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Remote Asymmetric Induction Using Neighboring Group Participation of a Sulfenyl Group

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Abstract: 2-[1-(Mesitylthio)alkyl]benzaldehydes and their dimethyl acetals react with silylated carbon nucleophiles under Lewis acidic conditions to give the corresponding aldol adducts with high diastereoselectivity, and in some cases, the products were obtained as almost a single diastereomer. Such a high diastereoselectivity is interpreted as the result of the 1,4-remote asymmetric induction through the benzene ring from the chiral ortho substituents of the substrates to the reaction centers. In the same manner, γ-mesitylthiolated aliphatic aldehydes and their acetals also react diastereoselectively to give the corresponding aldol adducts. In this case, the remote asymmetric induction occurs without the aid of a rigid benzene ring on the main chain of the substrates. In both reactions, a 5-membered cyclic sulfonium ion intermediate is thought to exist in the reaction pathway, which is formed by the intramolecular S_N2 reaction of the mesitylthio group, namely, the neighboring group participation of the sulfenyl group.

Introduction

Simple 1,4- or further remote stereocontrol in acyclic systems is one of the most important problems in organic synthesis[1] since there are still only a few effective methods for this strategy, in contrast to that a number of methods have already reported concerning the stereocontrol of 1,2- and 1,3-relationships. The strategies for introducing remote chiralities are classified into several types, including (i) the coupling of two chiral synthons, (ii) the removal of the mother chiral center(s) between newly generated, remote chiral centers formed as the result of 1,2- or 1,3-stereocontrol, (iii) the repeating of chirality transfer reactions from a chiral center to remote positions,[2] and so on. Relative asymmetric induction is among such devices[3] and superior to those cited above in the sense of maximum utilization of already-existing stereo-information.

On the other hand, we have recently focused on the development of synthetic methodologies using neighboring group participation, which is one of the well-known processes in organic molecules.[4-7] Among participating groups, an acyloxy group is the most famous and is widely used in the stereoselective glycosylation reactions.[4] Moreover, a sulfenyl group is known to participate in and stabilize a β-carbocation to form an episulfonium ion.[8] This phenomenon was brought to light by the experimental result on hydrolysis of β-sulfenylated alkyl chloride in water-dioxane.[9] Dramatic increase of first-order rate constant for the hydrolysis of 2-(phenylthio)ethyl chloride, compared with that of butyl chloride, revealed the existence of an intermediate episulfonium ion in the reaction pathway. As an application of this phenomenon, we have investigated the reactions of substrates having a sulfenyl group and already reported regio- and/or stereoselective reactions, such as regioselective pinacol rearrangement,[5] regioselective reaction of allyl acetates,[6] and stereoselective cationic cyclization.[7] In each case, an episulfonium ion intermediate plays an important role for determining the selectivity.

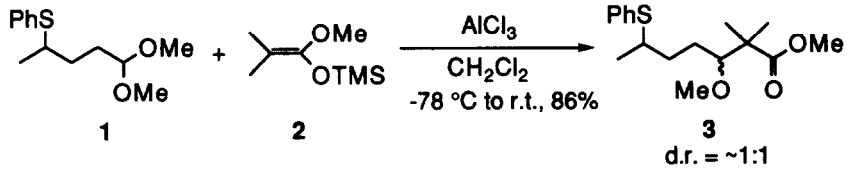
In addition to the enhancement of the hydrolysis rate of β-sulfenyl-substituted chloroalkanes, a similar acceleration of hydrolysis could be observed, when 4-(phenylthio)butyl chloride was used as a substrate.[9] The proposed intermediate in this reaction is a 5-membered cyclic sulfonium ion. We then focused our attention on the application of this "remote" neighboring group participation of a sulfenyl group toward 1,4-asymmetric induction.

Acetals, as well as aldehydes, can be activated with a Lewis acid and, extremely speaking, release one of the alkoxy groups to generate a cationic center. Subsequently, acetals react with rather weak nucleophiles, such as silyl enol ethers, ketene silyl acetals, enol ethers, and enamines to give the corresponding cross coupling (aldol) adducts.[10] Concerning the stereocontrol in aldol reactions, many researchers pay their attention on the relative stereochemistry between the newly generated chiral centers.[11] Only a few groups have reported on 1,2-asymmetric induction, namely Cram/*anti*-Cram selectivity, in aldol reaction.[12,13] For example, we have already presented the highly *anti*-selective aldol reaction of α-sulfenyl acetals with silylated carbon nucleophiles in the presence of a Lewis acid.[13] In this reaction, however, although the sulfenyl group plays a significant role, the formation of *anti*-isomers as major products is found not to attribute to the generation of an episulfonium intermediate by the neighboring group participation of the sulfenyl group, but to arise from the selective elimination of one of the alkoxy groups assisted by the sulfenyl function and successive attack of nucleophiles. Concerning the remote asymmetric induction from a chiral center to a position further away than β-position on the main chain of both aldehydes and acetals, only one example has been reported so far; the reaction of γ-alkoxy acetals with organosilane or organostannane reagents.[14]

In this paper, we report on the highly diastereoselective aldol reactions of (i) benzaldehydes and their dimethyl acetals having an α-sulfenylated chiral substituent at their *o*-position and (ii) their aliphatic versions with silylated carbon nucleophiles, based on the "remote" neighboring group participation of a sulfenyl group.[15]

Results and Discussion

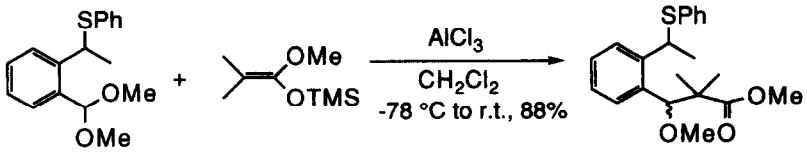
First of all, as an extension of the aldol reaction of α-sulfenyl acetals, we tried the reaction of γ-(phenylthio)valeraldehyde dimethyl acetal (**1**) with ketene silyl acetal **2**, derived from methyl isobutyrate, in the presence of $AlCl_3$ with expectation that 1,4-asymmetric induction would be observed through a five-membered cyclic sulfonium ion. However, the resulting aldol product, **3**, was found to be nearly a 1 : 1 mixture of diastereomers (Scheme 1).



1 **2** **3**
d.r. = ~1:1

Scheme 1

Concerning this non-selective manner in the reaction, three possible reasons would be considered: (i) The reaction proceeded without the formation of the expected, entropically unfavorable 5-membered cyclic sulfonium ion intermediate due to the flexibility of the carbon chain of the substrate. (ii) Although the expected intermediate was initially formed, it was not thermodynamically stable enough to survive until a nucleophile attacked. (iii) The intermediate was generated and stable enough, but it has no ability to induce an asymmetry at the reaction center owing to the lack of configurational and/or conformational rigidity. On the whole, the reason of this disappointing result could be attributed to the freedom of the substrate and/or the intermediate to some extent.

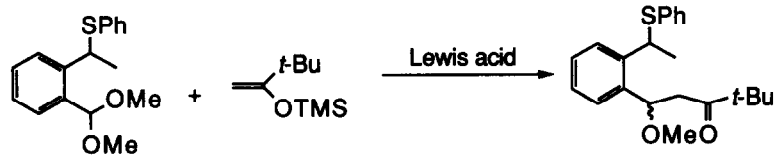


4 **2** **5**
d.r. = 99:1

Scheme 2

On the basis of this consideration, we next chose a benzo-substituted derivative in the place of two methylene groups of **1**, namely, 2-[1-(phenylthio)ethyl]benzaldehyde dimethyl acetal (**4**) as a substrate and tried again the aldol reaction with **2** under the same conditions for the reaction of **1** (Scheme 2). As expected, aldol adduct **5** was obtained in 88% yield with a satisfactory diastereomer ratio of 99 : 1.

This successful result prompted us to investigate the aldol reaction of 2-(1-sulfenylalkyl)benzaldehyde derivative in detail. A similar reaction of **4** with silyl enol ether **6**, derived from pinacolone, was also tried, but the diastereomer ratio of the product obtained was not satisfactory (Table 1, entry 4). Then, the reaction conditions, such as solvent, Lewis acid, and temperature, were optimized using this combination of reactants. The reaction was initiated at the indicated temperature by adding a Lewis acid to a mixture of substrate **4** and nucleophile **6**, because the diastereomer ratio slightly lowered when the nucleophile was added to a mixture of **4** and a Lewis acid.



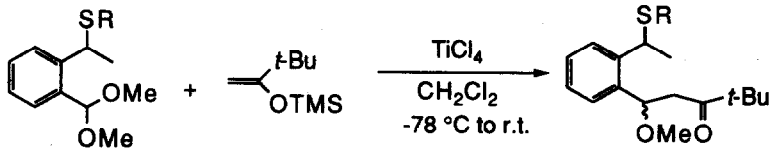
4 **6** **7**

Table 1. Reaction of **4** and **6** under various conditions

entry	solvent	Lewis acid	temperature / °C	reaction time / h	yield / %	diastereomer ratio
1	CH_2Cl_2	$AlCl_3$	-78	12	~ 0	——
2	CH_2Cl_2	$AlCl_3$	-23	3	74	72 : 28
3	CH_2Cl_2	$AlCl_3$	r.t.	1	81	66 : 34
4	CH_2Cl_2	$AlCl_3$	-78→ r.t.	2	85	72 : 28
5	toluene	$AlCl_3$	-78→ r.t.	2	52	56 : 44
6	MeCN	$AlCl_3$	-45→ r.t.	2	38	56 : 44
7	CCl_4	$AlCl_3$	-23→ r.t.	2	10	56 : 44
8	CH_2Cl_2	$BF_3{\cdot}OEt_2$	-78→ r.t.	2	82	68 : 32
9	CH_2Cl_2	TMSOTf	-78→ r.t.	2	74	51 : 49
10	CH_2Cl_2	$SbCl_5$	-78→ r.t.	4	~ 0	——
11	CH_2Cl_2	$TiCl_4$	-78→ r.t.	2	86	76 : 24
12	CH_2Cl_2	$SnCl_4$	-78→ r.t.	2	94	75 : 25

As a result, it was found that the reaction hardly proceeded at -78 °C but slowly at -23 °C, and quickly above 0 °C (entries 1-3). After some trials on the reaction, addition of a Lewis acid at -78 °C and gradual raising the temperature up to r.t. were proved to be the best way (entry 4). Among several solvents tested, dichloromethane was the best (entries 4-7). Concerning Lewis acid, only a little difference was observed, but strong, oxophilic Lewis acids, such as $TiCl_4$ and $AlCl_3$, gave good results (entries 4,11 and 12). Evaluating the highest diastereoselectivity (entry 11), we chose $TiCl_4$ as an optimized Lewis acid.

