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Syntheses of (*rac*)3-Substituted 4-Methoxycarbonyl-1,3-thiazolidine-2-thiones *via* Rearrangement of a Substituted Group from *exo*-S to N in (*rac*)2-Substituted Thio-4-methoxycarbonyl-Δ^2-1,3-thiazolines[1,2]

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Based on the previously obtained structural information, (*rac*)3-substituted 4-carboxy-1,3-thiazolidine-2-thiones **10** were designed as new aldose reductase inhibitors which might be helpful in treating the chronic complications of diabetes. After several trials to find efficient reaction conditions for preparation of the precursors **15** of compounds **10**, a catalytic thermal rearrangement reaction of **14** proved to be practically available. Thus, various 3-substituted 4-methoxycarbonyl-1,3-thiazolidine-2-thiones **15a** and **15d**—**t** were readily synthesized by heating the corresponding 2-substituted thio-Δ^2-1,3-thiazolines **14a** and **14d**—**t** at 120 °C in the presence of 0.1 mol eq of the corresponding halides **13a** and **13d**—**t** without any organic solvent (Sykes conditions). A plausible reaction pathway for the catalytic thermal rearrangement reaction of **14a** or **14d**—**t** is presented.

Keywords——aldose reductase inhibitor; (*rac*)2-substituted thio-4-methoxycarbonyl-Δ^2-1,3-thiazoline; (*rac*)3-substituted 4-methoxycarbonyl-1,3-thiazolidine-2-thione; Sykes-type reaction; rearrangement; stepwise cationic reaction; concerted bimolecular transition state

Diabetes is a serious disease which has several chronic complications, such as retinopathy, nephropathy, neuropathy and cataracts.[3] The tissues involved in these complications have been shown to accumulate unusually high amounts of D-sorbitol and D-fructose, which are derived *via* the reduction of D-glucose by the enzyme aldose reductase (AR).[4] The pathogenic potential of sorbitol accumulation in the lens has been proved.[4]

On the basis of the idea that AR inhibitors may have great potential as therapeutic agents for the chronic complications of diabetes, several candidate compounds **1**—**9** have been developed by various pharmaceutical companies.[4a,5] We were interested in the fact that some AR inhibitors have the 1,3-thiazolidine moiety and a carboxyl group in their molecules.[4a] It is also well-known that several types of 1,3-thiazolidines exhibit various biological and physiological activities.[6] Thus, we designed (*rac*)3-substituted 4-carboxy-1,3-thiazolidine-2-thiones **10** as a new kind of AR inhibitors. A part of the work on their syntheses and AR inhibitory activities was reported preliminarily in 1984.[2,7]

Here we wish to present the full details of the synthesis of (*rac*)3-substituted 4-methoxycarbonyl-1,3-thiazolidine-2-thiones **11**, which can be converted to the carboxylic acids **10** by alkaline hydrolysis.

Based on the previous information,[8-10] we adopted the Sykes-type reaction involving rearrangement of a substituent (RCH_2) from the *exo*-S atom to the N atom in (*rac*)2-substituted thio-4-methoxycarbonyl-Δ^2-1,3-thiazolines **14** (Chart 1). In 1970, Sykes and Clark reported a similar rearrangement reaction for two simple compounds, 2-benzylthio- (**16**) and

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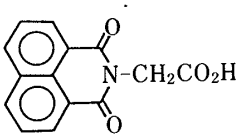

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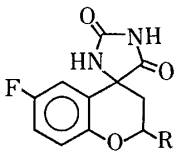
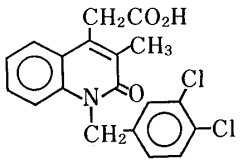


2 : R=H
3 : R=CH_3



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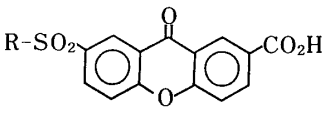
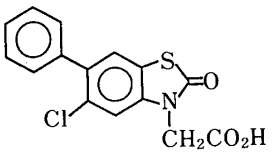


5 : R=$-N(CH_3)_2$
6 : R=$-N(CH_3)(CH_2)_2OH$



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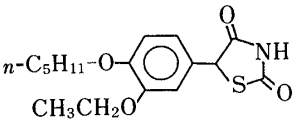

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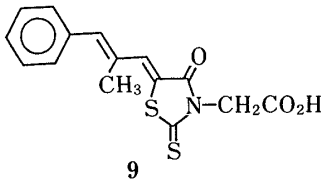

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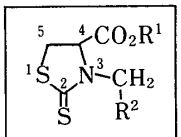
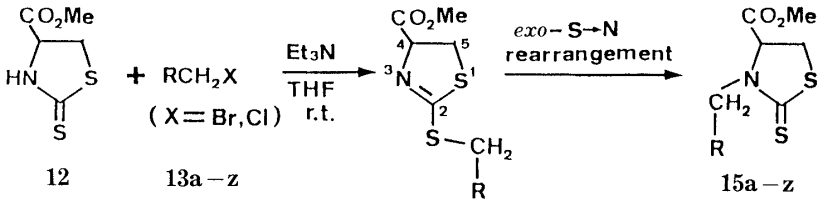


10 : R^1=H
11 : R^1=Me



12 13a–z 14a–z 15a–z

a : R=CO_2Me, X=Br
b : R=$(CH_2)_9CO_2Me$, X=Br
c : R=$(CH_2)_3CH_2-S-$(thiazolidine-2-thione-4-CO_2Me), X=Br
d : R=Ph, X=Br
e : R=2-OMe-Ph, X=Br
f : R=3-OMe-Ph, X=Br
g : R=4-OMe-Ph, X=Br
h : R=2-CO_2Me-Ph, X=Br
i : R=3-CO_2Me-Ph, X=Br
j : R=4-CO_2Me-Ph, X=Br
k : R=4-Me-Ph, X=Br
l : R=4-F-Ph, X=Br
m : R=4-Cl-Ph, X=Br
n : R=4-Br-Ph, X=Br
o : R=4-CN-Ph, X=Br
p : R=4-NO_2-Ph, X=Br
q : R=4-CH_2CO_2Me-Ph, X=Br
r : R=4-$CH=^{E}CHCO_2Me$-Ph, X=Br
s : R=$CH=^{E}CH$-Ph, X=Br
t : R=$CH=^{E}CH$-4-CO_2Me-Ph, X=Br
u : R=CH_2-phthalimide, X=Br
v : R=$(CH_2)_2$-phthalimide, X=Br
w : R=$(CH_2)_3$-phthalimide, X=Br
x : R=2-pyridyl, X=Cl·HCl
y : R=3-pyridyl, X=Cl·HCl
z : R=4-pyridyl, X=Cl·HCl

Chart 1

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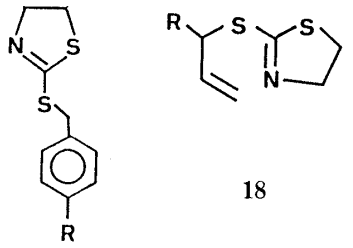
2-*p*-nitrobenzylthio-Δ^2-1,3-thiazoline (**17**).[8] Except for their two examples and Hirai and Kishida's results[9] on compounds **18** and **19**, there has been no detailed information about the rearrangement reaction in 4-substituted Δ^2-1,3-thiazolines. In order to obtain many kinds of test samples **10** in large amounts for AR inhibition studies, we wished to find efficient reaction conditions for the rearrangement (**14**→**15**). We also wished to clarify the relationship between the rearrangement and the structure of the thioethers **14**.

Various (*rac*)2-RCH_2S-4-methoxycarbonyl-Δ^2-1,3-thiazolines **14a**—**z** were readily prepared by treatment of (*rac*)4-methoxycarbonyl-1,3-thiazolidine-2-thione (**12**) with the corresponding halides (**13**: X=Br, Cl) (1 mol eq) in the presence of Et_3N (1 mol eq) in tetrahydrofuran (THF) at room temperature or under heating. The experimental results and physical data of the products **14a**—**z** are summarized in Tables I and II.

