amides.

Experimental

All melting points are uncorrected. ^1H NMR spectra were measured in a $CDCl_3$ solution with a JEOL FX-100 spectrometer. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion. Silica gel BW-127 ZH (Fuji–Devison) containing 2% fluorescence reagent 254 and a quartz column were used for column chromatography, and the products having UV absorption were detected by UV ir-

radiation. In experiments requiring a dry solvent, THF was distilled from diphenylketyl; diisopropylamine and CH_2Cl_2 were dried over CaH_2 and distilled.

2-Chloro-2-(*p*-tolylsulfonyl)-5-phenyl-3-pentanone (2a). A solution of 1-chloroethyl *p*-tolyl sulfoxide (**1**; $R_1=CH_3$; 1.2 g; 5.9 mmol) in 3 ml of dry THF was added dropwise to a solution of LDA (6 mmol) in 20 ml of THF at −60 °C. The mixture was stirred for 15 min and then 3-phenylpropanal (0.74 g; 6 mmol) was added. The reaction mixture was stirred for 5 min and then quenched with sat. aq NH_4Cl. The whole was extracted with ether–benzene. The organic layer was washed with brine, dried, and evaporated. The product was purified by silica-gel column chromatography to afford the adduct **7** (1.84 g; 93%) as a mixture of two diastereomers; IR (KBr) 3270 (OH) and 1030 (SO) cm^{-1}.

MCPBA (6 mmol) was added to a solution of **7** (1.74 g; 5.16 mmol) in CH_2Cl_2 (35 ml) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min and then at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 and the solution was washed successively with 5% NaOH, sat. aq sodium thiosulfate, and sat. aq $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by silica-gel column chromatography to give the sulfone (1.77 g; 96%) as colorless crystals (a mixture of two diastereomers). IR (KBr) 3525 (OH), 1315, 1140 (SO_2) cm^{-1}.

A solution of oxalyl chloride (0.38 ml; 4.5 mmol) in 12 ml of CH_2Cl_2 was cooled to −60 °C. A solution of DMSO (0.82 ml; 10.7 mmol) in 2 ml of dry CH_2Cl_2 was added to the reaction mixture and the solution was stirred at −60 °C for 5 min. A solution of the sulfone (1.4 g; 3.97 mmol) in 2 ml of CH_2Cl_2 was added dropwise to the mixture and the reaction mixture was stirred for 15 min. Triethylamine (2.5 ml) was added to the mixture and the solution was allowed to warm to 0 °C. Water (10 ml) was added and the whole was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The product was purified by silica-gel column chromatography to give the ketone **2a** (1.34 g; 96%) as a colorless oil. IR (neat) 1720 (CO), 1325, 1150 (SO_2) cm^{-1}; ^1H NMR δ=1.85 (3H, s), 2.45 (3H, s), 2.90 (2H, t, J=7 Hz), 3.2—3.4 (2H, m), and 7.1—7.7 (9H, m); MS m/z (%) 350 (M^+, 1), 218 (4), 194 (23), and 91 (100). Found: m/z 350.0751. Calcd for $C_{18}H_{19}ClO_3S$: M, 350.0742.

2-Chloro-2-(*p*-tolylsulfonyl)-3-nonanone (2b). Colorless oil; IR (neat) 1730 (CO), 1330, 1160 (SO_2) cm^{-1}; ^1H NMR δ=0.89 (3H, t, J=7 Hz), 1.1—1.8 (8H, m), 1.86 (3H, s), 2.47 (3H, s), 2.95 (2H, m), 7.36 (2H, d, J=8 Hz), and 7.76 (2H, d, J=8 Hz); MS m/z (%) 330 (M^+, 3.5), 218 (2.8), 155 (20), 139 (8), and 113 (100). Found: m/z 330.1055. Calcd for $C_{16}H_{23}ClO_3S$: M, 330.1055.

4-Chloro-5-methyl-1-phenyl-4-(*p*-tolylsulfonyl)-3-hexanone (2c). Colorless oil; IR (neat) 1720 (CO), 1340, 1160 (SO_2); ^1H NMR δ=0.90, 1.28 (each 3H, d, J=7 Hz), 2.44 (3H, s), 2.5—2.8 (2H, m), 3.08 (2H, quintet, J=7 Hz), and 6.9—7.7 (9H, m); MS m/z (%) 378 (M^+, 0.8), 231 (4), 222 (12), 157 (31), 133 (90), and 91 (100). Found: m/z 378.1044. Calcd for $C_{20}H_{23}ClO_3S$: M, 378.1034.

3-Chloro-2-methyl-3-(*p*-tolylsulfonyl)-4-decanone (2d). Colorless oil; IR (neat) 1720 (CO), 1340, 1160 (SO_2) cm^{-1}; ^1H NMR δ=0.82 (3H, d, J=7 Hz), 0.84 (3H, t, J=7 Hz), 1.28 (3H, d, J=7 Hz), 1.0—1.4 (9H, m), 2.2—2.5 (1H, m), 2.44 (3H, s), 3.06 (1H, quintet, J=6 Hz), 7.30, and 7.68 (each 2H, d, J=8 Hz); MS m/z (%) 358 (M^+, 4), 231 (3), 155 (9), and 113 (100). Found: m/z 358.1368. Calcd for $C_{18}H_{27}ClO_3S$: M, 358.1368.

***N*-Hexyl-2-benzyl-3-(*p*-tolylsulfonyl)butanamide (3a).** A mixture of NaH (0.35 mmol) and hexylamine (0.35 mmol) in 2.5 ml of dry THF was stirred at room temperature under N_2 for 5 min. To the mixture was added a solution of **2a** (100 mg; 0.29 mmol) in 1 ml of THF and the reaction mixture was stirred at room temperature for 4 h. The reaction was quenched with sat. aq NH_4Cl and the whole was extracted with ether–benzene. The product was purified by silica-gel column chromatography to afford **3a** (84 mg; 71%) as colorless crystals. Mp 122—123 °C (AcOEt–hexane); IR (KBr) 3370 (NH), 1645 (CO), 1300, 1140 (SO_2) cm^{-1}; ^1H NMR δ=0.87 (3H, t, J=7 Hz), 1.0—1.6 (methylene and methyl-H), 1.30 (3H, d, J=7 Hz), 2.44 (3H, s), 2.8—3.3 (6H, m), 6.01 (1H, t, J=6 Hz), and 6.9—7.7 (9H, m); MS m/z (%) 415 (M^+, 6) 260 (4), and 232 (100). Found: C, 69.26; H, 7.84; N, 3.27; S, 7.58%. Calcd for $C_{24}H_{33}NO_3S$: C, 69.36; H, 8.00; N, 3.37; S, 7.72%.