In addition to these external reaction conditions, the diastereoselectivity largely depended upon the sulfenyl group in the substrate. The results are summarized in Table 2. When alkylthio groups were employed instead of the phenylthio group (entries 5 and 6), the reactions proceeded sluggishly and the yields of the products were



6

Table 2. Effect of the sulfenyl group

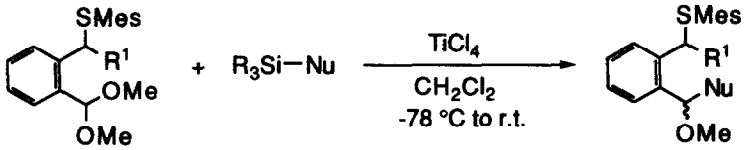
entry	R	reaction time / h	yield / %	diastereomer ratio
1	Ph (= **4**)	2	85	72 : 28
2	4-MeC_6H_4	2	90	85 : 15
3	2,4,6-$Me_3C_6H_2$ (= **8a**)	2	96	>99 : 1
4	4-$MeOC_6H_4$	2	90	73 : 27
5	Me	12	23	51 : 49
6	*t*-Bu	4	46	74 : 26

lower than that of the product from the substrate having a phenylthio group. If a cyclic sulfonium ion intermediate is truly generated, the first step of this reaction is thought to be a donation of the lone pair of a sulfenyl group to the reaction center. In this case, a substituent having electron-donative character is considered to be favorable. In fact, a dramatic improvement of diastereoselectivity was achieved in proportion to the increase of alkyl substituents on the phenyl group, which enhances the electron density in the pi-system (entries 1-3). Although *p*-methoxy group is also regarded as an electron-donative group to a benzene ring, the result of entry 4 would show that it could not work sufficiently as an electron donor under strong Lewis acidic conditions. Thus, mesitylthio group was turned out to be the most effective substituent in this reaction.[16] Then, by using mesitylthio group as a sulfenyl function, the aldol reactions of benzaldehyde derivatives **8a** and **8b** with various silylated carbon nucleophiles were carried out under the optimized conditions. The results are listed in Table 3.

Except for the reaction with trimethylsilyl cyanide (entry 6), all the reactions gave products **9** with almost perfect diastereoselectivity (minor diastereomers were not detectable in both ^1H NMR and gas chromatographic analyses of the crude products). In this reaction the methyl group seems to be bulky enough as a stereodifferentiating R^1 group on the chiral center. Subsequently, substrate **8b** having ethyl group as R^1 also gave similar results (entries 7,8). In the presence of strong Lewis acid $TiCl_4$, an elimination reaction occasionally occurred to liberate a MeOH molecule from the product having an acidic α-hydrogen atom, such as adducts **9c** and **9d**. As a result, enone like **10** was generated as a by-product. As already mentioned, a Lewis acid other than $TiCl_4$ could be employed in this reaction, and, for example, effectiveness of $AlCl_3$ was again realized in the reaction of **8a** with **2** (entry 2). Moreover, $AlCl_3$ was sometimes superior than $TiCl_4$ for suppressing the elimination reaction; the yield of the aldol product increased without depressing the diastereoselectivity in the reaction of **8a** with silyl enol ether derived from cyclohexanone (entry 5).

In order to confirm the real factor that caused this high diastereoselection, two control experiments were performed. When substrates **11a** and **11b** having a phenyl or a benzyloxy group instead of an arylthio group were submitted for the reaction with **2** under the same conditions, the corresponding aldol products, **12a** and **12b**, were obtained as almost 1 : 1 mixtures of diastereomers, respectively (Scheme 3).

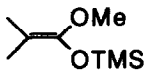
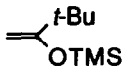
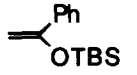
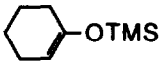
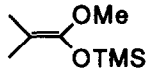
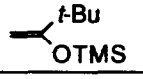
This striking difference indicates the indispensability of the sulfenyl group in the present reaction; the origin of the high diastereoselection is apparently not simple steric repulsion such as vinylogous Cram's rule,[17] but intermediacy of a 5-membered cyclic sulfonium ion. The result of the reaction of **11b** also indicates that the lone



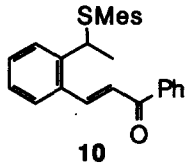
8a (R^1 = Me)
8b (R^1 = Et)

9a-g

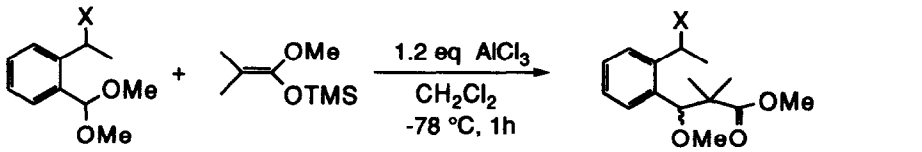
Table 3. Reactions of **8a** and **8b** with silylated carbon nucleophiles

entry	R^1		nucleophile	product	reaction time / h	yield / %	diastereomer ratio
1	CH_3	**8a**		**9a**	1	79	>99 : 1
2					1 [a]	92	>99 : 1
3				**9b**	2	96	>99 : 1
4				**9c**	3	57 [b]	>99 : 1
5				**9d**	2 [a]	81	>99 [c] : 1
6			TMSCN	**9e**	2	91	89 : 11
7	C_2H_5	**8b**		**9f**	1	86	>99 : 1
8				**9g**	2	90	>99 : 1

a) 1.2 eq. $AlCl_3$ was used as a Lewis acid.
b) Chalcone derivative **10** was obtained in 29% yield.
c) *Syn* : *anti* = 83 : 17.



10



11a (X = Ph)
11b (X = OBn)

2

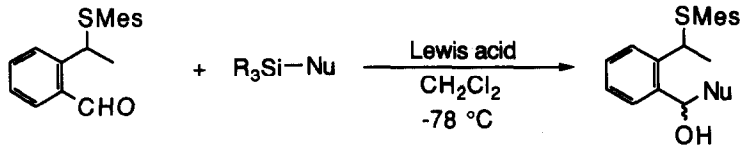
12a (X = Ph) yd: 75%, d.r.: 51 : 49
12b (X = OBn) yd: 86%, d.r.: 52 : 48

Scheme 3

pair of the ether oxygen cannot participate in this type of rigid substrate, that is, a benzo-substituted 5-membered oxonium ion is difficult to be formed. Although we tried to detect the intermediate sulfonium ion by analytical methods, no unambiguous evidence could be obtained in the reaction of acetal **8a**. However, it is clear, from the results of control experiments and the dependence on the sulfenyl group, that a cyclic sulfonium ion is a key intermediate to cause the diastereoselection.

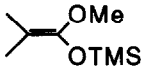
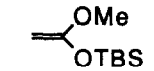
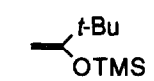
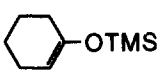
Thus, we achieved a new 1,4-remote asymmetric induction by using dimethyl acetals of ortho-substituted benzaldehydes as substrates. Then, we next investigated the reaction of the corresponding mother aldehyde. Although an aldehyde, unlike an acetal, cannot release an eliminating group to form a cationic species, an aldehyde would be converted into a Lewis acid-coordinated twitter-ionic sulfonium salt (**18**, *vide infra*). Through this intermediate, we expected the same type of 1,4-asymmetric induction, as was observed in the reaction of acetal **8**, and carried out the aldol reaction of aldehyde **13** with several kinds of silylated carbon nucleophiles.

In contrast to the case of dimethyl acetal **8**, we could not find unified reaction conditions to give the best result, independing nucleophiles. For example, there was a specific Lewis acid suitable for each nucleophile.[18] Among several combinations of a nucleophile and Lewis acids, we selected the best combination. The results are shown in Table 4. In many cases, $TiCl_4$, which was the optimized Lewis acid for the reaction of **8**, caused the elimination of a H_2O molecule from the aldol products, since H_2O is easier to be eliminated than MeOH under



13 **14a-d**

Table 4. Reactions of **13** with silylated carbon nucleophiles

entry	nucleophile	product	Lewis acid	reaction time / h	yield / %	diastereomer ratio
1		**14a**	$TiCl_4$	2	64	95 : 5
2			TMSOTf	2	75	94 : 6
3		**14b**	$TiCl_4$	2	22	95 : 5
4			TMSOTf	3	37	>99 : 1
5			cat. TMSOTf[a)]	8	80	97 : 3
6		**14c**	$TiCl_4$	2	48	95 : 5
7			$AlCl_3$	20	39	95 : 5
8		**14d**	$TiCl_4$	3[b)]	32	77[c)] : 23
9			$AlCl_3$	19	79	82[d)] : 18

a) 0.15 eq. of TMSOTf was used.
b) Temperature was raised up to r.t.
c) *Syn* : *anti* = 25 : 75.
d) *Syn* : *anti* = 45 : 55.

acidic conditions. From this reason, the yields were much lower in the reaction of **13** with silyl enol ethers (entries 6 and 8) than those in the reaction of its dimethyl acetal **8a**. On the other hand, TMSOTf gave satisfactory results in the reaction with more nucleophilic ketene silyl acetals (entries 2,4 and 5). As a whole, the major diastereomer of product **14** was proved to have the same relative stereochemistry as the major diastereomer of **9**, and its diastereomer ratio is a match for that of the reaction of the corresponding acetal.

As mentioned above, the reaction of aldehyde **13** is supposed to proceed through a twitter-ionic 5-membered sulfonium salt. In order to confirm the existence of such a twitter-ionic species, we tried to identify the intermediate, formed by mixing substrate **13** with an equimolar amount of $TiCl_4$ in CD_2Cl_2 at room temperature. The signals of aldehyde **13** completely faded upon the addition of $TiCl_4$, and new peaks appeared (Fig. 1). The conspicuous changes of chemical shifts are as following: (i) The aldehyde proton shifted in 1.23 ppm toward the higher field (from 9.81 ppm to 8.58 ppm). (ii) The methyl and methyne protons shifted in 0.3-0.4 ppm toward the lower field. (iii) The aromatic protons of mesitylthio group also shifted in 0.3 ppm toward the lower field. These changes of chemical shifts clearly show the formation of the supposed twitter-ionic sulfonium salt, because a simple 1:1 or 2:1 complex of **13** and $TiCl_4$ would show the change of chemical shift of aldehyde proton toward the lower field.[19]

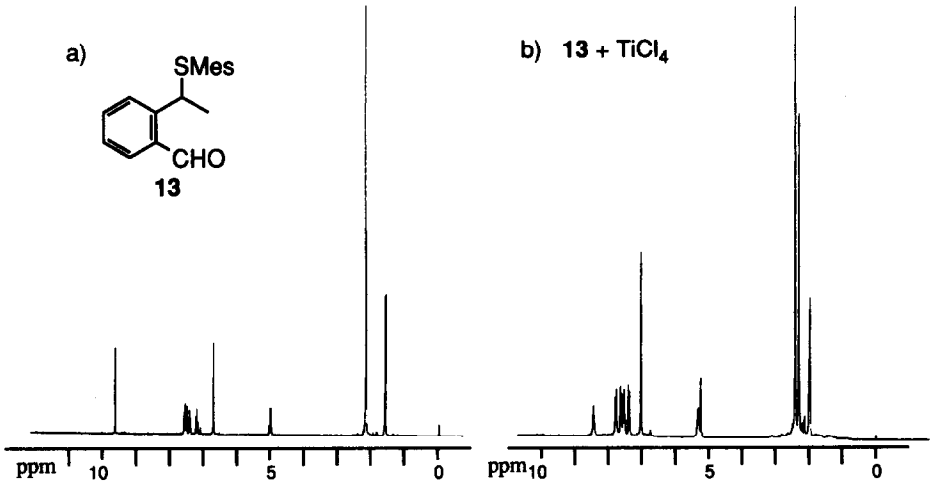
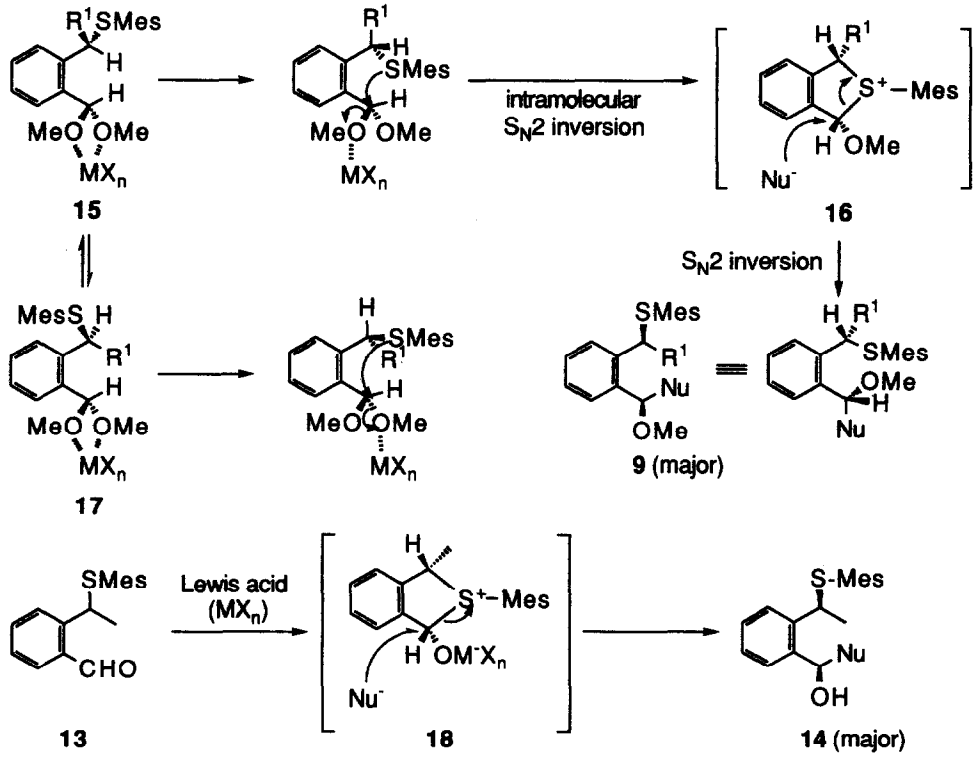