Because compound **12** shows an ambident anionic nature to nucleophiles under basic conditions, it can be converted to the N(3) or *exo*-S derivative depending on the nucleophiles employed. Here, *exo*-S derivatives **14** were exclusively obtained through soft–soft specific affinity.[10]

All halide compounds **13** except for **13r** and **13t** are commercially available; **13r** and **13t** were synthesized as follows. *p*-Formylcinnamic acid was treated with $NaBH_4$ in THF followed by methylation with CH_2N_2 to give the methyl ester **20** in 92% yield. Compound **20** was brominated with triphenylphosphine–bromine complex (1 mol eq) in acetonitrile, affording the bromide **13r** in 86% yield (Chart 2). Knoevenagel condensation between methyl *p*-formylbenzoate and malonic acid in piperidine–pyridine (1 : 10) at 60 °C gave *p*-



16 : R=H
17 : R=NO_2

18

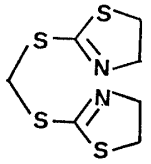


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TABLE I. Reaction of **12** with Halide Compounds **13**

Halide 13	Reaction conditions		Product 14	Yield (%)	Halide 13	Reaction conditions		Product 14	Yield (%)
	Temperature	Time (h)				Temperature	Time (h)		
13a	r.t.	1	**14a**	80	**13n**	r.t.	3	**14n**	85
13b	Reflux	18	**14b**	74	**13o**	r.t.	3	**14o**	89
13c	Reflux	18	**14c**	45	**13p**	r.t.	5	**14p**	95
13d	r.t.	4	**14d**	66	**13q**	r.t.	5	**14q**	89
13e	r.t.	1	**14e**	79	**13r**	r.t.	3	**14r**	64
13f	r.t.	3	**14f**	89	**13s**	r.t.	1	**14s**	85
13g	r.t.	1	**14g**	84	**13t**	r.t.	3	**14t**	61
13h	r.t.	5	**14h**	77	**13u**	Reflux	18	**14u**	37
13i	r.t.	5	**14i**	71	**13v**	Reflux	12	**14v**	49
13j	r.t.	5	**14j**	95	**13w**	Reflux	12	**14w**	60
13k	r.t.	2	**14k**	89	**13x**	r.t.	18	**14x**	59
13l	r.t.	3	**14l**	67	**13y**	r.t.	18	**14y**	63
13m	r.t.	3	**14m**	65	**13z**	r.t.	18	**14z**	50

r.t. = room temperature.

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TABLE II. Physical Data for **14**

Compound **14**	mp (°C)	Formula	Analysis (%) Calcd (Found) C H N	IR ν_{max} cm^{-1}	UV (EtOH) λ_{max} nm (log ε)
14a	Oil	$C_8H_{11}NO_4S_2$	M_r=249 (MS *m/z*: 249 (M^+))	1740 (film)	220 (3.78)
14b	Oil	$C_{17}H_{29}NO_4S_2$	M_r=375 (MS *m/z*: 375 (M^+))	1740 (film)	225 sh (3.82) 235 (3.85)
14c	Oil	$C_{15}H_{22}N_2O_4S_4$	M_r=422 (MS *m/z*: 422 (M^+))	1730 1560 (film)	226 sh (4.16) 235 (4.18)
14d	Oil	$C_{12}H_{13}NO_2S_2$	M_r=267 (MS *m/z*: 267 (M^+))	1740 (film)	222 (4.20)
14e	58	$C_{13}H_{15}NO_3S_2$	52.51 5.08 4.71 (53.00 5.24 4.47)	1730 ($CHCl_3$)	228 (4.17)
14f	Oil	$C_{13}H_{15}NO_3S_2$	M_r=297 (MS *m/z*: 297 (M^+))	1740 (film)	226 (4.22)
14g	61	$C_{13}H_{15}NO_3S_2$	52.51 5.08 4.71 (52.21 5.10 4.67)	1730 (KBr)	234 (4.28)
14h	77	$C_{14}H_{15}NO_4S_2$	51.68 4.65 4.30 (51.39 4.80 4.24)	1740 1710 ($CHCl_3$)	232 (4.21)
14i	60	$C_{14}H_{15}NO_4S_2$	51.68 4.65 4.30 (51.37 4.71 4.31)	1730 ($CHCl_3$)	231 (4.27)
14j	49	$C_{14}H_{15}NO_4S_2$	51.68 4.65 4.30 (51.29 4.75 4.28)	1725 (KBr)	240 (4.36)
14k	Oil	$C_{13}H_{15}NO_2S_2$	M_r=281 (MS *m/z*: 281 (M^+))	1740 (film)	227 (4.22)
14l	Oil	$C_{12}H_{12}FNO_2S_2$	M_r=285 (MS *m/z*: 285 (M^+))	1740 (film)	222 (4.14)
14m	Oil	$C_{12}H_{12}ClNO_2S_2$	M_r=301.5 (MS *m/z*: 301, 303 (M^+))	1740 (film)	229 (4.32)
14n	Oil	$C_{12}H_{12}BrNO_2S_2$	M_r=346 (MS *m/z*: 345, 347 (M^+))	1730 (film)	230 (4.32)
14o	79	$C_{13}H_{12}N_2O_2S_2$	53.41 4.14 9.58 (53.38 4.28 9.55)	2220 1740 ($CHCl_3$)	237 (4.31)
14p	50	$C_{12}H_{12}N_2O_4S_2$	46.14 3.87 8.97 (45.97 3.86 8.80)	1740 ($CHCl_3$)	219 (4.17)
14q	Oil	$C_{15}H_{17}NO_4S_2$	M_r=339 (MS *m/z*: 339 (M^+))	1730 (film)	227 (4.27)
14r	Amorphous	$C_{16}H_{17}NO_4S_2$	M_r=351 (MS *m/z*: 351 (M^+))	1710 1635 ($CHCl_3$)	222 (4.30) 288 (4.43)
14s	Oil	$C_{14}H_{15}NO_2S_2$	M_r=293 (MS *m/z*: 293 (M^+))	1740 (film)	258 (4.38)
14t	73	$C_{16}H_{17}NO_4S_2$	54.68 4.88 3.99 (54.46 4.98 4.00)	1710 (KBr)	221 (4.28) 284 (4.49)
14u	Oil	$C_{15}H_{14}N_2O_4S_2$	M_r=350 (MS *m/z*: 350 (M^+))	1730 (film)	221 (4.67)
14v	Oil	$C_{16}H_{16}N_2O_4S_2$	M_r=364 (MS *m/z*: 364 (M^+))	1770 1740 1710 ($CHCl_3$)	222 (4.68)
14w	Oil	$C_{17}H_{18}N_2O_4S_2$	M_r=378 (MS *m/z*: 378 (M^+))	1770 1740 1710 (film)	221 (4.66)
14x	Oil	$C_{11}H_{12}N_2O_2S_2$	M_r=268 (MS *m/z*: 268 (M^+))	1740 (film)	>210
14y	Oil	$C_{11}H_{12}N_2O_2S_2$	M_r=268 (MS *m/z*: 268 (M^+))	1740 (film)	>210
14z	Oil	$C_{11}H_{12}N_2O_2S_2$	M_r=268 (MS *m/z*: 268 (M^+))	1740 (film)	>210

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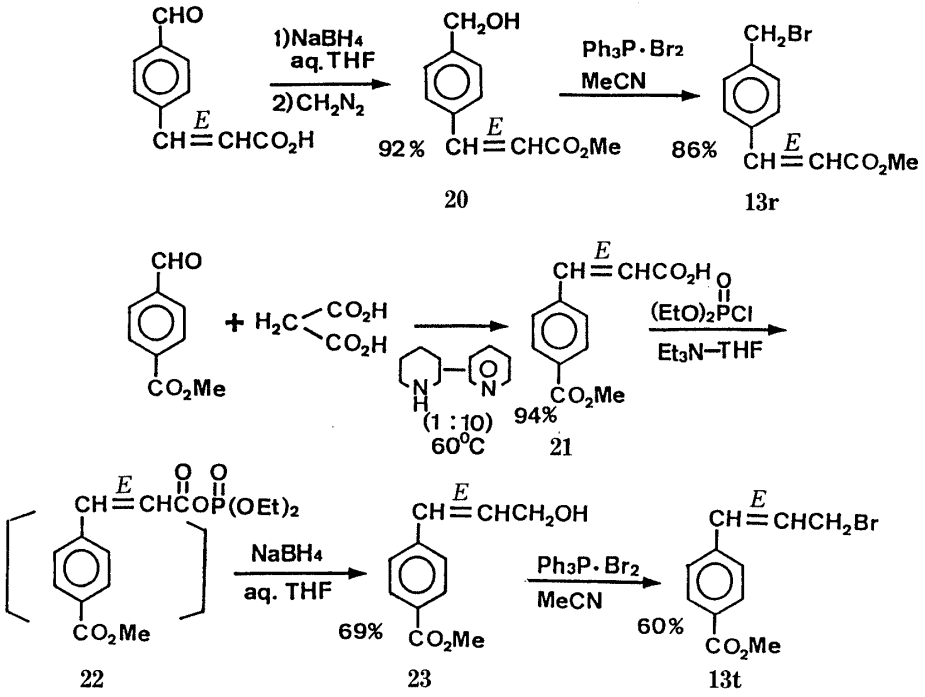

Chart 2

methoxycarbonylcinnamic acid (**21**) (94% yield), which was converted to the desired bromide **13t** *via* reduction of the mixed anhydride **22** with $NaBH_4$ followed by bromination (Chart 2).

Then, rearrangement of the RCH_2 group from the *exo*-S atom to the N atom in **14** was investigated in detail employing compound **14d** as a suitable model for the reaction.[8)]

First, a rearrangement reaction (**14d**→**15d**) was attempted in various organic solvents (see Table III) under reflux without benzyl bromide catalyst. However, the N-benzyl derivative **15d** was not obtained at all and the starting S-benzyl derivative **14d** was recovered in all cases (Table III). It was observed that compound **14d** decomposed at higher temperatures than 150 °C (*ca.* 3—5% decomposition in refluxing *N*,*N*-dimethylformamide (DMF) and *ca.* 80% decomposition in refluxing dimethyl sulfoxide (DMSO)). On the other hand, the rearrangement proceeded slightly in various refluxing solvents in the presence of 1 mol eq of benzyl bromide. Accordingly, this reaction seemed to be related to the boiling temperature of the solvents. It is noteworthy that this rearrangement proceeded in aprotic dipolar DMF at 120 °C without considerable decomposition, giving the N-benzyl derivative **15d** (55% yield) together with the starting material **14d** (34% recovery). Since the chemical yield of **15d** in DMF was higher than in non-polar solvents such as benzene, toluene, and xylene, this rearrangement was supposed to be ionic.