***N*,2-Dibenzyl-3-(*p*-tolylsulfonyl)butanamide (3b).** Mp 127—128 °C (AcOEt–hexane); IR (KBr) 3340 (NH), 1640 (CO), 1300, 1140, (SO_2) cm^{-1}; ^1H NMR δ=1.30 (3H, d, J=7 Hz), 2.43 (3H, s), 2.7—3.4 (4H, m), 4.32 (2H, m), 6.30 (1H, t, J=6 Hz, NH), and 6.9—7.7 (14H, m); MS m/z (%) 415 (M^+, 6), 260 (4), and 232 (100). Found: C, 70.89; H, 6.32; N, 3.23; S, 7.43%. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H,6.46; N, 3.32; S, 7.61%.

***N*,*N*-Diethyl-2-benzyl-3-(*p*-tolylsufonyl)butanamide (3c).** Mp 99—101 °C (AcOEt–hexane); IR (KBr) 1640 (CO), 1310, 1155 (SO_2) cm^{-1}; ^1H NMR δ=0.65 (3H, t, J=7 Hz), 0.97 (3H, t, J=7 Hz), 1.18 (3H, d, J=7 Hz), 2.44 (3H, s), 2.6—3.6 (8H, m), 7.19 (5H, s), 7.34, and 7.76 (each 2H, d, J=8 Hz); MS m/z (%) 387 (M^+, 3), 232 (23), and 204 (100). Found: C, 68.21; H, 7.53; N, 3.55; S, 8.31%. Calcd for $C_{22}H_{29}NO_3S$: C, 68.18; H, 7.54; N, 3.61; S, 8.27%.

***N*-[2-Benzyl-3-(*p*-tolylsulfonyl)butanoyl]piperidine (3d).** Mp 103–105 °C (AcOEt–hexane); IR (KBr) 1640 (CO), 1300, 1150 (SO_2) cm^{-1}; ^1H NMR δ=1.17 (3H, d, J=7 Hz), 1.1—1.6 (6H, m), 2.44 (3H, s), 2.9—3.8 (8H, m), 7.20 (5H, s), 7.32, and 7.75 (each 2H, d, J=8 Hz); MS m/z (%) 399 (M^+, 3), 244 (20), and 216 (100). Found: C, 68.84; H, 7.34; N, 3.45; S, 7.80%. Calcd for $C_{23}H_{29}NO_3S$: C, 68.97; H, 7.55; N, 3.50; S, 8.00%.

***N*-Hexyl-2-[1-(*p*-tolylsulfonyl)ethyl]heptanamide (3e).** Mp 96—98 °C (AcOEt–hexane); IR (KBr) 3350 (NH), 1650 (CO), 1300, 1140 (SO_2) cm^{-1}; ^1H NMR δ= 0.7—1.0 (6H, m), 1.1—1.6 (19H, d, J=7 Hz, and multiplet), 2.44 (3H, s), 2.7—3.4 (4H, m), 6.10 (1H, t, J=6 Hz, NH), 7.32, and 7.73 (each 2H, d, J=8 Hz); MS m/z (%) 395 (M^+, 4), 295 (5), 240 (34), 212 (22), and 170 (100). Found: C, 66.79; H, 9.41; N, 3.45; S, 8.01%. Calcd for $C_{22}H_{37}NO_3S$: C, 66.79; H, 9.43; N, 3.54; S, 8.11%.

***N*-Benzyl-2-[1-(*p*-tolylsulfonyl)ethyl]heptanamide (3f).** Mp 81—83 °C (AcOEt–hexane); IR (KBr) 3350 (NH), 1640 (CO), 1310, 1145 (SO_2) cm^{-1}; ^1H NMR δ=0.84 (3H, t, J=7 Hz), 1.23 (3H, d, J=7 Hz), 2.44 (3H, s), 2.8—3.3 (2H, m), 4.1—4.7 (2H, m), 6.42 (1H, t, J=6 Hz, NH), 7.30 (5H, s), 7.34, and 7.71 (each 2H, d, J=8 Hz); MS m/z (%) 401 (M^+, 3), 246 (4), 218 (4), and 106 (100). Found: C,

68.63; H, 7.87; N, 3.40; S, 7.87%. Calcd for $C_{23}H_{31}NO_3S$: C, 68.79; H, 7.78; N, 3.49; S, 7.98%.

***N,N*-Diethyl-2-[1-(*p*-tolylsulfonyl)ethyl]heptanamide (3g).** Mp 52—54 °C (AcOEt–hexane); IR (KBr) 1650 (CO), 1315, 1160, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.85 (3H, t, J=7 Hz), 1.0—2.0 (17H, m), 2.44 (3H, s), 3.0—3.8 (6H, m), 7.32, and 7.72 (each 2H, d, J=8 Hz); MS m/z (%) 367 (M^+, 0.3), 338 (0.6), and 212 (100). Found: C, 65.13; H, 9.05; N, 3.75; S, 8.68%. Calcd for $C_{20}H_{33}NO_3S$: C, 65.36; H, 9.05; N, 3.81; S, 8.72%.

***N*-[2-[1-(*p*-tolylsulfonyl)ethyl]heptanoyl]piperidine (3h).** Colorless oil; IR (neat) 1645 (CO), 1310, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.86 (3H, t, J=7 Hz), 1.16 (3H, d, J=7 Hz), 1.0—2.0 (methylene-H), 2.44 (3H, s), 3.0—3.8 (6H, m), 7.32, and 7.73 (each 2H, d, J=8 Hz); MS m/z (%) 379 (M^+, 0.7), 309 (0.5), and 224 (100). Found: m/z 379.2179. Calcd for $C_{21}H_{33}NO_3S$: M, 379.2179.