Fig.1 ^1H NMR of a) **13** in $CDCl_3$ and b) **13** + $TiCl_4$ (1 : 1) in CD_2Cl_2 at r.t.

On the basis of these results, a possible mechanism for the reaction of acetals **8** and aldehyde **13** is shown in Scheme 4. In the reaction of acetal **8**, the lone pair of the sulfenyl group assists the elimination of the particular diastereotopic methoxy group from the most stable conformation of Lewis acid-coordinated substrate **15** by an intramolecular S_N2 mechanism to form 5-membered cyclic sulfonium ion intermediate **16**. Participation from different conformer **17**, through which the other diastereomer would be formed, is supposed to be negligible because such a geometry is conformationally quite unfavorable. To diastereoselectively formed intermediate **16**, a nucleophile attacks in an S_N2 mechanism, and consequently aldol adduct **9** of the displayed relative stereochemistry is formed.

In the case of aldehyde **13**, the nucleophilic addition of the lone pair of the sulfenyl group occurs to form twitter-ionic cyclic sulfonium salt **18**, which was identified by the spectroscopic method (*vide supra*), having the same stereochemistry as **16**. A nucleophile attacks in the same manner as in the case of acetals to give aldol adduct **14** of the relative stereochemistry displayed.

So far, we found the diastereoselective aldol reaction of benzaldehyde and its dimethyl acetals having an α-sulfenylated chiral substituent at their ortho position. These substrates have a characteristic molecular shape,



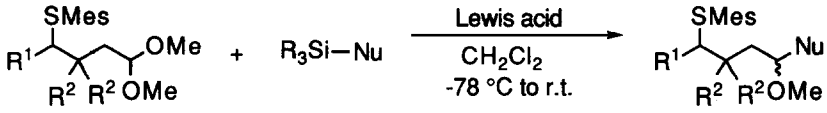
Scheme 4

which is advantageous to form a cyclic sulfonium ion easily and to maintain the intermediate stable and rigid. However, limitation of substrates in the present reaction leads to a restricted synthetic utility of this reaction. Then, we next tried to extend the idea of the 1,4-asymmetric induction to the reaction of aliphatic aldehyde derivatives, one of which gave an almost 1 : 1 mixture of diastereomers when phenylthio group was used as a sulfenyl function (Scheme 1). However, the displacement of phenylthio group into mesitylthio group resulted in improvement of the diastereoselectivity in the reaction of a benzaldehyde dimethyl acetal derivative with a silyl enol ether (Table 2). Then, we re-investigated the diastereoselective aldol reaction of acetal **19a**, by introducing mesitylthio instead of phenylthio group.

As is expected, the reaction with ketene silyl acetal **2** gave aldol product **20a** as a mixture of diastereomers in a ratio of 79 : 21 (Table 5, entry 1), of which the major isomer has the same relative stereochemistry as major diastereomers of **9** and **14**, namely the product arising from the substitution of the same diastereotopic methoxy group. This result shows that 1,4-asymmetric induction can be achieved without aid of benzene ring on the main chain of the substrate, although the selectivity was a little lower than that of benzaldehyde derivatives **8** and **13**. On the basis of the result, we carried out the aldol reaction of various aliphatic aldehydes and their acetals having a mesitylthio group at γ-position with silylated carbon nucleophiles in the presence of a Lewis acid. The results are shown in Tables 5 and 7.

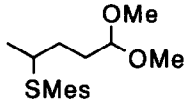
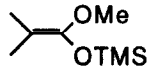
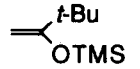
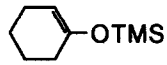
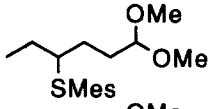
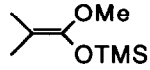
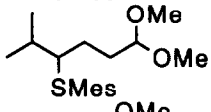
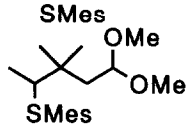
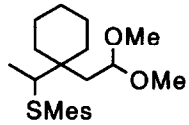
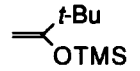
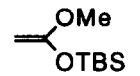
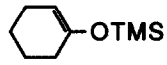
First, several Lewis acids were tested for the reaction of substrate **19a** with ketene silyl acetal **2** in CH_2Cl_2 at -78 °C. As a result, $TiCl_4$, again, gave the best result, which was favorable in the reaction of **8**. Then, we basically used $TiCl_4$ as a Lewis acid. The reaction with a less nucleophilic silyl enol ether gave the aldol product with lower diastereoselectivity (Table 5, entries 2 and 3), which implied that a rapid reaction gave good result.

Substrates having a different R^1 group gave the almost completely same result from the viewpoints of yield and diastereoselectivity (entries 4 and 5). In order to elucidate the effect of substituents on the alkyl chain, we carried out the aldol reaction of substrates having alkyl substituents at the β-position of the acetal moiety with **2**. Although the diastereomer ratio slightly lowered when dimethylated substrate **19d** was used (entry 6), substrate **19e** with a cyclohexane ring, to our surprise, gave the corresponding product **20g** as an almost single diastereomer (entry 7). Such a drastic increase of diastereoselectivity was also observed in the reaction with other silylated carbon nucleophiles (entries 8-10).

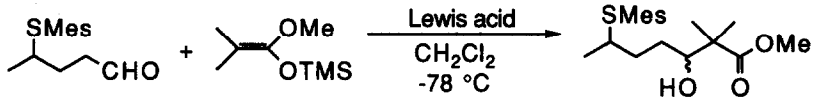


19a-e **20a-j**

Table 5. Reactions of **19** with silylated carbon nucleophiles

entry	substrate		nucleophile	product	Lewis acid	reaction time / h	yield / %	diastereomer ratio
1		**19a**		**20a**	$TiCl_4$	1	91	79 : 21
2				**20b**		3	44	70 : 30
3				**20c**	$AlCl_3$	1	76	77[a] : 23
4		**19b**		**20d**	$TiCl_4$	1	90	78 : 22
5		**19c**		**20e**		1	92	81 : 19
6		**19d**		**20f**		1	100	67 : 33
7		**19e**		**20g**		1	86	>99 : 1
8				**20h**		3	86	78 : 22
9				**20i**	TMSOTf	2	75	99 : 1
10				**20j**	$AlCl_3$	3	55	89[b] : 11

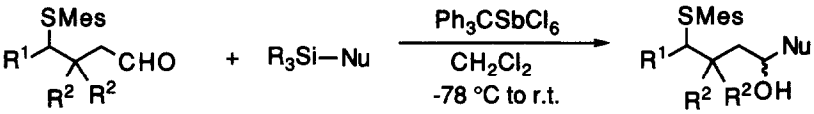
a) *Syn* : *anti* = 50 : 50.
b) *Syn* : *anti* = 37 : 63.



21a **2** **22a**

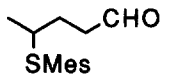
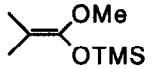
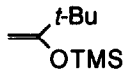
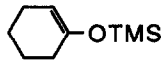
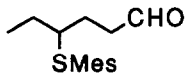
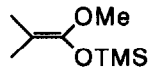
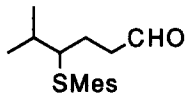
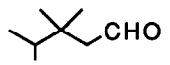
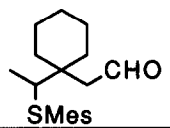
Table 6. Reactions of **21a** with **2** in the presence of various Lewis acids

entry	Lewis acid	reaction time / h	yield / %	diastereomer ratio
1	$TiCl_4$	1	83	67 : 33
2	$AlCl_3$	1	83	58 : 42
3	$BF_3{\cdot}OEt_2$	1	99	50 : 50
4	TMSOTf	1	90	57 : 43
5	Ph_3CSbCl_6	0.75	86	81 : 19



21a-e **22a-g**

Table 7. Reactions of **21** with silylated carbon nucleophiles

entry	substrate		nucleophile	product	reaction time / h	yield / %	diastereomer ratio
1		**21a**		**22a**	1	83	67 : 33
2				**22b**	5	40	58 : 42
3				**22c**	24	~0	——
4		**21b**		**22d**	12	57	91 : 9
5		**21c**		**22e**	12	50	91 : 9
6		**21d**		**22f**	12	35	72 : 28
7		**21e**		**22g**	48	16	66 : 34

In the case of the reaction of γ-sulfenylated aliphatic aldehydes with silylated carbon nucleophiles, an obvious effect of a Lewis acid was observed (Table 6). When Ph_3CSbCl_6 was used as a Lewis acid, the diastereomer ratio was much higher than those obtained by using the other Lewis acids (entry 5). However, the reaction rate with silyl enol ethers, was very slow under these conditions, and the diastereoselectivity was also unsatisfactory (Table 7, entries 2 and 3). Especially, the reaction with silyl enol ether, derived from cyclohexanone, hardly proceeded (entry 3). Contrary to the case of acetals, substrates having a different R^1 group gave the products with slightly different diastereoselectivity; a bulky R^1 group, such as Et and *i*-Pr, gave a favorable result (entries 4 and 5). Moreover, the effect of β-substituent groups was not remarkable (entries 6 and 7) in contrast to the reaction of acetals.

In order to know the mechanism for this reaction, we performed the aldol reaction with **2** upon changing the acetal functional groups (R^3) with expectation that the diastereoselectivity increases with increasing the bulkiness of R^3 on the basis of such an improvement reported in the reaction of γ-alkoxyacetals.[14,20] However, contrary to our expectation, R^3 group did not affect at all the diastereomer ratio in this case (Table 8). This result indicates the mechanism of this reaction different from that of γ-alkoxy acetals.