Subsequently, we carried out this rearrangement reaction in the presence of 0.1 mol eq of benzyl bromide[8)] without any solvent at 100, 120, and 150 °C (Table IV). After heating at each temperature for 3 h, the reaction mixture was analyzed by high performance liquid chromatography (HPLC) to give the results shown in Table III. This rearrangement reaction was also carried out at 120 °C for 3 h with or without 1 mol eq of benzyl bromide. The reaction conditions of heating at 120 °C in the presence of 0.1 mol eq of benzyl bromide without solvent were found to be the best among several trials.

Under the best reaction conditions, other similar *exo*-S derivatives **14a**—**c** and **14e**—**z** were subjected to the thermal catalytic rearrangement reaction. All results and physical data for **15** are listed in Tables V and VI.

As shown in Table V, all substituted benzyl groups on the *exo*-S position in **14** readily migrated to the N position, giving the corresponding N derivatives **15** in fairly good yields.

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TABLE III. Investigation of the Reaction Conditions for the *exo*-S→N Rearrangement of $PhCH_2$ Group in Refluxing Solvent[a]

Solvent	Without $PhCH_2Br$		With $PhCH_2Br$[b]	
	Recovery[c] of **14a** (%)	Yield[c] of **15a** (%)	Recovery[c] of **14a** (%)	Yield[c] of **15a** (%)
THF	99	0	97	3
Benzene	100	0	98	2
Toluene	100	0	97	3
Xylene	98	0	90	10
DMF	95	0	15	30
DMF (120 °C)			34	55
DMSO	19	0	Dec.	Dec.

a) All reactions were carried out for 3 h. *b*) One mol eq of $PhCH_2Br$ was employed with respect to **14d**. *c*) HPLC analysis.

TABLE IV. Investigation of the Reaction Conditions for the *exo*-S→N Rearrangement of $PhCH_2$ Group without Solvent[a]

Amounts[b] of $PhCH_2Br$ (mol eq)	Reaction temperature (°C)	Recovery[c] of **14a** (%)	Yield[c] of **15a** (%)
0.1	100	74	25
0.1	120	25	66
0.1	150	12	35
1	120	0	44
None	120	99	0

a) All reactions were carried out for 3 h. *b*) Based on compound **14a**. *c*) HPLC analysis.

Similar rearrangement of the cinnamyl derivatives **14s** and **14t** also proceeded smoothly to furnish the N-cinnamyl derivatives **15s** and **15t** in good yields. However, alkyl and phthalimidoalkyl groups in compounds **14b**, **14c**, and **14u**—**w** did not migrate to the N atom, but the starting material was recovered (in the cases of compounds **14b** and **14u**—**w**) or decomposition of the compound took place (for **14c**). Surprisingly, the *exo*-S→N rearrangement of the methoxycarbonylmethyl group in **14a** proceeded well, giving rise to **15a** in 52% yield. Although the *exo*-S picolyl derivatives **14x**—**z** were heated at 120 °C in the presence of 0.1 mol eq of the corresponding picolyl chloride hydrochloride and 0.5 mol eq of Et_3N, each reaction resulted in the decomposition of the starting material.

In order to get useful information for mechanistic consideration of this rearrangement reaction, we carried out the following experiments. Firstly, the rearrangement reaction of **14d** was carried out at 120 °C for 3 h in the presence of 0.1 mol eq of benzyl bromide and diphenylpicrylhydrazyl (**24**), a radical scavenger.[11] The result (**15d**, 63% yield; **14d**, 22% recovery) was in accord with that (Table IV) in the case without the radical scavenger **24**. Secondly, when compound **14v** was heated with 0.5 mol eq of *p*-methoxybenzyl bromide at 120 °C for 2 h, 3-*p*-methoxybenzyl-4-methoxycarbonyl-1,3-thiazolidine-2-thione (**15g**) was produced in 32% yield (Chart 3).

On the basis of all the results mentioned above, we reached the following conclusions. This catalytic thermal rearrangement from the *exo*-S atom to the N atom should proceed *via* an ionic pathway. Formation of the carbocation from the catalyst **13** seems to be essential for this rearrangement reaction, which has never been noted before.[8] This is also supported by

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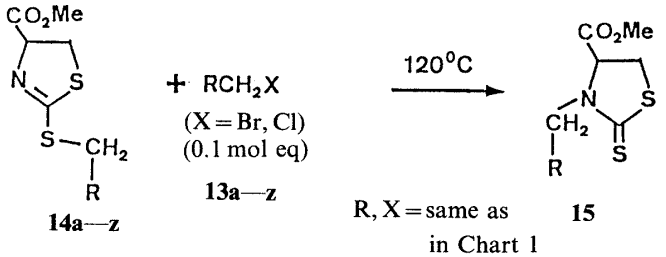
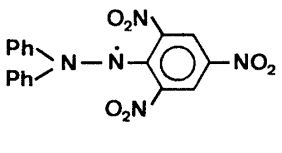
TABLE V. *exo*-S→N Rearrangement of RCH_2 Group in **14**



Compound		Reaction time (h)	Product	Yield[a] of **15** (%)	Compound		Reaction time (h)	Product	Yield[a] of **15** (%)
14	**13**		**15**		**14**	**13**		**15**	
14a	**13a**	6	**15a**	52	**14p**	**13p**	5	**15p**	66
14b	**13b**	16		Recovery (80%) of **14b**	**14q**	**13q**	6	**15q**	65
					14r	**13r**	6	**15r**	80
14c	**13c**	6		Decomposition of **14c**	**14s**	**13s**	2	**15s**	86
					14t	**13t**	4	**15t**	72
14d	**13d**	5	**15d**	78	**14u**	**13u**	16		Recovery (90%) of **14u**
14e	**13e**	1	**15e**	79					
14f	**13f**	3	**15f**	87	**14v**	**13v**	16		Recovery (90%) of **14v**
14g	**13g**	1	**15g**	98					
14h	**13h**	5	**15h**	51	**14w**	**13w**	16		Recovery (90%) of **14w**
14i	**13i**	5	**15i**	74					
14j	**13j**	5	**15j**	67	**14x**	**13x**	4[b]		Decomposition of **14x**
14k	**13k**	3	**15k**	74					
14l	**13l**	3	**15l**	73	**14y**	**13y**	4[b]		Decomposition of **14y**
14m	**13m**	3	**15m**	69					
14n	**13n**	3	**15n**	67	**14z**	**13z**	4[b]		Decomposition of **14z**
14o	**13o**	5	**15o**	62					

a) Isolation yield. *b*) The reaction was carried out in the presence of 0.5 mol eq of Et_3N with respect to **14x—z**.



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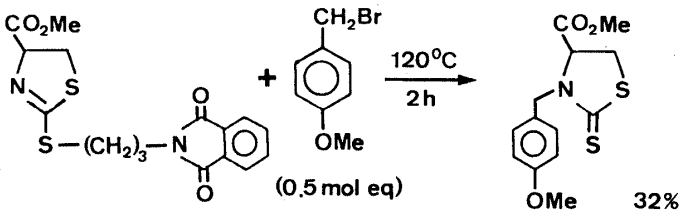

14v **13g** **15g**

Chart 3

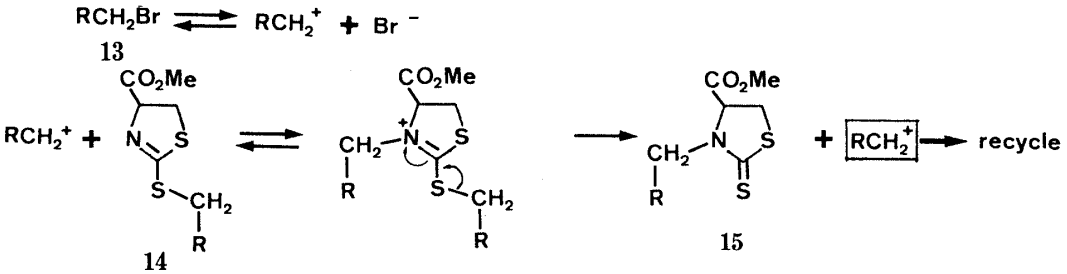

Chart 4

the substituent effect in the benzene ring of benzyl halides in the similar rearrangement of the substituted benzyl group in (*rac*)2-substituted benzylthio-4-methoxycarbonyl-Δ^2-1,3-thiazolines.[12] Thus, we can rationalize the rearrangement of the RCH_2 group from the *exo*-S

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TABLE VI. Physical Data for **15**