***N*-Hexyl-2-benzyl-4-methyl-3-(*p*-tolylsulfonyl)pentanamide (3i).** Mp 95—98 °C (AcOEt–hexane); IR (KBr) 3330 (NH), 1645 (CO), 1290, 1135 (SO_2) cm^{-1}; ^1H NMR δ=0.88 (3H, t, J=7 Hz), 1.22, 1.26 (each 3H, d, J=7 Hz), 1.1—1.6 (9H, m), 2.43 (3H, s), 2.7—3.4 (6H, m), 6.62 (1H, t, J=6 Hz, NH), and 6.7—7.6 (9H, m); MS m/z (%) 443 (M^+, 4), 288 (16), and 232 (100). Found: C, 70.38; H, 8.48; N, 3.08; S, 7.18%. Calcd for $C_{26}H_{37}NO_3S$: C, 70.39; H, 8.41; N, 3.16; S, 7.23%.

***N*,2-Dibenzyl-4-methyl-3-(*p*-tolylsulfonyl)pentanamide (3j).** Mp 130—133 °C (AcOEt–hexane); IR (KBr) 3280 (NH), 1640 (CO), 1310, 1140 (SO_2) cm^{-1}; ^1H NMR δ=1.19, 1.26 (each 3H, d, J=7 Hz), 2.43 (3H, s), 2.3—3.4 (5H, m), 4.1—4.7 (2H, m), and 6.7—7.6 (15H, m); MS m/z (%) 449 (M^+, 9), 294 (15), 238 (90), and 91 (100). Found: C, 72.03; H, 6.89; N, 3.03; S, 7.00%. Calcd for $C_{27}H_{31}NO_3S$:C, 72.29; H, 6.97; N, 3.12; S, 7.15%.

***N,N*-Diethyl-2-benzyl-4-methyl-3-(*p*-tolylsulfonyl)pentanamide (3k).** Mp 90—92 °C (AcOEt–hexane); IR (KBr) 1620 (CO), 1280, 1140 (SO_2) cm^{-1}; ^1H NMR δ=0.62, 0.95 (each 3H, t, J=7 Hz), 1.17 (6H, d, J=7 Hz), 2.44 (3H, s), 2.1—3.7 (9H, m), 7.12 (5H, m), 7.32, and 7.77 (each 2H, d, J=8 Hz); MS m/z (%) 415 (M^+, 0.4), 293 (0.5), and 260 (100). Found: C, 69.50; H, 8.06; N, 3.30; S, 7.52%. Calcd for $C_{24}H_{33}NO_3S$: C, 69.36; H, 8.00; N, 3.37; S, 7.72%.

***N*-[2-Benzyl-4-methyl-3-(*p*-tolylsulfonyl)pentanoyl]piperidine (3l).** Mp 90—92 °C (AcOEt–hexane); IR (KBr) 1630 (CO), 1290, 1145 (SO_2) cm^{-1}; ^1H NMR δ=1.06, 1.14 (each 3H, d, J=7 Hz), 1.0—1.4 (6H, m), 2.42 (3H, s), 2.0—3.8 (9H, m), 7.15 (5H, m), 7.31, and 7.78 (each 2H, d, J=8 Hz); MS m/z (%) 427 (M^+, 0.5), 294 (0.4), and 272 (100). Found: C, 70.32; H, 7.72; N, 3.23; S, 7.45%. Calcd for $C_{25}H_{33}NO_3S$: C, 70.22, H, 7.78; N, 3.28; S, 7.50%.

***N*-Hexyl-2-[2-methyl-1-(*p*-tolylsulfonyl)propyl]heptanamide (3m).** Colorless oil (1 : 1-diastereomeric mixture); IR (neat) 3320 (NH), 1650 (CO), 1300, 1145 (SO_2) cm^{-1}; ^1H NMR δ=0.87 (6H, m), 0.9—1.8 (methyl and methylene-H), 2.42, 2.44 (each s), 5.65, 6.81 (each t, J=6 Hz, NH); MS m/z (%) 423 (M^+, 4), 268 (100). Found: m/z 423.2796. Calcd for $C_{24}H_{41}NO_3S$: M, 423.2804.

***N*-Benzyl-2-[2-methyl-1-(*p*-tolylsulfonyl)propyl]heptanamide (3n).** Mp 111—113 °C (AcOEt–hexane); IR (KBr) 3280 (NH), 1640 (CO), 1300, 1140 (SO_2) cm^{-1}; ^1H NMR δ=0.82 (3H, t, J=7 Hz), 1.04, 1.13 (each 3H, d, J=7 Hz), 1.0—1.4 (8H, m), 2.28 (1H, m), 2.44 (3H, s), 2.70 (1H, m), 3.18 (1H, m), 4.2—4.7 (2H, m), and 7.0—7.7 (10H, m); MS m/z (%) 429 (M^+, 10), 274 (27), 204 (18), and 106 (100). Found: C, 70.11; H, 8.23; N, 3.20; S, 7.39%. Calcd for $C_{25}H_{35}NO_3S$: C, 69.89; H, 8.21; N, 3.26; S, 7.46%.

***N,N*-Diethyl-2-[2-methyl-1-(*p*-tolylsulfonyl)propyl]heptanamide (3o).** Mp 51–53.5 °C (hexane); IR (KBr) 1630 (CO), 1290, 1145 (SO_2) cm^{-1}; ^1H NMR δ= 0.7—1.8 (methyl and methylene-H), 2.30 (1H, m), 2.43 (3H, s), 3.1—3.8 (6H, m), 7.32, and 7.73 (each 2H, d, J=8 Hz); MS m/z (%) 396 ($[M+H]^+$, 0.4) and 240 (100). Found: C, 66.83; H, 9.53; N, 3.51; S, 8.01%. Calcd for $C_{22}H_{37}NO_3S$: C, 66.79; H, 9.43; N, 3.54; S, 8.10%

***N*-[2-[2-methyl-1-(*p*-tolylsulfonyl)propyl]heptanoyl]piperidine (3p).** Mp 72—75 °C (AcOEt–hexane); IR (KBr) 1640 (CO), 1300, 1140 (SO_2) cm^{-1}; ^1H NMR δ= 0.7—1.8 (methyl and methylene-H), 2.24 (1H, m), 2.43 (3H, s), 3.3—3.7 (6H, m), 7.30, and 7.73 (each 2H, d, J=8 Hz); MS m/z (%) 407 (M^+, trace) and 252 (100). Found: C, 67.63; H, 9.17; N, 3.41; S, 7.81%. Calcd for $C_{23}H_{37}NO_3S$: C, 67.77; H, 9.15; N, 3.44; S, 7.87%.