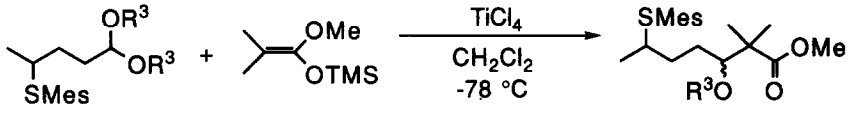
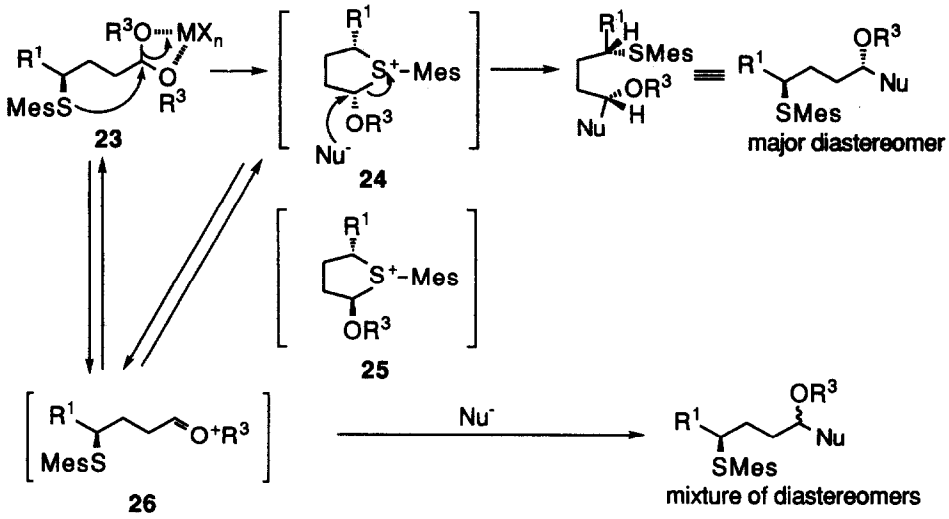


Table 8. Effect of R^3 group

entry	R^3	reaction time / h	yield / %	diastereomer ratio
1	Me (=**19a**)	1	91	79 : 21
2	Et	1	83	78 : 22
3	Pr^i	3	94	78 : 22

The characteristics of the reaction of aliphatic acetals and aldehydes are summarized: (i) A highly reactive nucleophile, such as ketene silyl acetal **2**, is favorable for the reaction of both acetals and aldehydes. (ii) Lewis acid-dependence of the selectivity is small for acetals, whereas bulky Ph_3CSbCl_6 gives good result in the case of aldehydes. (iii) Introduction of bulky R^1 and/or R^3 group brings no change of selectivity for acetals, but slightly better selectivity is observed by introducing a larger R^1 group to aldehydes. (iv) Effect of β-substituents is not remarkable for aldehydes, whereas clear enhancement of diastereoselectivity is observed for acetals. The β-substituents is supposed to make the carbon chains parallel, namely, the sulfenyl moiety close to the reaction center, resulting in the easy participation of the sulfenyl group. On the basis of these facts, a possible mechanism of the aldol reaction of aliphatic acetals can be proposed as following (Scheme 5).

As is the case of benzaldehyde derivatives **8** and **13**, by an intramolecular S_N2 attack of the lone pair of the sulfenyl group, 5-membered cyclic sulfonium ion **24** is formed with the elimination of an alkoxy group. The resulting sulfonium ion gives the major diastereomer upon an S_N2 attack of a nucleophile. However, another reaction pathway would exist to cause the generation of the minor diastereomer, that is, the intermediacy of open-chained oxocarbenium ion **26**, to which a non-selective nucleophilic addition occurs to give a mixture of the diastereomers. Sulfonium ion **24** is initially formed diastereoselectively; if the ratio of the diastereomers of the sulfonium ion reflects the distribution of the diastereomers, energetic difference between 1,3-*cis* **24** and 1,3-*trans* **25** would cause a change of the selectivity of the product ratio, depending on the R^1 and/or R^3 group. However, the present reaction is not the case. Then, we concluded that the most important factor to affect the diastereoselectivity of the product is not the difference in thermodynamic stability between two possible diastereomers of sulfonium ion **24** and **25**, but the content of oxocarbenium ion **26**. This explanation can be applied to understand the fact that bulky β-substituents improved the diastereoselectivity. On the other hand, in



Scheme 5

the case of aliphatic aldehydes, thermodynamic equilibrium, to some extent, between the two sulfonium ions is possible, which is suggested from the result that bulky R^1 group or bulky Lewis acid gave better results.

Conclusion

"Remote" neighboring group participation is still unexplored in remote-stereocontroled syntheses. Our 1,4-asymmetric induction using neighboring group participation of a sulfenyl function will be a clue to a new possibility of remote-stereocontrol. Although there are many unclear points in the mechanistic aspects, the high diastereoselectivity, especially in the reaction of benzaldehyde derivatives, is of much interest.

Experimental Section

General GC analyses were performed with a 25-m fused-silica capillary column using cyanopropyl silicone as a stationary phase. Melting points were determined using a metal block apparatus and an open capillary tube, and were uncorrected. NMR spectra were measured on a FT spectrometer operating at 270 MHz for ^1H and 68 MHz for ^{13}C. For ^1H NMR, the δ values are given in ppm with TMS as an internal standard, and the coupling constants are recorded in Hz. For ^{13}C NMR, the chemical shifts are reported in ppm relative to TMS or $CDCl_3$ (δ 77.0). The unit for the values of IR spectra is cm^{-1}. The mass spectra were recorded by the EI method (70 eV). Silica gel was used for column chromatography (particle size: 63-200 μm) and preparative TLC (<46 μm). Nucleophiles were synthesized according to the methods described in the literature.[10]

Compound **9e** was too unstable to obtain either combustion analysis or suitable high-resolution (exact mass) spectra.

Determination of relative stereochemistry of the products X-ray crystallographic analyses were performed in order to establish the structures of the following compounds, sulfone **27**, sulfoxide **28**, sulfone **29**, and sulfoxide **30** derived from the major diastereomers of **5**, **9b**, **14b**, and **20g**, respectively. The stereochemistries of the other compounds having a mesitylthio group were confirmed on the basis of a correlation of the ^1H NMR chemical shifts of *ortho*-methyl protons of mesitylthio group (the peak of the major product was observed in the lower field).

1,1-Dimethoxy-4-(phenylthio)pentane (1) and methyl 3-methoxy-2,2-dimethyl-6-(phenylthio)heptanoate (3) To a mixture of crotonaldehyde (20.5 ml, 247 mmol) and triethylamine (0.40 ml, 2.88 mmol) was slowly added thiophenol (30.5 ml, 297 mmol) at 0 °C. The resulting mixture was stirred for

30 min at that temperature. Concentration, followed by distillation, gave 44.32 g (99%) of 3-(phenylthio)butanal: bp 97-108 °C/0.2 mmHg. To a stirred solution of methoxymethyltriphenylphosphonium chloride (14.26 g, 41.6 mmol) in 100 ml of dry ether was added a hexane solution of *n*-BuLi (1.66 mol dm^{-3}, 25.0 ml, 41.6 mmol) at 0 °C and stirred at that temperature for 1 h. Then, a solution of the aldehyde obtained above (5.00 g, 27.7 mmol) in 10 ml of ether was slowly added at that temperature. Then, the cooling bath was removed, and the solution was additionally stirred at room temperature for 1 h. After an aqueous work up and silica gel column chromatography (eluent: ethyl acetate/hexane = 1/10), the resulting aldehyde was acetalized by an usual method (MeOH, $HC(OMe)_3$, catalytic TsOH) to give 1,1-dimethoxy-4-(phenylthio)pentane (**1**) as a colorless oil (5.47 g, 22.7 mmol, 82% from aldehyde). ^1H NMR ($CDCl_3$, 270 MHz) 1.29 (d, 3H, J = 7, CH_3CH), 1.56-1.82 (m, 4H, methylene), 3.18-3.26 (m, 1H, PhSC*H*), 3.30 (s, 6H, CH_3O), 4.35 (t, 1H, J = 5, $(MeO)_2CH$), 7.22-7.41 (m, 5H, phenyl); IR (neat) 1585, 1440, 1130, 1070, 745, 695; HRMS calcd for $C_{13}H_{20}O_2S$ 240.1184, found 240.1173.

To a mixture of **1** (51.3 mg, 0.213 mmol) and 1-methoxy-2-methyl-1-trimethylsilyloxypropene **2** (54.7 mg, 0.314 mmol) in 5 ml of dry dichloromethane was added aluminium trichloride (40.5 mg, 0.304 mmol) at -78 °C under an argon atmosphere, and the reaction mixture was stirred for 1 h at that temperature. After an aqueous work up, the organic materials were extracted with dichloromethane (2×10 ml). The combined organic layers were dried, concentrated under reduced pressure, and purified by silica-gel thin layer chromatography (eluent: ethyl acetate/hexane = 1/4) to give methyl 3-methoxy-2,2-dimethyl-6-(phenylthio)heptanoate (**3**) (61.8 mg, 93%). The 270 MHz ^1H NMR spectral and capillary gas chromatographic analyses showed that the product is a 1:1 mixture of diastereomers. ^1H NMR ($CDCl_3$, 270 MHz) 1.18 (s, 3×0.5H, $C(CH_3)CH_3$), 1.19 (s, 3×0.5H, $C(CH_3)CH_3$), 1.10 (s, 3×0.5H, $C(CH_3)CH_3$), 1.11 (s, 3×0.5H, $C(CH_3)CH_3$), 1.28 (d, 3×0.5H, J = 5, CH_3CH), 1.29 (d, 3×0.5H, J = 5, CH_3CH), 1.51-1.91 (m, 4H, methylene), 3.12-3.30 (m, 1H, PhSC*H*), 3.31-3.35 (m, 1H, MeOC*H*), 3.37 (s, 3×0.5H, CH_3O), 3.38 (s, 3×0.5H, CH_3O), 3.67 (s, 3H, $COOCH_3$), 7.21-7.41 (m, 5H, phenyl); IR (neat) 1725, 1580, 1435, 1270, 1130, 1095, 740, 685; HRMS calcd for $C_{17}H_{26}O_3S$ 310.1603, found 310.1607.

2-[1-(Phenylthio)ethyl]benzaldehyde dimethyl acetal (4) (Prepared by a similar procedure as **8a**, *vide infra*) ^1H NMR ($CDCl_3$, 270 MHz) 1.58 (d, 3H, J = 7, CH_3CH), 3.23 (s, 3H, CH_3O), 3.26 (s, 3H, CH_3O), 4.89 (q, 1H, J = 7, PhSC*H*), 5.44 (s, 1H, $(MeO)_2CH$), 7.13-7.60 (m, 9H, aryl); IR (neat) 1580, 1355, 1195, 1050, 980, 910, 745, 695; HRMS calcd for $C_{17}H_{20}O_2S$ 288.1184, found 288.1161.