Compound **15**	mp (°C)	Formula	Analysis (%) Calcd (Found) C H N	IR ν_{max} cm^{-1}	UV (EtOH) λ_{max} nm (log ε)
15a	Oil	$C_8H_{11}NO_4S_2$	M_r=249 (MS *m/z*: 249 (M^+))	1740 (film)	278 (3.90)
15d	Oil	$C_{12}H_{13}NO_2S_2$	M_r=267 (MS *m/z*: 267 (M^+))	1740 (film)	258 sh (4.05), 280 (4.23)
15e	Oil	$C_{13}H_{15}NO_3S_2$	M_r=297 (MS *m/z*: 297 (M^+))	1740 (film)	221 sh (3.72), 265 sh (3.58), 280 (3.76)
15f	58	$C_{13}H_{15}NO_3S_2$	52.51 5.08 4.71 (52.15 5.13 4.58)	1740 ($CHCl_3$)	221 sh (4.10), 265 sh (4.04), 279 (4.20)
15g	Amorphous	$C_{13}H_{15}NO_3S_2$	52.51 5.08 4.71 (52.15 4.95 4.44)	1750 ($CHCl_3$)	229 (4.10), 265 sh (4.09), 277 (4.19)
15h	Oil	$C_{14}H_{15}NO_4S_2$	M_r=325 (MS *m/z*: 325 (M^+))	1770, 1750, 1720 (film)	230 (4.13), 278 (4.07), 282 sh (4.07)
15i	104	$C_{14}H_{15}NO_4S_2$	51.68 4.65 4.30 (51.57 4.67 4.29)	1730 ($CHCl_3$)	232 (4.12), 265 sh (4.00), 281 (4.13)
15j	110	$C_{14}H_{15}NO_4S_2$	51.68 4.65 4.30 (51.54 4.60 4.23)	1740, 1720 ($CHCl_3$)	235 sh (4.09), 260 (4.15), 277 (4.14)
15k	67	$C_{13}H_{15}NO_2S_2$	55.49 5.37 4.98 (55.66 5.38 5.02)	1740 ($CHCl_3$)	225 sh (3.97), 260 sh (4.01), 280 (4.17)
15l	Oil	$C_{12}H_{12}FNO_2S_2$	M_r=285 (MS *m/z*: 285 (M^+))	1740 (film)	267 sh (4.02), 278 (4.10)
15m	67	$C_{12}H_{12}ClNO_2S_2$	47.76 4.01 4.64 (47.72 4.13 4.59)	1740 ($CHCl_3$)	224 (4.06), 263 sh (4.02), 280 (4.16)
15n	114	$C_{12}H_{12}BrNO_2S_2$	41.63 3.49 4.05 (41.33 3.53 4.01)	1745 ($CHCl_3$)	225 (4.18), 262 sh (4.15), 278 (4.26)
15o	92	$C_{13}H_{12}N_2O_2S_2$	53.41 4.14 9.58 (53.58 4.29 9.53)	2250, 1745 ($CHCl_3$)	231 (4.26), 263 sh (4.23), 277 (4.25)
15p	113	$C_{12}H_{12}N_2O_4S_2$	46.14 3.87 8.97 (45.87 3.85 8.76)	1750 ($CHCl_3$)	276 (4.32)
15q	95	$C_{15}H_{17}NO_4S_2$	53.08 5.05 4.13 (52.79 5.42 3.79)	1730 ($CHCl_3$)	225 sh (4.08), 261 sh (4.04), 279 (4.16)
15r	123	$C_{16}H_{17}NO_4S_2$	54.68 4.88 3.99 (54.43 5.01 3.98)	1740, 1705, 1640 ($CHCl_3$)	283 (4.60)
15s	Oil	$C_{14}H_{15}NO_2S_2$	M_r=293 (MS *m/z*: 293 (M^+))	1750 (film)	264 (4.46)
15t	82	$C_{16}H_{17}NO_4S_2$	54.68 4.88 3.99 (54.64 4.90 4.04)	1740 ($CHCl_3$)	280 (4.62)

atom to the N atom in compound **14** in terms of a modification (Chart 4) of the Sykes mechanism.[8]

However, we can not rationalize the rearrangement **14a**→**15a** in terms of the stepwise

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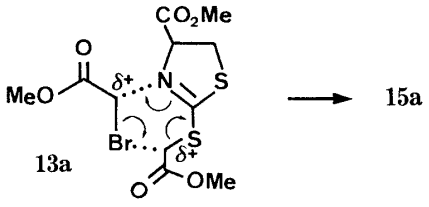

Fig. 1

cationic reaction pathway shown in Chart 4 because of the difficulty of formation of a cation such as $^{+}CH_2CO_2Me$. Presumably, this reaction can be explained in terms of a concerted bimolecular transition state (Fig. 1) where partial positive charge on the methylene carbons of the acetic acid derivatives, **13a** and **14a**, should be greater than those of **14b**, **14c** and **14u—w**.

Finally, we attempted a direct preparation of the desired N-benzyl derivative **15d** by treatment of (*rac*)4-methoxycarbonyl-1,3-thiazolidine-2-thione (**12**) with 1.5 mol eq of benzyl bromide (**13d**) in the presence of Et_3N (1.5 mol eq) or without Et_3N under heating at 120 °C. However, the reactions under both conditions resulted in the production of a mixture of **14d** and **15d** together with **12** (thin layer chromatography (TLC) analysis).

Thus, we established an efficient synthetic procedure for various (*rac*)3-substitued 4-methoxycarbonyl-1,3-thiazolidine-2-thiones **15**, which should be useful compounds for the development of new aldose reductase inhibitors.[2,7]

Experimental

Melting points (mp) were determined with Yanagimoto microapparatuses and are uncorrected. Infrared (IR) spectra were run on a Shimadzu IR 420 spectrophotometer. Ultraviolet (UV) spectra were recorded on a Hitachi 323 spectrophotometer. The ^{1}H- and ^{13}C-nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) spectra were recorded on a JEOL FX-200 spectrometer in $CDCl_3$ solutions unless otherwise noted. Chemical shifts are reported in δ values in ppm with tetramethylsilane as an internal standard. Mass spectra (MS) were determined with Hitachi RMU-6M and JEOL JMS-DX 300 mass spectrometers. HPLC analyses were carried out on a Shimadzu LC-3A instrument equipped with an SPD 2A detector. Extracts were dried over anhydrous Na_2SO_4. Kiesel gel 60 (70—230 mesh) (Merck) was employed for column chromatography.

(*rac*)4-Methoxycarbonyl-1,3-thiazolidine-2-thione (12)——Triethylamine (25 ml, 180 mmol) was added to a solution of *dl*-cysteine methyl ester hydrochloride (11.18 g, 65 mmol) and CS_2 (6 ml, 100 mmol) in CH_2Cl_2 (200 ml) with stirring under ice-cooling. After being stirred at room temperature for 4 h, the mixture was washed with aqueous saturated ammonium sulfate solution and dried. Evaporation of the solvent *in vacuo* gave an oily residue, which was chromatographed on a silica gel column with $CHCl_3$ to give compound **12** (7.5 g, 65%) as colorless prisms from CH_2Cl_2. mp 95—96 °C. ^{1}H-NMR δ: 3.82 (2H, d, J=7.4 Hz), 3.86 (3H, s), 4.87 (1H, t, J=7.4 Hz), 7.94—8.24 (1H, br s). ^{13}C-NMR δ: 35.6 (t), 53.5 (q), 63.8 (d), 168.9 (s), 201.4 (s). IR (KBr): 1730 cm^{-1}. UV λ_{max}^{EtOH} nm (log ε): 255 sh (3.81), 279 (4.81). MS *m/z*: 177 (M^+). *Anal.* Calcd for $C_5H_7NO_2S_2$: C, 33.87; H, 3.98; N, 7.91. Found: C, 33.67; H, 4.01; N, 7.92.

General Synthetic Method for (*rac*)2-RCH$_2$S-4-Methoxycarbonyl-Δ^2-1,3-thiazolines (14)——A mixture of a solution of compound **12** (10 mmol) in THF (40 ml) and Et_3N (10 mmol) was stirred at room temperature for 30 min. After addition of the halide compound **13** (10 mmol), the mixture was stirred at room temperature or refluxed under N_2. Insoluble materials were filtered off and the filtrate was evaporated *in vacuo*, giving an oily residue which was purified on a silica gel column to afford the corresponding (*rac*)2-RCH$_2$S-4-methoxycarbonyl-Δ^2-1,3-thiazoline (**14**). The results and some physical data are listed in Table I. The ^{1}H- and ^{13}C-NMR data of each thioether **14** are given below.

2-Methoxycarbonylmethylthio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14a)——Colorless oil. ^{1}H-NMR δ: 3.64 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.73 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.76, 3.79 (each 3H, s), 3.92, 4.01 (each 1H, d, J=16.0 Hz), 5.05 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), ^{13}C-NMR δ: 34.6 (t), 37.9 (t), 52.6 (q), 52.7 (q), 76.9 (d), 167.5 (s), 168.6 (s), 170.7 (s).