2-Chloro-2-(phenylsulfonyl)cyclohexanone (4a). NCS (260 mg; 1.95 mmol) was added to a solution of 2-(phenylthio)cyclohexanone (309 mg; 1.5 mmol) in 15 ml of CCl_4 and the reaction mixture was stirred at room temperature for 2.5 h. The reaction mixture was filtered and the CCl_4 was evaporated. The residue was dissolved in CH_2Cl_2 (5 ml) and MCPBA (3.3 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 2 h and then diluted with CH_2Cl_2. The solution was washed successively with 5% aq NaOH and sat. aq NH_4Cl. The product was purified by silica-gel column chromatography to afford the chloro sulfone **4a** (395 mg; 96%) as colorless crystals. Mp 70—71 °C (AcOEt–hexane); IR (KBr) 1730 (CO), 1315, 1165 (SO_2) cm^{-1}; ^1H NMR δ=1.7—2.6 (5H, m), 2.6—3.2 (1H, m), 2.83 (2H, dd, J=7, 6 Hz), and 7.4—8.0 (5H, m); MS m/z (%) 272 (M^+, 43), 141 (49), 131 (80), and 77 (100). Found: C, 52.91; H, 4.86; Cl, 12.71; S, 11.72%. Calcd for $C_{12}H_{13}ClO_3S$: C, 52.84; H, 4.80; Cl, 13.00; S, 11.75%.

2-Chloro-2-(phenylsulfonyl)cyclooctanone (4b). Yield, 92%: mp 107—109 °C (AcOEt–hexane); IR (KBr) 1725 (CO), 1320, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.5—1.1 (1H, m), 1.2—2.2 (7H, m), 2.3—2.7 (2H, m), 3.0—3.6 (2H, m), and 7.4—7.9 (5H, m); MS m/z (%) 300 (M^+, 4), 272 (7), 203 (7), 159 (45), 143 (53), and 77 (100). Found: C, 55.82; H, 5.54; Cl, 11.95; S, 10.85%. Calcd for $C_{14}H_{17}ClO_3S$: C, 55.90; H, 5.70; Cl, 11.79; S, 10.66%.

2-Chloro-2-(phenylsulfonyl)cyclododecanone (4c). Yield, 98%: mp 109—110 °C (AcOEt–hexane); IR (KBr) 1735 (CO), 1325, 1160, 1150 (SO_2) cm^{-1}; ^1H NMR δ= 0.9—1.8 (15H, m), 1.8—2.3 (2H, m), 3.6—4.4 (3H, m), and 7.4—8.0 (5H, m); MS m/z (%) 356 (M^+, 1), 328 (0.6), 215 (5), and 98 (100). Found: C, 60.48; H, 7.07; Cl, 10.08; S, 9.02%. Calcd for $C_{18}H_{25}ClO_3S$: C, 60.57; H, 7.06; Cl, 9.93; S, 8.98%.

***N*-[2-(Phenylsulfonyl)cyclopentylcarbonyl]piperidine (5a).** A mixture of the sulfone **4a** (89 mg; 0.33 mmol), piperidine (0.42 mmol), and NaH (0.42 mmol) in 5 ml of THF was stirred at room temperature for 4.5 h. The reaction was quenched with sat. aq NH_4Cl, and the whole was extracted with ether–benzene. The product was purified by silica-gel column chromatography to give **5a** (81 mg;

78%) as colorless crystals. Mp 74—76 °C; IR (KBr) 1640 (CO), 1305, 1150 (SO_2) cm^{-1}; ^1H NMR δ=1.1—2.4 (12H, m), 3.1—4.6 (5H, m), 4.2—4.5 (1H, m), and 7.3—8.0 (5H, m); MS *m/z* (%) 321 (M^+, 4), 225 (5), 180 (41), and 84 (100). Found: C, 63.35; H, 7.15; N, 4.25; S, 9.90%. Calcd for $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.21; N, 4.36; S, 9.98%.

***N*-Benzyl-2-(phenylsulfonyl)cyclopentane-1-carboxamide (5b).** Mp 92—95 °C (AcOEt–hexane); IR (KBr) 3390 (NH), 1655 (CO), 1300, 1155 (SO_2) cm^{-1}; ^1H NMR δ=1.6—2.2 (6H, m), 3.20 (1H, q, *J*=7 Hz), 3.7—4.0 (1H, m), 4.35 (2H, d, *J*=6 Hz), 6.46 (1H, t, *J*=6 Hz, NH), 7.26 (5H, m), and 7.4—7.9 (5H, m); MS *m/z* (%) 343 (M^+, 1.2), 247 (1), and 106 (100). Found: C, 66.46; H, 6.12; N, 3.99; S, 9.26%. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08; S, 9.34%.

***N*-Benzyl-6-chloro-6-(phenylsulfonyl)hexanamide (8).** Mp 87—88 °C (AcOEt–hexane); IR (KBr) 3320 (NH), 1660 (CO), 1330, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.4—2.0 (5H, m), 2.0—2.6 (3H, m), 4.40 (2H, d, *J*=6 Hz), 4.61 (1H, dd, *J*=10, 3 Hz), 5.81 (1H, m), 7.26 (5H, m), and 7.4—8.0 (5H, m); MS *m/z* (%) 379 (6), 202 (1), 149 (14), and 106 (100). Found: C, 60.07; H, 5.87; Cl, 9.34; N, 3.63; S, 8.31%. Calcd for $C_{19}H_{22}ClNO_3S$: C, 60.07; H, 5.84; Cl, 9.33; N, 3.69; S, 8.44%.