2-[1-(Mesitylthio)ethyl]benzaldehyde (13) and its dimethyl acetal (8a) To a stirred solution of 1-(2-chlorophenyl)ethanol (2.42 g, 15.4 mmol), prepared by the reduction of 2-chloroacetophenone, and triethylamine (2.34 g, 23.2 mmol) in 50 ml of dry dichloromethane was added a dichloromethane (20 ml) solution of mesyl chloride (1.95 g, 17.0 mmol) at -10 °C (ice-NaCl). After stirring for 20 min, the reaction mixture was poured into ice-water (100 ml). The organic materials were extracted with dichloromethane (2×50 ml), and the combined organic layers were dried over $MgSO_4$. After concentration under reduced pressure, the crude mesylate was added to a mechanically stirred solution of mesitylenethiol (2.35 g, 15.4 mmol) and sodium hydroxide (0.75 g, 18.5 mmol) in ethanol (30 ml). The reaction mixture was vigorously stirred for 15 min at room temperature. After an aqueous work up (100 ml of 1 N NaOH), organic materials were extracted with dichloromethane (3×20 ml). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (eluent: ethyl acetate/hexane = 1/100 to 1/25) gave 2.42 g (8.32 mmol, 54%) of 2-chloro-1-[1-(mesitylthio)ethyl]benzene. The resulting chloride was added into a suspension of activated magnesium turnings (202 mg, 8.32 mmol) in THF (10 ml). After the magnesium was disappeared, the reaction mixture was diluted with 50 ml of THF, and refluxed for 2 h. Then *N*,*N*-dimethylformamide (5 ml) was added to the refluxing solution and the reaction mixture was additionally stirred for 30 min. After an aqueous work up (100 ml of saturated aqueous solution of NH_4Cl), the organic layer was diluted with 100 ml of ether, washed successively with saturated aqueous solution of $NaHCO_3$ and brine, and dried over $MgSO_4$. Evaporation and purification by column chromatography (eluent: ethyl acetate/hexane = 1/100 to 1/10) gave 2-[1-(mesitylthio)ethyl]benzaldehyde (**13**) (0.86 g, 3.03 mmol, 36% from the chloride). ^1H NMR ($CDCl_3$, 270 MHz) 1.65 (d, 3H, J = 7, CH_3CH), 2.23 (s, 3H, mesityl), 2.25 (s, 6H, mesityl), 5.13 (q, 1H, J = 7, MesSC*H*), 6.85 (s, 2H, mesityl), 7.25-7.74 (m, 4H, aryl), 9.80 (s, 1H, C*H*O); IR (neat) 1695, 1380, 1200, 1035, 855, 760, 750; HRMS calcd for $C_{18}H_{20}OS$ 284.1235, found 284.1246.

Acetalization by an usual method gave 2-[1-(mesitylthio)ethyl]benzaldehyde dimethyl acetal (**8a**) as a colorless oil (0.90 g, 2.72 mmol, 90% from the aldehyde). ^1H NMR ($CDCl_3$, 270 MHz) 1.51 (d, 3H, J = 7, CH_3CH), 2.22 (s, 3H, mesityl), 2.37 (s, 6H, mesityl), 3.13 (s, 3H, CH_3O), 3.14 (s, 3H, CH_3O), 4.56 (q, 1H, J = 7, MesSC*H*), 5.03 (s, 1H, $(MeO)_2CH$), 6.88 (s, 2H, mesityl), 7.16-7.69 (m, 4H, aryl); IR (neat) 1600, 1455, 1195, 1055, 905, 850, 765, 745; HRMS calcd for $C_{20}H_{26}O_2S$ 330.1653, found 330.1689.

2-[1-(Mesitylthio)propyl]benzaldehyde dimethyl acetal (8b) (Prepared by a similar procedure as **8a**) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.88 (t, 3H, J = 7, CH_3CH_2), 1.92-1.99 (m, 2H, CH_3CH_2), 2.22 (s, 3H, mesityl), 2.29 (s, 6H, mesityl), 3.05 (s, 3H, CH_3O), 3.07 (s, 3H, CH_3O), 4.27 (dd, 1H, J = 9,7, MesSC*H*), 4.79 (s, 1H, $(MeO)_2CH$), 6.86 (s, 2H, mesityl), 7.16-7.62 (m, 4H, aryl); IR (neat) 1595, 1455, 1360, 1180, 1095, 990, 820, 765, 660; HRMS calcd for $C_{21}H_{28}O_2S$ 344.1810, found 344.1791.

Typical procedure for the aldol reaction of acetal 8 or aldehyde 13 with a silylated carbon nucleophile To a mixture of **8a** (21.2 mg, 0.0532 mmol) and 3,3-dimethyl-2-trimethylsilyloxy-1-butene **6** (11.3 mg, 0.0657 mmol) in 5 ml of dry dichloromethane was added a dichloromethane solution of titanium(IV) chloride (1.13 mol·dm^{-3}, 0.06 ml) at -78 °C under an argon atmosphere, and the reaction mixture was stirred for 1 h at that temperature. Then, the mixture was allowed to warm to room temperature and stirred for one hour. After an aqueous work up, the organic materials were extracted with dichloromethane (2×10 ml). The combined organic layers were dried, concentrated under reduced pressure, and purified by silica-gel thin layer chromatography (eluent: ethyl acetate/hexane = 1/6) to give 1-[2-[1-(mesitylthio)ethyl]phenyl]-1-methoxy-4,4-dimethyl-3-pentanone (**9b**) (24.5 mg, 96%). The 270 MHz ^{1}H NMR spectral and capillary gas chromatographic analyses showed a diastereomer ratio of >99:1 (the minor diastereomer was not detected). ^{1}H NMR ($CDCl_3$, 270 MHz) 1.06 (s, 9H, $C(CH_3)_3$), 1.48 (d, 3H, J = 7, CH_3CH), 2.20 (s, 3H, mesityl), 2.32 (dd, 1H, J = 17, 4, C*H*HCO), 2.43 (s, 6H, mesityl), 2.81 (s, 3H, CH_3O), 2.91 (dd, 1H, J = 17, 8, CH*H*CO), 4.44 (q, 1H, J = 7, MesSC*H*), 4,79 (dd, 1H, J = 8, 4, MeOC*H*), 6.89 (s, 2H, mesityl), 7.19-7.68 (m, 4H, aryl); IR (neat) 1680, 1605, 1480, 1080, 910, 850, 735; HRMS calcd for $C_{25}H_{34}O_2S$ 398.2279, found 398.2307.

Methyl 3-methoxy-2,2-dimethyl-3-[2-[1-(phenylthio)ethyl]phenyl]propionate (5) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.01 (s, 3H, $C(CH_3)CH_3$),1.16 (s, 3H, $C(CH_3)CH_3$), 1.63 (d, 3H, J = 7, CH_3CH), 2.94 (s, 3H, CH_3O), 3.75 (s, 3H, $COOCH_3$), 4.74 (q, 1H, J = 7, PhSC*H*), 5.09 (s, 1H, MeOC*H*), 7.23-7.47 (m, 9H, aryl); IR (neat) 1725, 1475, 1440, 1260, 1135, 1090, 910, 735; HRMS calcd for $C_{21}H_{26}O_3S$ 358.1602, found 358.1588.

Methyl 3-methoxy-2,2-dimethyl-3-[2-[1-(phenylsulfonyl)ethyl]phenyl]propionate (27) To a stirred solution of sulfide **5** (787 mg, 2.20 mmol) in 20 ml of ether was added an ethereal solution of m-CPBA (0.99 g, 4.6 mmol) at room temperature. The reaction mixture was stirred for 6 h, then quenched by 50 ml of saturated aqueous solution of $NaHCO_3$. Organic materials were washed (sat. $NaHCO_3$ 20 ml×2), dried, and concentrated under reduced pressure. Recrystalization from EtOH gave the title compound as colorless plates (mp 147 °C). ^{1}H NMR ($CDCl_3$, 270 MHz) 0.93 (s, 3H, $C(CH_3)CH_3$),1.07 (s, 3H, $C(CH_3)CH_3$), 1.71 (d, 3H, J = 7, CH_3CH), 2.86 (s, 3H, CH_3O), 3.73 (s, 3H, $COOCH_3$), 4.82 (q, 1H, J = 7, $PhSO_2CH$), 4.94 (s, 1H, MeOC*H*), 7.26-7.72 (m, 9H, aryl) IR (KBr) 1740, 1305, 1245, 1150, 885, 760, 725; HRMS calcd for $C_{21}H_{26}O_5S$ 390.1501, found 390.1487; Crystal data: chemical formula $C_{21}H_{26}O_5S_1$; formula weight 390.0; crystal system triclinic; space group $P\bar{1}$; Z=2; a=8.471(1), b=13.551(2), c=10.097(3) Å; α=105.70(2)°, β=112.17(2)°, γ=81.54(1)°; V=1032.0(4) Å^3; D_c=1.25 g cm^{-3}; R=0.072; R_w=0.103 (used 3353 reflections).

1-Methoxy-4,4-dimethyl-1-[2-[1-(phenylthio)ethyl]phenyl]-3-pentanone (7) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.07 (s, 9×0.76H, $C(CH_3)_3$), 1.09 (s, 9×0.24H, $C(CH_3)_3$), 1.58 (d, 3×0.76H, J = 7, CH_3CH), 1.61 (d, 3×0.24H, J = 7, CH_3CH), 2.42 (dd, 0.24H, J = 17, 2, C*H*HCO), 2.47 (dd, 0.76H, J = 17, 4, C*H*HCO), 3.00 (dd, 0.24H, J = 17, 10, CH*H*CO), 3.05 (s, 3×0.76H, CH_3O), 3.10 (dd, 0.24H, J = 17, 9, CH*H*CO), 3.19 (s, 3×0.24H, CH_3O), 4.71 (q, 0.24H, J = 7, PhSC*H*), 4.76 (q, 0.76H, J = 7, PhSC*H*), 5.10 (dd, 0.76H, J = 9, 4, MeOC*H*), 5.16 (dd, 0.24H, J = 10, 2, MeOC*H*), 7.22-7.56 (m, 9H, aryl); IR (neat) 1680, 1605, 1480, 1370, 1080, 910, 735, 695; HRMS calcd for $C_{22}H_{28}O_2S$ 356.1810, found 356.1822.

Methyl 3-[2-[1-(mesitylthio)ethyl]phenyl]-3-methoxy-2,2-dimethylpropionate (9a) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.95 (s, 3H, $C(CH_3)CH_3$), 1.09 (s, 3H, $C(CH_3)CH_3$), 1.53 (d, 3H, J = 7, CH_3CH), 2.22 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.70 (s, 3H, CH_3O), 3.74 (s, 3H, $COOCH_3$), 4.57 (q, 1H, J = 7, MesSC*H*), 4.86 (s, 1H, MeOC*H*), 6.88 (s, 2H, mesityl), 7.20-7.68 (m, 4H, aryl); IR (neat) 1735, 1595, 1460, 1245, 1125, 845, 760, 730; HRMS calcd for $C_{24}H_{32}O_3S$ 400.2072, found 400.2082.

1-[2-[1-(Mesitylsulfinyl)ethyl]phenyl]-1-methoxy-4,4-dimethyl-3-pentanone (28) Colorless plates ^{1}H NMR ($CDCl_3$, 270 MHz) 1.05 (s, 9H, $C(CH_3)_3$), 1.37 (d, 3H, J = 7, CH_3CH), 2.27 (s, 3H, mesityl), 2.54 (s, 6H, mesityl), 2.66 (dd, 1H, J = 17, 5, C*H*HCO), 3.02 (s, 3H, CH_3O), 3.07 (dd, 1H, J = 17, 8, CH*H*CO), 4.91(dd, 1H, J = 8, 5, MeOC*H*), 5.01 (q, 1H, J = 7, MesSOC*H*), 6.86 (s, 2H, mesityl), 7.32-7.60 (m, 4H, aryl); HRMS calcd for $C_{25}H_{34}O_3S$ 414.2228, found 414.2260; Crystal data: chemical formula $C_{25}H_{34}O_3S_1$; formula weight 414.0; crystal system monoclinic; space group $P2_1/n$; Z=4; a=15.774(4), b=11.909(2), c=13.102(2) Å; β=101.99(2)°; V=2407.6(8) Å^3; D_c=1.19 g cm^{-3}; R=0.082; R_w=0.093 (used 2426 reflections).