2-[10-(Methoxycarbonyl)decyl]thio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14b)——Colorless oil. ^{1}H-NMR δ: 1.27—1.70 (16H, m), 2.30 (2H, t, J=7.3 Hz), 3.12, 3.14 (each 1H, t, J=7.1 Hz), 3.58 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.67 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.67, 3.80 (each 3H, s), 5.07 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz). ^{13}C-NMR δ: 28.7 (t), 29.2 (t), 29.4 (t), 33.2 (t), 34.1 (t), 37.1 (t), 51.4 (q), 52.6 (q), 77.4 (d), 169.4 (s), 171.1 (s), 174.2 (s).

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The Dithioether (14c)——Colorless oil. ^{1}H-NMR δ: 1.67—1.78 (6H, m), 3.13, 3.15 (each 2H, t, J=7.3 Hz), 3.59 (1H, dd, J_{AB}=10.7 Hz, J_{AX}=8.8 Hz), 3.68 (1H, dd, J_{AB}=10.7 Hz, J_{BX}=7.8 Hz), 3.80 (6H, s), 5.06 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz). ^{13}C-NMR δ: 27.6 (t), 28.6 (t), 32.7 (t), 37.1 (t), 52.6 (q), 77.2 (d), 169. 1 (s), 171.0 (s).

2-Benzylthio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14d)——Colorless oil. ^{1}H-NMR δ: 3.26 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.70 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81 (3H, s), 4.37, 4.43 (each 1H, d, J=13.2 Hz), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 7.25—7.39 (5H, m). ^{13}C-NMR δ: 37.3 (t), 37.4 (t), 52.6 (q), 77.2 (d), 127.0 (d), 128.6 (d), 129.1 (d), 136.4 (s), 168.7 (s), 170.9 (s).

2-(2-Methoxybenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14e)——Colorless needles. mp 58 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.59 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.69 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81 (3H, s), 3.85 (3H, s), 4.42 (2H, s), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 6.81 (2H, m), 7.25, 7.38 (each 1H, m). ^{13}C-NMR δ: 32.1 (t), 37.3 (t), 52.6 (q), 55.5 (q), 77.3 (d), 110.6 (d), 120.4 (d), 125.0 (s), 129.0 (d), 130.9 (d), 157.6 (s), 169.3 (s), 171.1 (s).

2-(3-Methoxybenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14f)——Colorless oil. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.80 (3H, s), 3.81 (3H, s), 4.32, 4.42 (each 1H, d, J=13.1 Hz), 5.08 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 6.80, 6.93, 6.95, 7.24 (each 1H). ^{13}C-NMR δ: 37.3 (t), 37.4 (t), 52.6 (q), 55.3 (q), 77.2 (d), 113.3 (d), 114.8 (d), 121.4 (d), 129.6 (d), 138.0 (s), 159.8 (s), 168.7 (s), 170.9 (s).

2-(4-Methoxybenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14g)——Colorless needles. mp 61 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.61 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.70 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.79 (3H, s), 3.82 (3H, s), 4.32, 4.40 (each 1H, d, J=12.9 Hz), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 6.84, 7.29 (each 2H, AB type, J=8.8 Hz). ^{13}C-NMR δ: 36.9 (t), 37.3 (t), 52.6 (q), 55.3 (q), 77.3 (d), 114.1 (d), 128.4 (s), 130.3 (d), 159.2 (s), 168.9 (s), 171.0 (s).

2-(2-Methoxycarbonylbenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14h)——Colorless needles. mp 77 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.59 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.68 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81, 3.91 (each 3H, s), 4.77 (2H, s), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 7.33, 7.45, 7.62, 7.97 (each 1H). ^{13}C-NMR δ: 35.7 (t), 37.4 (t), 52.1 (q), 52.6 (q), 77.6 (d), 127.6 (d), 128.9 (s), 131.1 (d), 132.0 (d), 132.3 (d), 139.5 (s), 167.4 (s), 169.4 (s), 171.0 (s).

2-(3-Methoxycarbonylbenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14i)——Colorless needles. mp 60 °C ($CHCl_3$–*n*-hexane). ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=9.0 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.80, 3.92 (each 3H, s), 4.38, 4.47 (each 1H, d, J=13.5 Hz), 5.08 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 7.39, 7.60, 7.94, 8.04 (each 1H). ^{13}C-NMR δ: 36.7 (t), 37.5 (t), 52.1 (q), 52.6 (q), 77.1 (d), 128.7 (d), 128.8 (d), 130.2 (d), 130.6 (s), 133.6 (d), 137.2 (s), 166.7 (s), 168.3 (s), 170.8 (s).

2-(4-Methoxycarbonylbenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14j)——Colorless needles. mp 49 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.63 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.72 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.81, 3.91 (each 3H, s), 4.37, 4.48 (each 1H, d, J=13.6 Hz), 5.08 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.45, 7.98 (each 2H, AB type, J=8.5 Hz). ^{13}C-NMR δ: 36.8 (t), 37.6 (t), 52.1 (q), 52.7 (q), 77.1 (d), 129.1 (d), 129.9 (d), 130.2 (s), 142.1 (s), 166.8 (s), 168.3 (s), 170.8 (s).

2-(4-Methylbenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14k)——Colorless oil. ^{1}H-NMR δ: 2.32 (3H, s), 3.61 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.70 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81 (3H, s), 4.32, 4.41 (each 1H, d, J=13.1 Hz), 5.08 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 7.11, 7.26 (each 2H, AB type, J=8.0 Hz). ^{13}C-NMR δ: 21.1 (q), 37.1 (t), 37.3 (t), 52.6 (q), 77.3 (d), 129.0 (d), 129.3 (d), 133.3 (s), 137.3 (s), 168.9 (s), 171.0 (s).

2-(4-Fluorobenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14l)——Colorless oil. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81 (3H, s), 4.31, 4.41 (each 1H, d, J=13.4 Hz), 5.06 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=8.1 Hz), 6.99 (2H, dd, J=8.8, 8.8 Hz), 7.35 (2H, dd, J=8.8, 5.1 Hz). ^{13}C-NMR δ: 36.4 (t), 37.4 (t), 52.6 (q), 77.2 (d), 115.2 (d), 115.7 (d), 130.7 (d), 130.9 (d), 132. 4(s), 132.8 (s), 159.8 (s), 164.7 (s), 168.5 (s), 170.8 (s).

2-(4-Chlorobenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14m)——Colorless oil. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=9.0 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.81 (3H, s), 4.29, 4.40 (each 1H, d, J=13.4 Hz), 5.08 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 7.26, 7.32 (each 2H, AB type, J=9.0 Hz). ^{13}C-NMR δ: 36.4 (t), 37.5 (t), 52.6 (q), 77.1 (d), 128.7 (d), 130.5 (d), 133.4 (s), 135.3 (s), 168.3 (s), 170.8 (s).

2-(4-Bromobenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14n)——Colorless oil. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.80 (3H, s), 4.27, 4.38 (each 1H, d, J=13.6 Hz), 5.08 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.25, 7.43 (each 2H, AB type, J=8.5 Hz). ^{13}C-NMR δ: 36.4 (t), 37.5 (t), 52.6 (q), 77.1 (d), 121.4 (s), 130.8 (d), 131.6 (d), 135.8 (s), 168.2 (s), 170.7 (s).

2-(4-Cyanobenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14o)——Colorless needles. mp 79 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.64 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=9.0 Hz), 3.72 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.80 (3H, s), 4.33, 4.47 (each 1H, d, J=13.8 Hz), 5.07 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 7.50, 7.60 (each 2H, AB type, J=8.5 Hz). ^{13}C-NMR δ: 36.4 (t), 37.7 (t), 52.6 (q), 77.0 (d), 111.4 (s), 118.6 (s), 129.9 (d), 132.3 (d), 142.6 (s), 167.8 (s), 170.7 (s).

2-(4-Nitrobenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14p)——Colorless needles. mp 50 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.65 (1H, dd, J_{AB}=16.3 Hz, J_{AX}=9.0 Hz), 3.73 (1H, dd, J_{AB}=16.3 Hz, J_{BX}=8.1 Hz), 3.80 (3H,

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s), 4.30, 4.51 (each 1H, d, J=13.9 Hz), 5.08 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 7.58, 8.16 (each 2H, AB type, J=8.9 Hz). ^{13}C-NMR δ: 36.1 (t), 37.8 (t), 52.7 (q), 76.9 (d), 123.7 (d), 130.1 (d), 144.8 (s), 147.4 (s), 167. 8 (s), 170.7 (s).

2-(4-Methoxycarbonylmethylbenzylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14q)——Colorless oil. ^{1}H-NMR δ: 3.61 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=9.0 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 3.60 (2H, s), 3.69, 3.81 (each 3H, s), 4.33, 4.42 (each 1H, d, J=13.2 Hz), 5.08 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 7.22, 7.33 (each 2H, AB type, J=8.2 Hz). ^{13}C-NMR δ: 36.9 (t), 37.4 (t), 40.8 (t), 52.0 (q), 52.2 (q), 77.2 (d), 129.4 (d), 129.5 (d), 133.4 (s), 135.4 (s), 168.7 (s), 170.9 (s), 171.7 (s).