***N*-*t*-Butyl-2-(phenylsulfonyl)cyclopentane-1-carboxamide (5c).** Mp 117—118 °C (AcOEt–hexane); IR (KBr) 3430 (NH), 1685 (CO), 1310, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.27 (9H, s), 1.5—2.2 (6H, m), 3.06 (1H, q, *J*=7 Hz), 3.6—3.9 (1H, m), 6.84 (1H, m), 7.4—7.7 (3H, m), and 7.7—8.0 (2H, m); MS *m/z* (%) 309 (M^+, 7), 294 (41), 254 (18), and 58 (100). Found: C, 62.16; H, 7.47; N, 4.46; S, 10.12%. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53; S, 10.36%.

***N*-2-(phenylsulfonyl)cycloheptylcarbonylpiperidine (5d).** Mp 114—116 °C (AcOEt–hexane); IR (KBr) 1630 (CO), 1295, 1150 (SO_2) cm^{-1}; ^1H NMR δ=1.0—2.2 (16H, m), 3.1—3.6 (5H, m), 4.1—4.3 (1H, m), 7.3—7.7 (3H, m), and 7.7—8.0 (2H, m); MS *m/z* (%) 349 (M^+, 1), 263 (1), 239 (1), and 208 (100). Found: C, 65.29; H, 7.79; N, 3.91; S, 9.08%. Calcd for $C_{19}H_{27}NO_3S$: C, 65.30; H, 7.79; N, 4.01; S, 9.17%

***N*-Benzyl-1-cycloheptene-1-carboxamide (9).** Mp 68—70 °C (AcOEt–hexane); IR (KBr) 3380 (NH), 1670, 1625 (CO) cm^{-1}; ^1H NMR δ=1.4—1.9 (6H, m), 2.24 (2H, m), 2.47 (2H, m), 4.46 (2H, d, *J*=6 Hz), 6.00 (1H, m), 6.54 (1H, t, *J*=6 Hz), and 7.27 (5H, s); MS *m/z* (%) 229 (M^+, 100), 186 (75), and 172 (28). Found: C, 78.63; H, 8.36; N, 6.04%. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11%.

***N*-Hexyl-2-(phenylsulfonyl)cycloheptanecarboxamide (5f).** Colorless oil; IR (neat) 3350 (NH), 1660 (CO), 1300, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.86 (3H, t, *J*=7 Hz), 1.0—2.2 (18H, m), 2.8—3.4 (3H, m), 3.9—4.2 (1H, m), 5.76 (1H, t, *J*=6 Hz, NH), 7.3—7.7 (3H, m), and 7.7—8.0 (2H, m); MS *m/z* (%) 365 (M^+, 3), 265 (9), and 224 (100). Found: *m/z* 365.2031. Calcd for $C_{20}H_{31}NO_3S$: M, 365.2023.

***N*-Hexyl-1-cycloheptene-1-carboxamide (10).** Colorless oil; IR (neat) 3340 (NH), 1670, 1630 (CO) cm^{-1}; ^1H NMR δ=0.88 (3H, t, *J*=7 Hz), 1.0—1.9 (14H, m), 2.0—2.5 (4H, m), 3.1—3.4 (2H, m), 5.87 (1H, s), and 6.49 (1H, t, *J*=7 Hz); MS *m/z* (%) 223 (M^+, 77), 208 (7), 194 (20), 180 (47), 153 (47), and 123 (100). Found: *m/z* 223.1934. Calcd for $C_{14}H_{25}NO$: M, 223.1934.

***N*-[2-(Phenylsulfonyl)cycloundecyl]carbonylpiperidine (5g).** Less polar product (18%): colorless oil; IR (neat) 1640 (CO), 1305, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.9—2.2 (24H, m), 2.4—2.8 (1H, m), 3.30 (1H, m), 3.4—3.8 (4H, m), and 7.3—8.0 (5H, m); MS *m/z* (%) 406 ($[M+H]^+$, 0.5), 294 (1), 275 (2), and 264 (100). Found: *m/z* 406.2394. Calcd for $C_{23}H_{36}NO_3S$: M, 406.2413.

More polar product (76%): colorless oil; IR (neat) 1650, 1640 (CO), 1310, 1150 (SO_2) cm^{-1}; ^1H NMR δ=1.1—2.1 (24H, m), 3.2—3.7 (5H, m), 3.9—4.2 (1H, m), and 7.4—8.0 (5H, m); MS *m/z* (%) 405 (M^+, 0.1), 341 (0.2), and 264 (100). Found: *m/z* 405.2337. Calcd for $C_{23}H_{35}NO_3S$: M, 405.2336.

***N*-Benzyl-2-(phenylsulfonyl)cycloundecanecarboxamide (5h).** Less polar product (20%): colorless oil; IR (neat) 3350 (NH), 1660 (CO), 1300, 1145 (SO_2) cm^{-1}; ^1H NMR δ=0.8—2.4 (methylene-H), 3.01 (1H, m), 3.51 (1H, m), 4.44 (2H, m), 6.53 (1H, t, *J*=6 Hz, NH), 7.31 (5H, m), and 7.4—8.0 (5H, m); MS *m/z* (%) 427 (M^+, 7), 286 (27), and 106 (100). Found: *m/z* 427.2174. Calcd for $C_{25}H_{33}NO_3S$: M, 427.2178.

More polar product (39%): mp 147—150 °C (AcOEt–hexane); IR (KBr) 3350 (NH), 1660 (CO), 1300, 1150 (SO_2) cm^{-1}; ^1H NMR δ=0.8—1.0 (1H, m), 1.1—1.9 (17H, m), 2.7—3.0 (1H, m), 3.8—4.0 (1H, m), 4.1—4.6 (2H, m), 6.01 (1H, t, *J*=6 Hz), 7.27 (5H, m), and 7.4—8.0 (5H, m); MS *m/z* (%) 427 (M^+, 3), 286 (16), 279 (5), and 106 (100). Found: C, 70.23; H, 7.79; N, 3.22; S, 7.43%. Calcd for $C_{25}H_{33}NO_3S$: C, 70.22; H, 7.78; N, 3.28; S, 7.50%.