3-Methoxy-3-[2-[1-(mesitylthio)ethyl]phenyl]propiophenone (9c) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.50 (d, 3H, J = 7, CH_3CH), 2.20 (s, 3H, mesityl), 2.43 (s, 6H, mesityl), 2.78 (dd, 1H, J = 16, 3,

C*H*HCO), 2.84 (s, 3H, C*H*$_3$O), 3.46 (dd, 1H, *J* = 16, 9, CH*H*CO), 4.49 (q, 1H, *J* = 7, MesSC*H*), 4.95 (dd, 1H, *J* = 9, 3, MeOC*H*), 6.89 (s, 2H, mesityl), 7.23-7.98 (m, 9H, aryl); IR (neat) 1680, 1595, 1445, 1100, 845, 750, 735, 685; HRMS calcd for $C_{27}H_{30}O_2S$ 418.1966, found 418.1963.

2-[1-Methoxy-1-[2-[1-(mesitylthio)ethyl]phenyl]methyl]cyclohexanone (9d) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.42 (d, 3×0.17H, *J* = 7, C*H*$_3$CH), 1.51 (d, 3×0.83H, *J* = 7, C*H*$_3$CH), 1.59-2.46 (m, 9H, methylenes, C*H*CO), 2.20 (s, 3×0.83H, mesityl), 2.23 (s, 3×0.17H, mesityl), 2.39 (s, 6×0.83H, mesityl), 2.48 (s, 6×0.17H, mesityl), 2.81 (s, 3×0.83H, C*H*$_3$O), 2.91 (s, 3×0.17H, C*H*$_3$O), 4.27 (q, 0.83H, *J* = 7, MesSC*H*), 4.54 (q, 0.17H, *J* = 7, MesSC*H*), 4.75 (d, 0.17H, *J* = 9, MeOC*H*), 4.85 (d, 0.17H, *J* = 3, MeOC*H*), 6.88 (s, 2×0.83H, mesityl), 6.90 (s, 2×0.17H, mesityl), 7.16-7.73 (m, 4H, aryl); IR (neat) 1705, 1595, 1445, 1365, 1135, 760, 725; HRMS calcd for $C_{25}H_{32}O_2S$ 396.2123, found 396.2110.

2-Methoxy-2-[2-[1-(mesitylthio)ethyl]phenyl]acetonitrile (9e) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.57 (d, 3×0.89H, *J* = 7, C*H*$_3$CH), 1.60 (d, 3×0.11H, *J* = 7, C*H*$_3$CH), 2.24 (s, 3H, mesityl), 2.26 (s, 6×0.11H, mesityl), 2.35 (s, 6×0.89H, mesityl), 3.28 (s, 3×0.89H, C*H*$_3$O), 3.31 (s, 3×0.11H, C*H*$_3$O), 4.12 (q, 0.11H, *J* = 7, MesSC*H*), 4.23 (q, 0.89H, *J* = 7, MesSC*H*), 4.72 (s, 0.11H, MeOC*H*), 5.02 (s, 0.89H, MeOC*H*), 6.90 (s, 2H, mesityl), 7.24-7.68 (m, 4H, aryl); IR (neat) 1595, 1450, 1080, 845, 760, 735.

Methyl 3-methoxy-3-[2-[1-(mesitylthio)propyl]phenyl]-2,2-dimethylpropionate (9f) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.97 (s, 3H, C(C*H*$_3$)CH$_3$),1.07 (s, 3H, C(CH$_3$)C*H*$_3$), 1.11 (t, 3H, *J* = 7, C*H*$_3$CH$_2$), 1.86-1.97 (m, 2H, CH$_3$C*H*$_2$), 2.19 (s, 3H, mesityl), 2.40 (s, 6H, mesityl), 2.51 (s, 3H, C*H*$_3$O), 3.75 (s, 3H, COOC*H*$_3$), 4.32 (dd, 1H, *J* = 7, 8, MesSC*H*), 4.74 (s, 1H, MeOC*H*), 6.84 (s, 2H, mesityl), 7.18-7.62 (m, 4H, aryl); IR (neat) 1740, 1595, 1460, 1380, 1245, 1125, 845, 760; HRMS calcd for $C_{25}H_{34}O_3S$ 414.2228, found 414.2235.

1-[2-[1-(Mesitylthio)propyl]phenyl]-1-methoxy-4,4-dimethyl-3-pentanone (9g) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.98 (t, 3H, *J* = 7, C*H*$_3$CH$_2$), 1.17 (s, 9H, C(C*H*$_3$)$_3$), 1.88-2.09 (m, 2H, CH$_3$C*H*$_2$), 2.28 (s, 3H, mesityl), 2.36 (d, 1H, *J* = 17, C*H*HCO), 2.49 (s, 6H, mesityl), 2.78 (s, 3H, C*H*$_3$O), 3.02 (dd, 1H, *J* = 17, 9, CH*H*CO), 4.25 (t, 1H, *J* = 7, MesSC*H*), 4,79 (d, 1H, *J* = 9, MeOC*H*), 6.96 (s, 2H, mesityl), 7.29-7.71 (m, 4H, aryl); IR (neat) 1700, 1595, 1460, 1365, 1100, 995, 845, 755; HRMS calcd for $C_{26}H_{36}O_2S$ 412.2436, found 412.2446.

Methyl 3-hydroxy-3-[2-[1-(mesitylthio)ethyl]phenyl]-2,2-dimethylpropionate (14a) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.69 (d, 1H, *J* = 3, O*H*), 0.86 (s, 3H, C(C*H*$_3$)CH$_3$), 1.01 (s, 3H, C(CH$_3$)C*H*$_3$), 1.68 (d, 3H, *J* = 7, C*H*$_3$CH), 2.18 (s, 6H, mesityl), 2.20 (s, 3H, mesityl), 3.72 (s, 3H, COOC*H*$_3$), 4.75 (q, 0.90H, *J* = 7, PhSC*H*), 4.59 (q, 1H, *J* = 7, MesSC*H*), 4.59 (d, 1H, *J* = 3, HOC*H*), 6.86 (s, 2H, mesityl), 7.15-7.59 (m, 4H, aryl) IR 3560 (br), 1740, 1380, 1250, 1130, 1040, 855, 765, 740; HRMS calcd for $C_{23}H_{30}O_3S$ 386.1916, found 386.1914.

Methyl 3-hydroxy-3-[2-[1-(mesitylthio)ethyl]phenyl]propionate (14b) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.49 (d, 1H, *J* = 3, O*H*), 1.61 (d, 3H, *J* = 7, C*H*$_3$CH), 2.23 (s, 3H, mesityl), 2.29 (s, 6H, mesityl), 2.42 (dd, 1H, *J* = 16, 5, C*H*HCO), 2.63 (dd, 1H, *J* = 16, 9, CH*H*CO), 3.67 (s, 3H, COOC*H*$_3$), 4.51 (q, 1H, *J* = 7, MesSC*H*), 4.97 (ddd, 1H, *J* = 9, 5, 3, HOC*H*), 6.90 (s, 2H, mesityl), 7.20-7.59 (m, 4H, aryl); IR (neat) 3425 (br), 1740, 1260, 1160, 1040, 850, 765, 720; HRMS calcd for $C_{21}H_{26}O_3S$ 358.1602, found 358.1609.

Methyl 3-hydroxy-3-[2-[1-(mesitylsulfonyl)ethyl]phenyl]propionate (29) Colorless plates (mp 162 °C) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.74 (d, 3H, *J* = 7, C*H*$_3$CH), 1.94 (s, 1H, O*H*), 2.29 (s, 3H, mesityl), 2.48 (s, 6H, mesityl), 2.58 (dd, 1H, *J* = 16, 6, C*H*HCO), 2.83 (dd, 1H, *J* = 16, 8, CH*H*CO), 3.65 (s, 3H, COOC*H*$_3$), 4.96 (q, 1H, *J* = 7, MesSO$_2$C*H*), 5.09-5.13 (m, 1H, HOC*H*), 6.94 (s, 2H, mesityl), 7.26-7.61 (m, 4H, aryl); IR (neat) 3500 (br), 1720, 1310, 1215, 1140, 860, 780, 730; HRMS calcd for $C_{21}H_{27}O_5S$ (M+1) 391.1579, found 391.1583; Crystal data: chemical formula $C_{21}H_{26}O_5S_1$; formula weight 390.0; crystal system monoclinic; space group $P2_1/c$; *Z*=4; *a*=16.686(5), *b*=10.508(3), *c*=11.624(3) Å; *β*=104.41(2)°; *V*=1974.0(1) Å^3; D_c=1.31 g cm^{-3}; *R*=0.076; R_w=0.097 (used 3095 reflections).

1-Hydroxy-1-[2-[1-(mesitylthio)ethyl]phenyl]-4,4-dimethyl-3-pentanone (14c) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.03 (s, 9H, C(C*H*$_3$)$_3$), 1.59 (d, 3H, *J* = 7, C*H*$_3$CH), 1.87 (d, 1H, *J* = 2, O*H*), 2.23 (s, 3H, mesityl), 2.31 (s, 6H, mesityl), 2.65 (dd, 1H, *J* = 17, 5, C*H*HCO), 2.79 (dd, 1H, *J* = 17, 8, CH*H*CO), 4.51 (q, 1H, *J* = 7, MesSC*H*), 5.05 (m, 1H, HOC*H*), 6.91 (s, 2H, mesityl), 7.19-7.58 (m, 4H, aryl); IR (neat) 3550 (br), 1700, 1370, 1080, 1040, 850, 765, 750; HRMS calcd for $C_{24}H_{32}O_2S$ 384.2123, found 384.2156.

2-[1-Hydroxy-1-[2-[1-(mesitylthio)ethyl]phenyl]methyl]cyclohexanone (14d) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.08-2.74 (m, 9H, methylenes, C*H*CO), 1.48 (d, 3×0.12H, *J* = 7, C*H*$_3$CH), 1.52 (d, 3×0.44H, *J* = 7, C*H*$_3$CH), 1.60 (d, 3×0.38H, *J* = 7, C*H*$_3$CH), 2.22 (s, 3×0.12H, mesityl), 2.25 (s, 3×0.44H, mesityl), 2.30 (s, 6×0.38H, mesityl), 2.35 (s, 3×0.38H, mesityl), 2.38 (s, 6×0.44H, mesityl), 2.43 (s, 6×0.12H, mesityl), 3.03 (s, 3×0.44H, C*H*$_3$O), 3.68 (s, 3×0.38H, C*H*$_3$O), 3.83 (s, 3×0.12H, C*H*$_3$O), 4.15 (q, 0.06H, *J* = 7, MesSC*H*), 4.37 (q, 0.38H, *J* = 7, MesSC*H*), 4.57 (q, 0.12H, *J* = 7, MesSC*H*), 4.63 (q, 0.44H,

J = 7, MesSC*H*), 4.89 (pseudo d, 0.44H, J = 9, HOC*H*), 5.03 (pseudo d, 0.12H, J = 9, HOC*H*), 5.10 (pseudo d, 0.38H, J = 4, HOC*H*), 5.62 (s, 0.06H, HOC*H*), 6.87 (s, 2×0.12H, mesityl), 6.90 (s, 2×0.38H, mesityl), 6.93 (s, 2×0.44H, mesityl), 7.16-7.66 (m, 4H, aryl); IR (neat) 3500 (br), 1700, 1600, 1450, 1130, 1040, 855, 765; HRMS calcd for $C_{24}H_{30}O_2S$ 381.1967, found 381.1973.