The Thioether (14r)——Amorphous. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=9.0 Hz), 3.72 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=8.1 Hz), 4.35, 4.45 (each 1H, d, J=13.6 Hz), 5.09 (1H, dd, J_{AX}=9.0 Hz, J_{BX}=8.1 Hz), 6.42 (1H, d, J=16.1 Hz), 7.40, 7.47 (each 2H, AB type, J=8.3 Hz), 7.67 (1H, d, J=16.1 Hz). ^{13}C-NMR δ: 36.7 (t), 37.5 (t), 51.6 (q), 52.6 (q), 77.0 (d), 117.9 (d), 128.2 (d), 129.6 (d), 133.6 (s), 139.1 (s), 144.1 (d), 167.2 (s), 168.2 (s), 170.8 (s).

2-Cinnamylthio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14s)——Colorless oil. ^{1}H-NMR δ: 3.61 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.78 (3H, s), 3.93, 4.02 (each 1H, dd, J=13.4, 7.3 Hz), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 6.30 (1H, dt, J=15.6, 7.3 Hz), 6.62 (1H, d, J=15.6 Hz), 7.19—7.39 (5H, m). ^{13}C-NMR δ: 35.5 (t), 37.3 (t), 52.6 (q), 77.2 (d), 123.7 (d), 126.5 (d), 127.8 (d), 128.5 (d), 133.9 (d), 136.6 (s), 168.5 (s), 170.9 (s).

2-(4-Methoxycarbonylcinnamylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14t)——Colorless needles. mp 73 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.63. (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.72 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.78, 3.91 (each 3H, s), 3.57, 3.62 (each 1H, d, J=7.1 Hz), 5.10 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 6.44 (1H, dt, J=15.6, 7.1 Hz), 6.66 (1H, d, J=15.6 Hz), 7.42, 7.98 (each 2H, AB type, J=8.5 Hz). ^{13}C-NMR δ: 35.2 (t), 37.4 (t), 52.0 (q), 52.7 (q), 77.2 (d), 126.3 (d), 126.8 (d), 129.3 (s), 129.9 (d), 132.9 (d), 141.1 (s), 166.8 (s), 168.3 (s), 170.9 (s).

The Thioether (14u)——Colorless oil. ^{1}H-NMR δ: 3.46 (2H, t, J=6.6 Hz), 3.59 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.82 (3H, s), 4.08, 4.09 (each 1H, t, J=6.6 Hz), 5.05 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.70—7.74, 7.83—7.88 (each 2H, m). ^{13}C-NMR δ: 31.1 (t), 36.9 (t), 37.4 (t), 52.6 (q), 77.2 (d), 123.4 (d), 132.2 (s), 134.0 (d), 167.8 (s), 168.0 (s), 170.8 (s).

The Thioether (14v)——Colorless oil. ^{1}H-NMR δ: 2.13 (2H, m), 3.16,.3.17 (each 1H, t, J=7.1 Hz), 3.58 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.67 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.77 (3H, s), 3.80 (2H, t, J=6.8 Hz), 5.12 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.70—7.77, 7.80—7.87 (each 2H, m). ^{13}C-NMR δ: 28.6 (t), 30.3 (t), 36.9 (t), 37.3 (t), 52.6 (q), 77.1 (d), 123.2 (d), 132.2 (s), 133.9 (d), 168.2 (s), 168.5 (s), 170.9 (s).

The Thioether (14w)——Colorless oil. ^{1}H-NMR δ: 1.78—1.81 (4H, m), 3.17 (2H, t, J=6.8 Hz), 3.58 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.67 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.71 (2H, t, J=6.8 Hz), 3.79 (3H, s), 5.05 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.69—7.76, 7.80—7.87 (each 2H, m). ^{13}C-NMR δ: 26.7 (t), 27.6 (t), 32.4 (t), 37.2 (t), 37.4 (t), 52.6 (q), 77.2 (d), 123.2 (d), 132.2 (s), 133.9 (d), 168.2 (s), 168.8 (s), 171.0 (s).

2-(2-Picolylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14x)——Colorless oil. ^{1}H-NMR δ: 3.62 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.71 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.80 (3H, s), 4.49, 4.59 (each 1H, d, J=13.9 Hz), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.18, 7.46, 7.64, 8.55 (each 1H, m). ^{13}C-NMR δ: 37.6 (t), 38.9 (t), 52.6 (q), 77.2 (d), 122.3 (d), 123.5 (d) 136.6 (d), 149.4 (d), 156.8 (s), 168.6 (s), 170.9 (s).

2-(3-Picolylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14y)——Colorless oil. ^{1}H-NMR δ: 3.63 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.72 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 3.81 (3H, s), 4.31, 4.43 (each 1H, d, J=13.7 Hz), 5.09 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.25, 7.74, 8.17, 8.62 (each 1H, m). ^{13}C-NMR δ: 34.1 (t), 37.6 (t), 52.6 (q), 77.1 (d), 123.4 (d), 133.0 (s), 136.6 (d), 148.7 (d), 150.3 (d), 168.0 (s), 170.8 (s).

2-(4-Picolylthio)-4-methoxycarbonyl-Δ^2-1,3-thiazoline (14z)——Colorless oil. ^{1}H-NMR δ: 3.64 (1H, dd, J_{AB}=11.0 Hz, J_{AX}=8.8 Hz), 3.73 (1H, dd, J_{AB}=11.0 Hz, J_{BX}=7.8 Hz), 4.28, 4.40 (each 1H, d, J=14.2 Hz), 5.08 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=7.8 Hz), 7.32, 8.54 (each 2H). ^{13}C-NMR δ: 35.7 (t), 37.7 (t), 52.6 (q), 77.0 (d), 124.0 (d), 146.1 (s), 149.9 (d), 167.8 (s), 170.7 (s).

Methyl *p*-Hydroxymethylcinnamate (20)——A solution of $NaBH_4$ (1.1 g, 28 mmol) in THF–H_2O (4:1) (25 ml) was added dropwise to a solution of *p*-formylcinnamic acid (5 g, 28 mmol) in THF (50 ml) with stirring. After being stirred at room temperature for 3 h, the reaction mixture was treated with 10% HCl and extracted with AcOEt. The extract was washed with aqueous Na_2CO_3 solution, then with brine, and dried. Evaporation of the organic solvents gave a colorless powder, which was dissolved in Et_2O–MeOH and treated with CH_2N_2 to afford a crude methyl ester **20**. This crude product was purified on a silica gel column with $CHCl_3$ to give pure compound **20** (5 g, 92%) as pale yellow needles from benzene. mp 89—90 °C. ^{1}H-NMR δ: 3.79 (3H, s), 4.69 (2H, s), 6.40 (1H, d, J=16.1 Hz), 7.36, 7.48 (each 2H, AB type, J=8.2 Hz), 7.65 (1H, d, J=16.1 Hz). IR (KBr): 3450, 1690, 1630 cm^{-1}. MS m/z: 192 (M^+). *Anal.* Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.62; H, 6.32.

Methyl *p*-Bromomethylcinnamate (13r)——Bromine (1.33 ml, 26 mmol) was added dropwise to a solution of triphenylphosphine (6.8 g, 26 mmol) in anhydrous CH_3CN (40 ml) under ice-cooling. To this solution was added a solution of compound **20** (5 g, 26 mmol) in anhydrous CH_3CN (20 ml) at room temperature with stirring. After being stirred for 1 h, the reaction mixture was evaporated *in vacuo* to give an oily residue, which was dissolved in Et_2O. The ethereal solution was washed with aqueous Na_2CO_3 solution, dried and evaporated *in vacuo* to give a crude product. Purification of the crude bromide on a silica gel column with benzene yielded the pure bromide **13r** (5.7 g, 86%) as

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colorless needles from Et_2O–*n*-hexane. mp 57—58 °C. ^{1}H-NMR δ: 3.81 (3H, s), 4.49 (2H, s), 6.44 (1H, d, J=16.0 Hz), 7.41, 7.50 (each 2H, AB type, J=8.3 Hz), 7.67 (1H, d, J=16.1 Hz). IR (KBr): 1720 cm^{-1}. MS *m/z*: 254, 256 (M^+). *Anal.* Calcd for $C_{11}H_{11}BrO_2$: C, 51.79; H, 4.35. Found: C, 51.59; H, 4.20.

***p*-Methoxycarbonylcinnamic Acid (21)**——A mixture of methyl *p*-formylbenzoate (20 g, 0.12 mol), malonic acid (32 g, 0.31 mol), piperidine (10 ml) and pyridine (100 ml) was heated at 60 °C for 1 h and then at 100 °C for 2 h with stirring. After being acidified with 10% HCl, the mixture was subjected to the usual work-up to give compound **21** (23.5 g, 94%) as a colorless amorphous powder from aqueous methanol. mp 246—247 °C. ^{1}H-NMR δ: 3.94 (3H, s), 6.54 (1H, d, J=16.1 Hz), 7.61, 8.07 (each 2H, d, J=8.2 Hz), 7.77 (1H, d, J=16.1 Hz). IR (KBr): 1710, 1670, 1630 cm^{-1}. MS *m/z*: 206 (M^+). *Anal.* Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.09; H, 4.83.