***N*-*t*-Butyl-2-(phenylsulfonyl)cycloundecanecarboxamide (5i).** Less polar product (16%): mp 180—182 °C (AcOEt–hexane); IR (KBr) 3375 (NH), 1680 (CO), 1300, 1140 (SO_2) cm^{-1}; ^1H NMR δ=1.0—2.4 (methylene-H), 1.37 (9H, s), 2.8—3.0 (1H, m), 3.46 (1H, m), 6.11 (1H, s), and 7.4—8.0 (5H, m); MS *m/z* (%) 393 (M^+, 10), 375 (3), 321 (21), 252 (32), and 179 (100). Found: *m/z* 393.2361. Calcd for $C_{22}H_{35}NO_3S$: M, 393.2336.

More polar product (43%): mp 152—154 °C (AcOEt–hexane); IR (KBr) 3400 (NH), 1670 (CO), 1300, 1145 (SO_2) cm^{-1}; ^1H NMR δ=1.0—2.4 (methylene-H), 1.32 (9H, s), 2.6—2.9 (1H, m), 3.7—4.0 (1H, m), 5.48 (1H, s), and 7.3—8.0 (5H, m); MS *m/z* (%) 393 (M^+, 0.2), 378 (4), 321 (20), and 252 (100). Found: C, 67.14; H, 9.01; N, 3.49%. Calcd for $C_{22}H_{35}NO_3S$: C, 67.14; H, 8.96; N, 3.56%.

***N*-Benzyl-2-ethylheptanamide (11).** To a refluxing suspension of Na (180 mg) in 3 ml of dry toluene was added Hg (3 g) dropwise with stirring. After a violent reaction, the solvent was evaporated under vacuum. To the residue (6% Na–Hg) methanol (3 ml) and Na_2HPO_4 (31 mg) were added. A solution of the sulfone **3f** (110 mg; 0.27 mmol) in 2 ml of methanol was added to the mixture and the suspension was stirred at room temperature for 4 h. The reaction mixture was filtered and the methanol was evaporated. The residue was dissoved in ether—benzene and the resulting solution was washed once with sat. aq NH_4Cl. The product was purified by silica-gel column chromatography to afford the amide **11** (54 mg; 80%) as a colorless oil. IR (neat) 3300 (NH), 1640 (CO) cm^{-1}; ^1H NMR δ=0.88, 0.90 (each 3H, t, *J*=7 Hz), 1.1—2.1 (11H, m), 4.44 (2H, d, *J*=6 Hz), 5.72 (1H, m), and 7.27 (5H, m); MS *m/z* (%) 247 (M^+, 54), 218 (10), 190 (26), and 177 (100). Found: *m/z* 247.1934. Calcd for $C_{16}H_{25}NO$: M, 247.1934.

***N*-(2-Ethylheptanoyl)piperidine (12).** Colorless oil; IR (neat) 1640 (CO) cm^{-1}; ^1H NMR δ=0.85 (6H, t, J=7 Hz), 1.0—1.8 (16H, m), 2.4—2.7 (1H, m), and 3.3—3.7 (4H, m); MS m/z (%) 225 (M^+, 6), 210 (4), 196 (15), 168 (23), and 155 (100). Found: m/z 225.2095. Calcd for $C_{14}H_{27}NO$: M, 225.2091.

(*E*)-*N*-Hexyl-2-pentyl-2-butenamide (13). A solution of **3e** (80 mg; 0.2 mmol), NaH (1 mmol), and hexylamine (1 mmol) in 5 ml of dry THF was stirred under N_2 at room temperature for 4 d. The reaction mixture was diluted with ether—benzene and the reaction was quenched with sat. aq NH_4Cl. The organic layer was washed once with sat. aq NH_4Cl. The product was purified by silica-gel column chromatography to afford **13** (48 mg; 62%) as a colorless oil and 32 mg of the starting material. Colorless oil; IR (neat) 3320 (NH), 1660 (CO) cm^{-1}; ^1H NMR δ=0.87 (6H, t, J=7 Hz), 1.0—1.7 (methylene-H), 1.72 (3H, d, J=7 Hz), 2.1—2.3 (2H, m), 3.28 (2H, q, J=6 Hz), 5.71 (1H, bs), and 6.20 (1H, q, J=7 Hz); MS m/z (%) 239 (M^+, 65), 224 (54), 210 (48), 182 (63), and 139 (100). Found: m/z 239.2251. Calcd for $C_{15}H_{29}NO$: M, 239.2248.

(*E*)-*N*-Benzyl-2-pentyl-2-butenamide (14). Mp 58—59.5 °C (AcOEt–hexane); IR (KBr) 3330 (NH), 1665, 1630 (CO) cm^{-1}; ^1H NMR δ=0.87 (3H, t, J=7 Hz), 1.1—1.5 (6H, m), 1.74 (3H, d, J=7 Hz), 2.32 (2H, t, J=7 Hz), 4.48 (2H, d, J=6 Hz), 5.96 (1H, bs), 6.26 (1H, q, J=7 Hz), and 7.27 (5H, m); MS m/z (%) 245 (M^+, 26), 230 (27), 188 (96), and 91 (100). Found: C, 78.15; H, 9.46; N, 5.63%. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71%.

2,*N*-Dibenzyl-4-methyl-2-pentenamide (15). A mixture of geometrica isomers; E/Z=4/1. Colorless oil; IR (neat) 3330 (NH), 1665, 1630 (CO) cm^{-1}; ^1H NMR δ=0.98, 1.04 (6H, d, J=7 Hz), 2.5—3.0 (1H, m), 3.52, 3.71 (2H, s), 4.36 (2H, d, J=6 Hz), 5.38, 6.28 (1H, d, J=7 Hz), 5.88 (1H, bs), and 6.8—7.4 (10H, m); MS m/z (%) 293 (M^+, 55), 278 (5), 250 (53), and 91 (100). Found: m/z 293.1783. Calcd for $C_{20}H_{23}NO$: M, 293.1779.

***N*-Benzyl-1-cyclopentenecarboxamide (16).** Mp 112—114 °C (AcOEt–hexane); IR (KBr) 3320 (NH), 1645, 1610 (CO) cm^{-1}; ^1H NMR δ=1.8—2.1 (2H, m), 2.48 (4H, m), 4.48 (2H, d, J=7 Hz), 5.96 (1H, bs), 6.52 (1H, t, J=2 Hz), and 7.26 (5H, m); MS m/z (%) 201 (M^+, 100), 173 (64), and 172 (51). Found: C, 77.75; H, 7.49; N, 6.88%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96%.