4-(Mesitylthio)pentanal (21a) and 4-mesitylthio-1,1-dimethoxypentane (19a) Ethyl 3-hydroxybutyrate (5.00 g, 37.8 mmol) was mesylated by the same procedure as described for **4** (mesyl chloride, triethylamine). To a stirred solution of mesitylenethiol (6.33 g, 41.6 mmol) in 20 ml of THF was added a hexane solution of *n*-BuLi (1.66 mol dm^{-3}, 23.9 ml, 39.7 mmol) and then a THF (15 ml) solution of the crude mesylate at 0 °C. After removal of the cooling bath, the reaction mixture was stirred at room temperature for 12 h. Then, 100 ml of saturated aqueous solution of NH_4Cl was added, and the organic layer was diluted with 100 ml of ether, partitioned, and washed with aqueous NaOH (1 N solution, 50 ml). The organic layer was dried and concentrated under reduced pressure. Purification by column chromatography (eluent: ethyl acetate/hexane = 1/50 to 1/5) gave ethyl 3-(mesitylthio)butyrate (8.87 g, 33.3 mmol, 88%). To a dichloromethane solution (50 ml) of the resulting ester was added a dichloromethane solution of DIBAL-H (0.93 mol dm^{-3}, 35.8 ml, 33.3 mmol) at -78 °C and stirred at that temperature for 15 min. After an aqueous work up (15 ml of saturated aqueous solution of NH_4Cl), 20 g of anhydrous $MgSO_4$ was added and organic materials were filtrated through celite and silica-gel pads and concentrated. The Wittig reaction of this crude aldehyde ((methoxymethyl)triphenylphosphonium chloride, *n*-BuLi), followed by hydrolysis with a mixture of 4 ml of trifluoroacetic acid and 10 ml of water (15 min at room temperature) and purification by column chromatgraphy (eluent: ethyl acetate/hexane = 1/25 to 1/10), gave 4-(mesitylthio)pentanal (**21a**) (3.51 g, 14.8 mmol, 45% from the ester). ^{1}H NMR ($CDCl_3$, 270 MHz) 1.16 (d, 3H, J = 7, CH_3CH), 1.85 (pseudo q, 2H, J = 7, MesSCHCH_2), 2.26 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.63 (ddt, 2H, J = 7, 3, 1, CH_2CHO), 2.98 (pseudo sextet, 1H, J = 7, MesSC*H*), 6.93 (s, 2H, mesityl), 9.76 (t, 1H, J = 1, C*H*O); IR (neat) 2730, 1725, 1600, 1450, 1375, 1130, 1060, 850; HRMS calcd for $C_{14}H_{20}OS$ 236.1235, found 236.1255.

Acetalization by an usual method gave 4-mesitylthio-1,1-dimethoxypentane (**19a**) as a colorless oil (3.81 g, 13.5 mmol, 91% from the aldehyde). ^{1}H NMR ($CDCl_3$, 270 MHz) 1.14 (d, 3H, J = 7, CH_3CH), 1.56-1.79 (m, 4H, methylene), 2.26 (s, 3H, mesityl), 2.48 (s, 6H, mesityl), 2.95 (pseudo sextet, 1H, J = 7, MesSC*H*), 3.30 (s, 3H, CH_3O), 3.31 (s, 3H, CH_3O), 4.33 (t, 1H, J = 5, $(MeO)_2$C*H*), 6.92 (s, 2H, mesityl); IR (neat) 1595, 1450, 1375, 1195, 1125, 1060, 845; HRMS calcd for $C_{16}H_{26}O_2S$ 282.1654, found 282.1651.

The following aldehydes **21b-21d** and the corresponsing acetals **19b-19d** were synthesized by a similar procedure as **21a** and **19a**.

4-Mesitylthio-1,1-dimethoxyhexane (19b) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.95 (t, 3H, J = 7, CH_3CH$_2$), 1.47-1.81 (m, 6H, methylenes), 2.25 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.82 (pseudo quintet, 1H, J = 7, MesSC*H*), 3.29 (s, 3H, CH_3O), 3.30 (s, 3H, CH_3O), 4.31 (t, 1H, J = 6, $(MeO)_2$C*H*), 6.91 (s, 2H, mesityl); IR (neat) 1605, 1460, 1380, 1195, 1135, 1060, 855; HRMS calcd for $C_{17}H_{28}O_2S$ 296.1810, found 296.1794.

4-Mesitylthio-1,1-dimethoxy-5-methylhexane (19c) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.91 (d, 3H, J = 7, isopropyl), 1.03 (d, 3H, J = 7, isopropyl), 1.28-1.81 (m, 4H, methylenes), 1.85-1.98 (m, 1H, isopropyl), 2.25 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.55-2.78 (m, 1H, MesSC*H*), 3.28 (s, 3H, CH_3O), 3.30 (s, 3H, CH_3O), 4.31 (t, 1H, J = 6, $(MeO)_2$C*H*), 6.90 (s, 2H, mesityl); IR (neat) 1605, 1460, 1390, 1125, 1065, 855; HRMS calcd for $C_{18}H_{30}O_2S$ 310.1967, found 310.1924.

4-Mesitylthio-1,1-dimethoxy-3,3-dimethylpentane (19d) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.99 (d, 3H, J = 7, CH_3CH), 1.10 (s, 3H, C(CH_3)CH$_3$), 1.13 (s, 3H, C(CH$_3$)CH_3), 1.79 (d, 2H, J = 5, CH_2CH), 2.26 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.93 (q, 1H, J = 7, MesSC*H*), 3.31 (s, 3H, CH_3O), 3.32 (s, 3H, CH_3O), 4.53 (d, 1H, J = 5, $(MeO)_2$C*H*), 6.92 (s, 2H, mesityl); IR (neat) 1605, 1470, 1380, 1125, 1055, 855; HRMS calcd for $C_{18}H_{30}O_2S$ 310.1967, found 310.1907.

4-(Mesitylthio)hexanal (21b) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.98 (t, 3H, J = 7, CH_3CH$_2$), 1.47-1.58 (m, 2H, CH$_3$CH_2), 1.71-1.98 (m, 2H, CH_2CH$_2$CHO), 2.25 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.59-2.67 (m, 2H, CH_2CHO), 2.84 (pseudo quintet, 1H, J = 7, MesSC*H*), 6.92 (s, 2H, mesityl), 9.76 (t, 1H, J = 1, C*H*O); IR (neat) 2670, 1725, 1605, 1460, 1380, 1060, 1040, 855; HRMS calcd for $C_{15}H_{22}OS$ 250.1392, found 250.1396.

4-Mesitylthio-5-methylhexanal (21c) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.94 (d, 3H, J = 7, isopropyl), 1.05 (d, 3H, J = 7, isopropyl), 1.55-1.81 (m, 2H, CH_2CH$_2$CHO), 1.86-1.98 (m, 2H, isopropyl), 2.25 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.63-2.71 (m, 2H, CH_2CHO), 2.72-2.79 (m, 1H, MesSC*H*), 6.91 (s, 2H, mesityl), 9.75 (t, 1H, J = 2, C*H*O); IR (neat) 2725, 1725, 1600, 1465, 1390, 855; HRMS calcd for $C_{16}H_{24}OS$ 264.1548, found 264.1534.

4-Mesitylthio-3,3-dimethylpentanal (21d) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.02 (d, 3H, J = 7, CH_3CH), 1.22 (s, 3H, C(CH_3)CH_3), 1.24 (s, 3H, C(CH_3)CH_3), 2.26 (s, 3H, mesityl), 2.47 (s, 6H, mesityl), 2.50 (dd, 1H, J = 15, 3, CHHCHO), 2.64 (dd, 1H, J = 15, 3, CHHCHO), 3.02 (q, 1H, J = 7, MesSCH), 6.92 (s, 2H, mesityl), 9.88 (t, 1H, J = 3, CHO); IR (neat) 2740, 1720, 1600, 1465, 1380, 1060, 855; HRMS calcd for $C_{16}H_{24}OS$ 264.1547, found 264.1559.

2-[1-[1-(Mesitylthio)ethyl]cyclohexyl]acetaldehyde (21e) and 1-(2,2-dimethoxyethyl)-1-[1-(mesitylthio)ethyl]cyclohexane (19e) To a stirred solution of LDA, prepared from diisopropylamine (24.6 ml, 176 mmol) and a hexane solution of n-BuLi (1.66 mol dm^{-3}, 106 ml, 176 mmol), was slowly added methyl cyclohexanecarboxylate (25.0 g, 176 mmol) in 10 ml of THF at 0 °C, and the reaction mixture was stirred at that temperature for 1 h. Then, acetaldehyde (5.1 ml, 176 mmol) was added drop by drop to the solution, and the mixture was stirred for 1 h. After an aqueous work up, the organic layer was diluted with ether, partitioned, and dried over $MgSO_4$. Evaporation of the solvents and distillation gave methyl 1-(1-hydroxyethyl)cyclohexanecarboxylate: bp 100 °C/4 mmHg (24.2 g, 130 mmol, 74%). Mesylation of the resulting alcohol (6.94 g, 39.0 mmol) by mesyl chloride (6.71 g, 58.5 mmol) and triethylamine (7.90 g, 78.0 mmol), followed by sulfenylation by lithium mesitylenethiolate prepared from mesitylenethiol (7.13 g, 46.8 mmol) and a hexane solution of n-BuLi (1.66 mol dm^{-3}, 28.2 ml, 46.8 mmol), gave methyl 1-[1-(mesitylthio)ethyl]cyclohexanecarboxylate (3.67 g, 11.3 mmol, 29%). To a suspension of LAH (0.75 g, 19.8 mmol) in dry ether (100 ml) was added an ethereal solution (10 ml) of the resulting ester at 0 °C, and after removal of cooling bath, the reaction mixture was stirred at room temperature for 2 h. After a work up (3 ml of ethyl acetate and 5 ml of saturated aqueous solution of NH_4Cl), 10 g of anhydrous $MgSO_4$ was added, and organic solution was filtrated through celite and silica-gel pads and concentrated to give the corresponding alcohol. To a suspension of PCC (6.10 g, 28.3 mmol) and MS4A (10 g) in 50 ml of dry dichloromethane was added the resulting crude alcohol at room temperature, and the reaction mixture was stirred at that temperature for 15 min. Then the reaction mixture was filtrated through celite and silica-gel pads and concentrated to give the corresponding aldehyde. The Wittig reaction ((methoxymethyl)-triphenylphosphonium chloride, n-BuLi), followed by hydrolysis (trifluoroacetic acid, water) gave 2-[1-[1-(mesitylthio)ethyl]cyclohexyl]acetaldehyde (**21e**) (0.73 g, 2.41 mmol, 21% from the sulfenyl ester). ^{1}H NMR ($CDCl_3$, 270 MHz) 0.98 (d, 3H, J = 7, CH_3CH), 1.26-1.86 (m, 10H, -(CH_2)$_5$-), 2.26 (s, 3H, mesityl), 2.46 (s, 6H, mesityl), 2.50 (dd, 1H, J = 15, 3, CHHCHO), 2.73 (dd, 1H, J = 15, 3, CHHCHO), 3.31 (q, 1H, J = 7, MesSCH), 6.92 (s, 2H, mesityl), 10.01 (t, 1H, J = 3, CHO); IR (neat) 2675, 1720, 1605, 1460, 1380, 1035, 855; HRMS calcd for $C_{19}H_{28}OS$ 304.1861, found 304.1868.