***p*-Methoxycarbonylcinnamic Alcohol (23)**——A mixture of a solution of carboxylic acid **21** (3 g, 14.6 mmol) in THF (150 ml), Et_3N (3 g, 29.7 mmol) and diethyl chlorophosphate (2.5 ml, 17.3 mmol) was stirred at room temperature for 3 h. The precipitate was filtered off. After evaporation of the filtrate, the residue was dissolved in THF (30 ml). This solution was reacted with a solution of $NaBH_4$ (550 mg, 14.6 mmol) in aqueous THF solution (30 ml) for 2 h at room temperature. The usual work-up of the reaction mixture afforded the alcohol **23** (3.3 g, 70%) as a colorless amorphous powder from Et_2O–*n*-hexane. mp 78 °C. ^{1}H-NMR δ: 3.91 (3H, s), 4.36, 4.37 (each 1H, d, J=5.1 Hz), 6.47 (1H, dt, J=15.9, 5.1 Hz), 6.67 (1H, d, J=15.9 Hz), 7.44, 7.99 (each 2H, AB type, J=8.3 Hz). IR (KBr): 3200, 1710 cm^{-1}. M_r Calcd for $C_{11}H_{12}O_3$: 192.079. Found: MS *m/z*: 192.078 (M^+).

***p*-Methoxycarbonylcinnamyl Bromide (13t)**——Bromine (0.93 ml, 18.2 mmol) was added dropwise to a solution of triphenylphosphine (4.8 g, 18.2 mmol) in anhydrous CH_3CN (40 ml) under ice-cooling. Next, a solution of the alcohol **23** (3.5 g, 18.2 mmol) in anhydrous CH_3CN (20 ml) was added with stirring. After being stirred at room temperature for 1 h, the reaction mixture was treated as usual to give the bromide **13t** (2.8 g, 60%) as colorless needles from Et_2O–*n*-hexane. mp 119 °C. ^{1}H-NMR δ: 3.92 (3H, s), 4.16 (2H, d, J=7.3 Hz), 6.50 (1H, dt, J=15.6, 7.3 Hz), 6.68 (1H, d, J=15.6 Hz), 7.44, 8.00 (each 2H, AB type, J=8.4 Hz). IR (KBr): 1715 cm^{-1}. MS *m/z*: 254, 256 (M^+). *Anal.* Calcd for $C_{11}H_{11}BrO_2$: C, 51.79; H, 4.35. Found: C, 52.09; H, 4.47.

Investigation of the Reaction Conditions for the Rearrangement of the Benzyl Group from the *exo*-S Atom to the N Atom in Compound 14d——In Refluxing Solvent: 2-Benzylthio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (**14d**) (267 mg, 1 mmol) was added to an organic solvent (2 ml) such as benzene, toluene, xylene, THF, DMF or DMSO and then the mixture with or without benzyl bromide (0.12 ml, 1 mmol) was refluxed for 3 h under N_2. The reactions were checked by HPLC analysis, and the results are listed in Table II.

Without Organic Solvent: A mixture of 2-benzylthio-4-methoxycarbonyl-Δ^2-1,3-thiazoline (**14d**) (267 mg, 1 mmol) with benzyl bromide (0.012 ml, 0.1 mmol or 0.12 ml, 1 mmol) was heated under the several reaction conditions shown in Table IV for 3 h. All experimental results determined by HPLC are summarized in Table IV.

Analytical Conditions by HPLC——Machine, Shimadzu LC-3A instrument; column, μ-Porasil i.d. 4 mm × 25 cm (Waters); detection, UV 245 nm; elution solvent system, CH_2Cl_2–EtOH (1000 : 1); flow rate, 2 ml/min; retention times, **15d** = 1.97 min and **14d** = 3.25 min. Absolute yields of **14d** and **15d** were calculated based on their calibration curves.

General Synthetic Method for (*rac*)3-RCH$_2$-4-Methoxycarbonyl-1,3-thiazolidine-2-thiones (15)——A mixture of (*rac*)2-RCH$_2$S-4-methoxycarbonyl-Δ^2-1,3-thiazoline (**14**) (10 mmol) and the corresponding halide (**13**) (1 mmol) was heated at 120 °C under N_2 with monitoring of the reaction by TLC. The reaction mixture was chromatographed on a silica gel column to give pure **15**. The results and some physical data are listed in Tables V and VI. The ^{1}H- and ^{13}C-NMR data of each racemic compound **15** are recorded below.

3-Methoxycarbonylmethyl-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15a)——Pale yellow oil. ^{1}H-NMR δ: 3.52 (1H, dd, J_{AB}=11.2 Hz, J_{AX}=3.4 Hz), 3.76 (1H, dd, J_{AB}=11.2 Hz, J_{BX}=8.8 Hz), 3.78, 3.84 (each 3H, s), 4.07, 5.43 (each 1H, d, J=18.0 Hz), 5.07 (1H, dd, J_{AX}=3.4 Hz, J_{BX}=8.8 Hz). ^{13}C-NMR δ: 30.8 (t), 48.9 (t), 52.5 (q), 53.3 (q), 67.6 (d), 168.2 (s), 168.9 (s), 199.3 (s).

3-Benzyl-4-methoxycarbonyl-1,3-thiazoline-2-thione (15d)——Colorless oil. ^{1}H-NMR δ: 3.39 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.9 Hz), 3.52 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.8 Hz), 3.80 (3H, s), 4.59 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.8 Hz), 4.30, 5.89 (each 1H, d, J=14.9 Hz), 7.26—7.83 (5H, m). ^{13}C-NMR δ: 30.9 (t), 51.9 (q), 53.2 (t), 66.7 (d), 128.4 (d), 129.0 (d), 135.0 (s), 169.0 (s), 198.0 (s).

3-(2-Methoxybenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15e)——Colorless oil. ^{1}H-NMR δ: 3.31 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.4 Hz), 3.53 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.8 Hz), 3.80 (3H, s), 3.82 (3H, s), 4.74 (1H, dd, J_{AX}=2.4 Hz, J_{BX}=8.8 Hz), 4.54, 5.58 (each 1H, d, J=14.7 Hz), 6.89, 6.96, 7.29, 7.37 (each 1H, m). ^{13}C-NMR δ: 31.2 (t), 47.2 (t), 53.0 (q), 55.4 (q), 67.5 (d), 110.7 (d), 120.9 (d), 123.0 (s), 129.9 (d), 131.3 (d), 157.7 (s), 169.5 (s), 197.5 (s).

3-(3-Methoxybenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15f)——Colorless needles. mp 58 °C (Et_2O–*n*-hexane). ^{1}H-NMR δ: 3.39 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=2.9 Hz), 3.53 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.8 Hz), 3.80 (3H, s), 3.82 (3H, s), 4.61 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.8 Hz), 4.25, 5.88 (each 1H, d, J=15.0 Hz), 6.84, 7.27 (each 1H), 6.86 (2H). ^{13}C-NMR δ: 30.9 (t), 51.8 (t), 53.1 (q), 55.3 (q), 66.7 (d), 113.8 (d), 114.1 (d), 120.5 (d), 130.1 (d), 136.4 (s), 160.1 (s), 169.0 (s), 198.0 (s).

3-(4-Methoxybenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15g)——Amorphous. ^{1}H-NMR δ: 3.36 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.9 Hz), 3.50 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.5 Hz), 3.81 (6H, s), 4.58 (1H, dd, J_{AX}=2.9 Hz,

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J_{BX}=8.5 Hz), 4.24, 5.80 (each 1H, d, J=14.8 Hz), 6.88, 7.22 (each 2H, AB type, J=8.6 Hz). ^{13}C-NMR δ: 30.9 (t), 51.4 (t), 53.1 (q), 55.3 (q), 66.6 (d), 114.7 (d), 127.0 (s), 130.0 (d), 159.8 (s), 169.2 (s), 197.7 (s).

3-(2-Methoxycarbonylbenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15h)——Colorless oil. ^{1}H-NMR δ: 3.37 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.2 Hz), 3.56 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.8 Hz), 3.80, 3.90 (each 3H, s), 4.72 (1H, dd, J_{AX}=2.2 Hz, J_{BX}=8.8 Hz), 4.97, 5.93 (each 1H, d, J=15.4 Hz), 7.52, 7.93 (each 2H, m). ^{13}C-NMR δ: 31.2 (t), 49.5 (t), 52.4 (q), 51.3 (q), 67.3 (d), 128.2 (d), 130.0 (s), 130.1 (d), 130.8 (d), 132.6 (d), 136.3 (s), 167.5 (s), 169.2 (s), 198.3 (s).

3-(3-Methoxycarbonylbenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15i)——Colorless needles. mp 104 °C (Et_2O–n-hexane). ^{1}H-NMR δ: 3.41 (1H, dd, J_{AB}=11.6 Hz, J_{AX}=2.9 Hz), 3.55 (1H, dd, J_{AB}=11.6 Hz, J_{BX}=8.5 Hz), 3.81, 3.93 (each 3H, s), 4.59 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.5 Hz), 4.39, 5.92 (each 1H, d, J=15.0 Hz), 7.45, 7.54, 7.93, 8.01 (each 1H). ^{13}C-NMR δ: 31.0 (t), 51.5 (t), 52.3 (q), 53.3 (q), 66.8 (d), 129.3 (d), 129.4 (d), 129.6 (d), 131.1 (s), 132.9 (d), 135.6 (s), 166.5 (s), 168.9 (s), 198.4 (s).