***N*-*t*-Butyl-1-cyclopentenecarboxamide (17).** Mp 112—114 °C (AcOEt–hexane); IR (KBr) 3350 (NH), 1645, 1620 (CO) cm^{-1}; ^1H NMR δ=1.38 (9H, s), 1.8—2.2 (2H, m), 2.3—2.6 (4H, m), 5.42 (1H, bs), and 6.42 (1H, t, J=2 Hz); MS m/z (%) 167 (M^+, 24), 152 (8), 112 (23), and 95 (100). Found: C, 71.49; H, 10.21; N, 8.28%. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.31%.

(*Z*)-*N*-Benzyl-1-cycloundecenecarboxamide (18). Mp 103—104 °C (AcOEt–hexane); IR (KBr) 3330 (NH), 1655, 1625 (CO) cm^{-1}; ^1H NMR δ=0.7—1.8 (14H, m), 2.1—2.4 (4H, m), 4.49 (2H, d, J=6 Hz), 5.67 (1H, t, J=7 Hz), 5.80 (1H, bs), and 7.28 (5H, m); MS m/z (%) 285 (M^+, 100), 242 (14), and 228 (31). Found: C, 80.01; H, 9.54; N, 4.84%. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91%.

(*E*)-**18**: Mp 99—101 °C (AcOEt–hexane); IR (KBr) 3360 (NH), 1660, 1620 (CO) cm^{-1}; ^1H NMR δ=0.9—1.7 (14H, m), 1.1—1.6 (4H, m), 4.50 (2H, d, J=6 Hz), 6.04 (1H, bs), 6.12 (1H, t, J=7 Hz), and 7.28 (5H, m); MS m/z (%) 285 (M^+, 100), 242 (7), and 228 (12). Found: C, 80.06; H, 9.56; N, 4.87%. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91%.

The geometry (E/Z) of **18** and **19** was determined by comparison of the chemical shift of the vinyl-H of **18** and **19** with that of **10**.

(*Z*)-*N*-*t*-Butyl-1-cycloundecenecarboxamide (19). Mp 136—138.5 °C (hexane); IR (KBr) 3350 (NH), 1655, 1630 (CO) cm^{-1}; ^1H NMR δ=0.8—1.8 (methylene-H), 1.38 (9H, s), 2.0—2.4 (4H, m), 5.27 (1H, bs), and 5.54 (1H, t, J=7 Hz); MS m/z (%) 251 (M^+, 100), 208 (8), and 195 (55). Found: C, 76.23; H, 11.63; N, 5.49%. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57%.

(*E*)-**19**: Mp 103—105.5 °C (hexane); IR (KBr) 3340 (NH), 1655, 1625 (CO) cm^{-1}; ^1H NMR δ=1.0—1.7 (methylene-H), 1.38 (9H, s), 2.1—2.5 (4H, m), 5.45 (1H, bs), and 5.97 (1H, t, J=7 Hz); MS m/z (%) 251 (100), 236 (7), 208 (9), 195 (36), and 179 (71). Found: m/z 251.2252. Calcd for $C_{16}H_{29}NO$: M, 251.2248.

Methyl 6-Chloro-6-(phenylsulfonyl)hexanoate (6a). The sulfonyl ketone **4a** (68 mg; 0.25 mmol) was dissolved in 1 ml of THF and 3 ml of methanol was added. To this solution was added a solution of sodium methoxide (0.38 mmol; prepared from NaH and methanol) in 1 ml of methanol. The reaction mixture was stirred at room temperature for 10 min. The reaction was quenched with sat. aq NH_4Cl and the solvent was evaporated. The residue was extracted with ether–benzene. The product was purified by silica-gel column chromatography to afford **6a** (76 mg; 99%) as colorless low melting solid. IR (neat) 1730 (CO), 1320, 1145 (SO_2) cm^{-1}; ^1H NMR δ=1.3—2.1 (5H, m), 2.2—2.6 (3H, m), 3.66 (3H, s), 4.62 (1H, dd, J=11, 3 Hz), and 7.4—8.0 (5H, m); MS m/z (%) 304 (M^+, 2), 273 (14), 163 (87), and 85 (100). Found: m/z 304.0535. Calcd for $C_{13}H_{17}ClO_4S$: M, 304.0535.

Ethyl 6-Chloro-6-(phenylsulfonyl)hexanoate (6b). Mp 49—52 °C (AcOEt–hexane); IR (KBr) 1740 (CO), 1315, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.25 (3H, t, J=7 Hz), 1.4—2.1 (5H, m), 2.1—2.6 (3H, m), 4.11 (2H, q, J=7 Hz), 4.63 (1H, dd, J=11, 4 Hz), and 7.4—8.0 (5H, m); MS m/z (%) 318 (M^+, 2), 273 (28), and 177 (100). Found: C, 52.79; H, 5.99; Cl, 10.91; S, 10.16%. Calcd for $C_{14}H_{19}ClO_4S$: C, 52.74; H, 6.01; Cl, 11.12; S, 10.06%.

6-Chloro-6-(phenylsulfonyl)hexanoic Acid (6c). To a solution of **4a** (82 mg; 0.3 mmol) in 4 ml of THF was added 5% aqueous NaOH (0.36 ml) with stirring. The reaction mixture was stirred at room temperature for 10 min, then quenched with sat. aq NH_4Cl. The whole was extracted with ether–benzene. The product was purified by silica-gel column chromatography to give 74 mg (85%) of **6c** as colorless crystals. Mp 82—83 °C (AcOEt–hexane); IR (KBr) 1705 (CO), 1340, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.2—2.1 (5H, m), 2.1—2.6 (3H, m), 4.64 (1H, dd, J=10, 3 Hz), 7.4—8.0 (5H, m), and 9.88 (1H, bs); MS m/z (%) 291 ($[M+H]^+$, 0.3), 273 (5), 149 (75), 113 (97), and 71 (100). Found: C, 49.63; H, 5.20; Cl, 12.33; S, 11.22%. Calcd for $C_{12}H_{15}ClO_4S$: C, 49.57; H, 5.20; Cl, 12.19; S, 11.03%.