3-(4-Methoxycarbonylbenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15j)——Colorless powder. mp 110 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.42 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.9 Hz), 3.56 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.6 Hz), 3.80, 3.92 (each 3H, s), 4.58 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.6 Hz), 4.40, 5.93 (1H, d, J=15.4 Hz), 7.37, 8.03 (each 2H, AB type, J=8.2 Hz). ^{13}C-NMR δ: 30.9 (t), 51.5 (t), 52.2 (q), 53.2 (q), 66.8 (d), 128.2 (d), 130.3 (d), 140.1 (s), 166.5 (s), 168.8 (s), 198.5 (s).

3-(4-Methylbenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15k)——Colorless needles. mp 67 °C (Et_2O–n-hexane). ^{1}H-NMR δ: 2.35 (3H, s), 3.37 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.8 Hz), 3.51 (1H, dd, J_{AX}=11.5 Hz, J_{BX}=8.7 Hz), 3.80 (3H, s), 4.58 (1H, dd, J_{AX}=2.8 Hz, J_{BX}=8.7 Hz), 4.24, 5.85 (each 1H, d, J=14.9 Hz), 7.17 (4H, s). ^{13}C-NMR δ: 21.1 (q), 30.9 (t), 51.7 (t), 53.1 (q), 66.7 (d), 128.4 (d), 129.7 (d), 131.9 (s), 138.2 (s), 169.0 (s), 197.8 (s).

3-(4-Fluorobenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15l)——Colorless oil. ^{1}H-NMR δ: 3.39 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.9 Hz), 3.53 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.5 Hz), 3.81 (3H, s), 4.58 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.5 Hz), 4.31, 5.83 (1H, dd, J=14.9 Hz), 7.05 (2H, dd, J=8.7, 8.6 Hz), 7.29 (2H, dd, J=8.7, 5.4 Hz). ^{13}C-NMR δ: 30.8 (t), 51.1 (t), 53.2 (q), 66.7 (d), 115.7 (d), 116.2 (d), 130.2 (d), 130.4 (d), 130.9 (s), 160.3 (s), 165.2 (s), 168.9 (s), 198.2 (s).

3-(4-Chlorobenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15m)——Colorless needles. mp 67 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.40 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=3.2 Hz), 3.54 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.6 Hz), 3.80 (3H, s), 4.58 (1H, dd, J_{AX}=3.2 Hz, J_{BX}=8.6 Hz), 4.30, 5.83 (each 1H, d, J=15.1 Hz), 7.24, 7.34 (each 2H, AB type, J=8.6 Hz). ^{13}C-NMR δ: 30.9 (t), 51.2 (t), 53.2 (q), 66.7 (d), 129.2 (d), 129.8 (d), 133.5 (s), 134.4 (s), 168.9 (s), 198.3 (s).

3-(4-Bromobenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15n)——Colorless needles. mp 114 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.40 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=3.2 Hz), 3.54 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.5 Hz), 3.80 (3H, s), 4.58 (1H, dd, J_{AX}=3.2 Hz, J_{BX}=8.5 Hz), 4.29, 5.82 (each 1H, d, J=15.1 Hz), 7.18, 7.49 (each 2H, AB type, J=8.2 Hz). ^{13}C-NMR δ: 30.8 (t), 51.2 (t), 53.2 (q), 66.7 (d), 122.5 (s), 130.1 (d), 132.2 (d), 134.1 (s), 168.9 (s), 198.3 (s).

3-(4-Cyanobenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15o)——Colorless powder. mp 92 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.45 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=3.2 Hz), 3.59 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.6 Hz), 3.80 (3H, s), 4.60 (1H, dd, J_{AX}=3.2 Hz, J_{BX}=8.6 Hz), 4.44, 5.88 (each 1H, d, J=15.5 Hz), 7.42, 7.66 (each 2H, AB type, J=8.5 Hz). ^{13}C-NMR δ: 31.0 (t), 51.3 (t), 53.3 (q), 67.1 (d), 111.9 (s), 118.4 (s), 128.8 (d), 132.7 (d), 140.4 (s), 168.7 (s), 198.8 (s).

3-(4-Nitrobenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15p)——Colorless powder. mp 113 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.47 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=3.2 Hz), 3.61 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.6 Hz), 3.82 (3H, s), 4.63 (1H, dd, J_{AX}=3.2 Hz, J_{BX}=8.6 Hz), 4.50, 5.92 (each 1H, d, J=15.8 Hz), 7.48, 8.22 (each 2H, AB type, J=8.7 Hz). ^{13}C-NMR δ: 30.9 (t), 51.1 (t), 53.3 (q), 67.1 (d), 124.2 (d), 128.9 (d), 142.4 (s), 148.0 (s), 168.7 (s), 199.0 (s).

3-(4-Methoxycarbonylmethylbenzyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15q)——Colorless needles. mp 95 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.38 (1H, dd, J_{AB}=11.5 Hz, J_{AX}=2.9 Hz), 3.53 (1H, dd, J_{AB}=11.5 Hz, J_{BX}=8.8 Hz), 3.63 (2H, s), 3.70 3.80 (each 3H, s), 4.60 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.8 Hz), 4.29, 5.87 (each 1H, d, J=14.9 Hz), 7.26 (4H, s). ^{13}C-NMR δ: 30.9 (t), 40.8 (t), 51.5 (t), 52.0 (q), 53.1 (q), 66.7 (d), 128.7 (d), 129.9 (d), 133.8 (s), 134.3 (s), 169.0 (s), 171.7 (s), 198.1 (s).

1,3-Thiazolidine-2-thione (15r)——Colorless powder. mp 123 °C ($CHCl_3$–n-hexane). ^{1}H-NMR δ: 3.41 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=2.9 Hz), 3.55 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=8.5 Hz), 3.81, 3.82 (each 3H, s), 4.60 (1H, dd, J_{AX}=2.9 Hz, J_{BX}=8.5 Hz), 4.34, 5.90 (each 1H, d, J=15.3 Hz), 6.44, 7.66 (each 1H, d, J=16.0 Hz), 7.18, 7.52 (each 2H, AB type, J=8.3 Hz). ^{13}C-NMR δ: 30.9 (t), 51.5 (t), 51.7 (q), 55.3 (q), 66.7 (d), 118.5 (s), 128.6 (d), 128.9 (d), 134.6 (s), 137.2 (s), 143.8 (d), 167.2 (s), 168.9 (s), 198.3 (s).

3-Cinnamyl-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15s)——Colorless oil. ^{1}H-NMR δ: 3.41 (1H, dd, J_{AB}=11.7 Hz, J_{AX}=8.8 Hz), 3.63 (1H, dd, J_{AB}=11.7 Hz, J_{BX}=2.9 Hz), 3.81 (3H, s), 4.08 (1H, dd, J=15.1, 8.8 Hz), 4.86 (1H, dd, J_{AX}=8.8 Hz, J_{BX}=2.9 Hz), 5.22 (1H, dd, J=15.1, 5.4 Hz), 6.17 (1H, ddd, J=15.9, 8.8, 5.4 Hz), 6.59 (1H, d, J=15.9 Hz), 7.26—7.41 (5H, m). ^{13}C-NMR δ: 31.0 (t), 50.7 (t), 53.2 (q), 67.1 (d), 121.7 (d), 126.6 (d), 128.3 (d), 128.7 (d), 135.4 (d), 135.9 (s), 169.2 (s), 197.6 (s).

3-(4-Methoxycarbonylcinnamyl)-4-methoxycarbonyl-1,3-thiazolidine-2-thione (15t)——Colorless powder. mp

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82 °C. ($CHCl_3$–*n*-hexane). ^{1}H-NMR δ: 3.44 (1H, dd, $J_{AB}=11.5$ Hz, $J_{AX}=2.9$ Hz), 3.66 (1H, dd, $J_{AB}=11.5$ Hz, $J_{BX}=8.8$ Hz), 3.82, 3.92 (each 3H, s), 4.13 (1H, dd, $J=15.4$, 8.1 Hz), 4.85 (1H, dd, $J_{AX}=2.9$ Hz, $J_{BX}=8.8$ Hz), 5.24 (1H, dd, $J=15.4$, 5.4 Hz), 6.30 (1H, ddd, $J=15.9$, 8.1, 5.4 Hz), 6.62 (1H, d, $J=15.9$ Hz), 7.43, 8.00 (each 2H, AB type, $J=8.3$ Hz). ^{13}C-NMR δ: 31.0 (t), 50.6 (t), 52.1 (q), 53.3 (q), 67.3 (d), 124.6 (d), 126.5 (d), 129.8 (s), 130.0 (d), 134.1 (d), 140.3 (s), 166.6 (s), 169.1 (s), 197.8 (s).

References and Notes

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