Methyl 8-Chloro-8-(phenylsulfonyl)octanoate (6d). Colorless oil; IR (neat) 1740 (CO), 1330, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.2—2.0 (9H, m), 2.2—2.4 (3H, m), 3.65 (3H, s), 4.64 (1H, dd, J=10, 3Hz), and 7.4—8.0 (5H, m); MS m/z (%) 333 ($[M+H]^+$, 0.4), 301 (15), and 191 (100). Found: m/z 333.0924. Calcd for $C_{15}H_{22}ClO_4S$: M, 333.0925.

Ethyl 8-Chloro-8-(phenylsulfonyl)octanoate (6e). Mp 51—53 °C (AcOEt–hexane);IR (KBr) 1740 (CO), 1320, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.24 (3H, t, J=7 Hz), 1.2—2.0 (9H, m), 2.1—2.6 (3H, m), 4.10 (2H, q, J=7 Hz), 4.62 (1H, dd, J=11, 3 Hz), and 7.4—8.0 (5H, m); MS m/z (%) 347 ($[M+H]^+$, 2), 301 (20), and 205 (100). Found: C, 55.35; H, 6.67; Cl, 10.15; S, 9.36%. Calcd for $C_{16}H_{23}ClO_4S$: C, 55.40; H, 6.08; Cl, 10.13; S, 9.24%.

8-Chloro-8-(phenylsulfonyl)octanoic Acid (6f). Mp 87—89 °C (AcOEt–hexane); IR (KBr) 1710 (CO), 1330, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1,1—2.1 (9H, m), 2.1—2.6 (3H, m), 4.63 (1H, dd, J=11, 3 Hz), 7.4—8.0 (5H, m), and 9.40 (1H, bs); MS m/z (%) 319 ($[M+H]^+$, 0.6), 301 (8), 177 (58), and 123 (100). Found: C, 52.95; H, 6.03; Cl, 10.93; S, 10.02%. Calcd for $C_{14}H_{19}ClO_4S$: C, 52.74; H, 6.01; Cl, 11.12; S, 10.06%.

Methyl 12-Chloro-12-(phenylsulfonyl)dodecanoate (6g). Mp 63—65 °C (AcOEt–hexane); IR (KBr) 1740 (CO), 1320, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.0—2.0 (17H, m), 2.1—2.6 (3H, m), 3.65 (3H, s), 4.63 (1H, dd, J=10, 3 Hz), and 7.4—8.0 (5H, m); MS m/z (%) 388 (M^+, 0.4), 357 (12), and 247 (100). Found: C, 58.49; H, 7.53; Cl, 8.99; S, 8.24%. Calcd for $C_{19}H_{29}ClO_4S$: C, 58.67; H, 7.52; Cl, 9.11; S, 8.24%.

12-Chloro-12-(phenylsulfonyl)dodecanoic Acid (6h). Colorless oil; IR (neat) 1720 (CO), 1330, 1160 (SO_2) cm^{-1}; ^1H NMR δ=1.0—2.1 (17H, m), 2.1—2.6 (3H, m), 4.63 (1H, dd, J=10, 3 Hz), 7.4—8.0 (5H, m), and 10.03 (1H, bs); MS m/z (%) 374 (M^+, 0.1), 356 (3), 197 (87), and 143 (100). Found: m/z 347.1322. Calcd for $C_{18}H_{27}ClO_4S$: M, 374.1317.

We are grateful to Dr. Mikio Takeda and Dr. Norio Takamura, Tanabe Seiyaku Co., Ltd., for elemental analysis, to Noriko Sawabe and Fukiko Hasegawa of this laboratory for NMR and MS measurements, to Kenji Matsuda for technical assistance. This work was supported by a Grant-in-Aid for Scientific Research No. 01571168 from the Ministry of Education, Science and Culture, which is gratefully acknowledged.

References

1) S. Patai, "The Chemistry of Carboxylic Acids and Esters," John Wiley and Sons, London (1969); S. Patai, "The Chemistry of Amides," John Wiley and Sons, London (1970); S. Patai, "The Chemistry of Acyl Halides," John Wiley and Sons, London (1972); I. O. Sutherland, "Comprehensive Organic Chemisty," Pergamon Press, Oxford (1979), Vol. 2, pp. 593—1118.

2) A. S. Kende, *Org. React.*, **11**, 261 (1960); J. Mann, "Comprehensive Organic Synthesis," ed by G. Pattenden, Pergamon Press, Oxford (1991), Vol. 3, p. 839.

3) T. Satoh, *Yakugaku Zasshi*, **111**, 205 (1991); T. Satoh and K. Yamakawa, *Synlett*, **1992**, 455.

4) Preliminary communication of this study: T. Satoh, K. Oguro, J. Shishikura, N. Kanetaka, R. Okada, and K. Yamakawa, *Tetrahedron Lett.*, **33**, 1455 (1992).

5) T. Satoh, N. Itoh, K. Onda, Y. Kitoh, and K. Yamakawa, *Bull. Chem. Soc. Jpn.*, **65**, 2800 (1992).

6) T. Satoh, Y. Kaneko, T. Izawa, K. Sakata, and K. Yamakawa, *Bull. Chem. Soc. Jpn.*, **58**, 1983 (1985); T. Satoh, T. Oohara, Y. Ueda, and K. Yamakawa, *J. Org. Chem.*, **54**, 3130 (1989).

7) J. A. Marshall and D. E. Seitz, *J. Org. Chem.*, **39**, 1814 (1974); B. M. Trost and G. S. Massiot, *J. Am. Chem. Soc.*, **99**, 4405 (1977); D. Scholz, *Chem. Ber.*, **114**, 909 (1981); D. Scholz, *Justus Liebigs Ann. Chem.*, **1984**, 264.

8) B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, **98**, 4887 (1976); B. M. Trost and G. S. Massiot, *J. Am. Chem. Soc.*, **99**, 4405 (1972).

9) B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, *Tetrahedron Lett.*, **1976**, 3477; B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, **100**, 3435 (1978).

10) E. Block, "Reaction of Organosulfur Compounds," Academic Press, New York (1978), p. 46.