Acetalization by an usual method gave 1-(2,2-dimethoxyethyl)-1-[1-(mesitylthio)ethyl]cyclohexane (**19e**) as a colorless oil (0.57 g, 1.64 mmol, 68% from the aldehyde). ^{1}H NMR ($CDCl_3$, 270 MHz) 0.97 (d, 3H, J = 7, CH_3CH), 1.44-1.80 (m, 10H, -(CH_2)$_5$-), 1.96 (dd, 1H, J = 15, 6, CHHCH), 2.03 (dd, 1H, J = 15, 5, CHHCH), 2.26 (s, 3H, mesityl), 2.50 (s, 6H, mesityl), 3.33 (s, 3H, CH_3O), 3.33 (q, 1H, J = 7, MesSCH), 3.34 (s, 3H, CH_3O), 4.63 (dd, 1H, J = 6, 5, (MeO)$_2$CH), 6.92 (s, 2H, mesityl); IR (neat) 1500, 1355, 1275, 1090, 1025, 955, 750; HRMS calcd for $C_{21}H_{34}O_2S$ 350.2279, found 350.2261.

Typical procedure for the aldol reaction of acetal 19 with a silylated carbon nucleophile To a mixture of **19a** (76.6 mg, 0.272 mmol) and 1-methoxy-2-methyl-1-trimethylsilyloxypropene **2** (74.3 mg, 0.426 mmol) in 5 ml of dry dichloromethane was added a dichloromethane solution of titanium(IV) chloride (1.02 mol·dm^{-3}, 0.32 ml, 0.326 mmol) at -78 °C under an argon atmosphere, and the reaction mixture was stirred for 1 h at that temperature. After an aqueous work up, the organic materials were extracted with dichloromethane (2×10 ml). The combined organic layers were dried, concentrated under reduced pressure, and purified by silica-gel thin layer chromatography (eluent: ethyl acetate/hexane = 1/10) to give methyl 6-mesitylthio-3-methoxy-2,2-dimethylheptanoate (**20a**) (86.7 mg, 91%). The 270 MHz ^{1}H NMR spectral and capillary gas chromatographic analyses showed a diastereomer ratio of 79:21. ^{1}H NMR ($CDCl_3$, 270 MHz) 1.09 (s, 3×0.79H, C(CH_3)CH_3), 1.10 (s, 3×0.21H, C(CH_3)CH_3), 1.15 (d, 3H, J = 7, CH_3CH), 1.18 (s, 3×0.79H, C(CH_3)CH_3), 1.19 (s, 3×0.21H, C(CH_3)CH_3), 1.45-1.76 (m, 4H, methylenes), 2.25 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.89-2.96 (m, 1H, MesSCH), 3.28-3.33 (m, 1H, MeOCH), 3.35 (s, 3×0.79H, CH_3O), 3.37 (s, 3×0.21H, CH_3O), 3.67 (s, 3×0.79H, COOCH_3), 3.68 (s, 3×0.21H, COOCH_3), 6.92 (s, 2H, mesityl); IR (neat) 1730, 1595, 1460, 1270, 1130, 1100, 845, 730; HRMS calcd for $C_{20}H_{32}O_3S$ 352.2072, found 352.2061.

8-Mesitylthio-5-methoxy-2,2-dimethyl-3-nonanone (20b) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.12 (s, 9H, C(CH_3)$_3$), 1.12-1.17 (m, 3H, CH_3CH), 1.53-1.65 (m, 4H, methylene), 2.25 (s, 3H, mesityl), 2.40 (dd, 1H, J = 17, 5, CHHCO), 2.48 (s, 6×0.30H, mesityl), 2.49 (s, 6×0.70H, mesityl), 2.78 (dd, 0.30H, J = 17, 7, CHHCO), 2.80 (dd, 0.70H, J = 17, 7, CHHCO), 2.93-2.96 (m, 1H, MesSCH), 3.28 (s, 3×0.70H, CH_3O), 3.29 (s, 3×0.30H, CH_3O), 3.66-3.70 (m, 1H, MeOCH), 6.92 (s, 2H, mesityl); IR (neat) 1705, 1600, 1460, 1370, 1090, 850, 735; HRMS calcd for $C_{21}H_{34}O_2S$ 350.2279, found 350.2299.

2-[4-(Mesitylthio)-1-methoxypentyl]cyclohexanone (20c) Less polar diastereomers (mixture of *anti* isomers) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.13 (d, 3×0.74H, J = 7, CH_3CH), 1.14 (d, 3×0.74H, J = 7, CH_3CH), 1.53-2.42 (m, 13H, methylenes, COCH), 2.26 (s, 3H, mesityl), 2.48 (s, 6×0.26H, mesityl), 2.49 (s, 6×0.74H, mesityl), 2.90-2.97 (m, 1H, MesSCH), 3.32 (s, 3H, CH_3O), 3.63-3.67 (m, 1H, MeOCH), 6.92 (s, 2H, mesityl); IR (neat) 1705, 1600, 1450, 1375, 1095, 850, 735; HRMS calcd for $C_{21}H_{32}O_2S$ 348.2023, found 348.2096. More polar diastereomers (mixture of *syn* isomers) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.14 (d, 3×0.19H, J = 7, CH_3CH), 1.15 (d, 3×0.81H, J = 7, CH_3CH), 1.39-2.43 (m, 12H, methylenes), 2.25 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.54-2.62 (m, 1H, COCH), 2.94-3.01 (m, 1H, MesSCH), 3.27 (s, 3×0.81H, CH_3O), 3.30 (s, 3×0.19H, CH_3O), 3.56-3.61 (m, 1H, MeOCH), 6.92 (s, 2H, mesityl); IR (neat)1705, 1600, 1450, 1375, 1090, 850, 735; HRMS calcd for $C_{21}H_{32}O_2S$ 348.2023, found 348.2096.

Methyl 6-mesitylthio-3-methoxy-2,2-dimethyloctanoate (20d) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.98 (t, 3H, J = 8, CH_3CH$_2$), 1.08 (s, 3×0.78H, C(CH_3)CH$_3$), 1.10 (s, 3×0.22H, C(CH_3)CH$_3$), 1.17 (s, 3×0.78H, C(CH$_3$)CH_3), 1.18 (s, 3×0.22H, C(CH$_3$)CH_3), 1.44-1.84 (m, 6H, methylenes), 2.25 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.78-2.85 (m, 1H, MesSCH), 3.26-3.37 (m, 1H, MeOCH), 3.32 (s, 3×0.78H, CH_3O), 3.35 (s, 3×0.22H, CH_3O), 3.66 (s, 3×0.78H, COOCH_3), 3.68 (s, 3×0.22H, COOCH_3), 6.91 (s, 2H, mesityl); IR (neat) 1740, 1605, 1460, 1380, 1270, 1105, 910, 855, 735; HRMS calcd for $C_{21}H_{34}O_3S$ 366.2229, found 366.2217.

Methyl 6-mesitylthio-3-methoxy-2,2,7-trimethyloctanoate (20e) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.93 (d, 3×0.81H, J = 7, isopropyl), 0.95 (d, 3×0.19H, J = 7, isopropyl), 1.05 (d, 3×0.19H, J = 7, isopropyl), 1.06 (d, 3×0.81H, J = 7, isopropyl), 1.07 (s, 3H, C(CH_3)CH$_3$), 1.16 (s, 3H, C(CH$_3$)CH_3), 1.33-1.64 (m, 4H, methylenes), 1.74-1.88 (m, 2H, isopropyl), 2.25 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.73-2.79 (m, 1H, MesSCH), 3.27 (dd, 1H, J = 9, 3, MeOCH), 3.32 (s, 3×0.81H, CH_3O), 3.34 (s, 3×0.19H, CH_3O), 3.66 (s, 3×0.81H, COOCH_3), 3.67 (s, 3×0.19H, COOCH_3), 6.90 (s, 2H, mesityl); IR (neat) 1725, 1465, 1275, 1105, 910, 855, 740; HRMS calcd for $C_{22}H_{36}O_3S$ 380.2385, found 380.2406.

Methyl 6-mesitylthio-3-methoxy-2,2,5,5-tetramethylheptanoate (20f) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.98 (d, 3×0.67H, J = 7, CH_3CH), 0.99 (d, 3×0.33H, J = 7, CH_3CH), 1.08 (s, 3×0.33H, CH$_2$C(CH_3)CH$_3$), 1.09 (s, 3×0.67H, CH$_2$C(CH_3)CH$_3$), 1.12 (s, (3×0.33+3)H, CH$_2$C(CH$_3$)CH_3, COC(CH_3)CH$_3$), 1.14 (s, 3×0.67H, CH$_2$C(CH$_3$)CH_3), 1.23 (s, 3H, COC(CH$_3$)CH_3), 1.35-1.68 (m, 2H, CH_2CH), 2.26 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.89 (q, 0.67H, J = 7, MesSCH), 2.96 (q, 0.33H, J = 7, MesSCH), 3.39 (s, 3×0.33H, CH_3O), 3.42 (s, 3×0.67H, CH_3O), 3.55 (dd, 0.67H, J = 6, 4, MeOCH), 3.64 (pseudo d, 0.33H, J = 9, MeOCH), 3.67 (s, 3×0.67H, COOCH_3), 3.69 (s, 3×0.33H, COOCH_3), 6.92 (s, 2H, mesityl); IR (neat) 1740, 1605, 1470, 1265, 1105, 855, 735; HRMS calcd for $C_{22}H_{36}O_3S$ 380.2385, found 380.2387.

Methyl 4-[1-[1-(mesitylthio)ethyl]cyclohexyl]-3-methoxy-2,2-dimethylbutyrate (20g) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.94 (d, 3H, J = 7, CH_3CH), 1.17 (s, 3H, C(CH_3)CH$_3$), 1.24 (s, 3H, C(CH$_3$)CH_3), 1.43-1.82 (m, 12H, methylenes), 2.26 (s, 3H, mesityl), 2.50 (s, 6H, mesityl), 3.38 (s, 3H, CH_3O), 3.45 (q, 1H, J = 7, MesSCH), 3.70 (s, 3H, COOCH_3), 3.75 (dd, 1H, J = 9, 1, MeOCH), 6.91 (s, 2H, mesityl), ^{13}C NMR ($CDCl_3$, 270 MHz) 14.4, 20.9, 21.4, 21.6, 21.7, 22.3, 26.1, 32.1, 33.1, 35.2, 39.2, 48.7, 49.3, 51.7, 59.9, 83.5, 128.8, 130.1, 137.5, 143.5, 177.5; IR (neat) 1740, 1460, 1375, 1265, 1105, 755, 735; HRMS calcd for $C_{25}H_{40}O_3S$ 420.2698, found 420.2727.

Methyl 4-[1-[1-(mesitylsulfinyl)ethyl]cyclohexyl]-3-methoxy-2,2-dimethylbutyrate (30) Colorless plates (mp 125 °C) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.74 (d, 3H, J = 7, CH_3CH), 1.16 (s, 3H, C(CH_3)CH$_3$), 1.25 (s, 3H, C(CH$_3$)CH_3), 1.39-2.08 (m, 12H, methylenes), 2.28 (s, 3H, mesityl), 2.39 (s, 3H, mesityl), 2.75 (s, 3H, mesityl), 3.44 (s, 3H, CH_3O), 3.65-3.72 (m, 2H, MesSCH, MeOCH), 3.70 (s, 3H, COOCH_3), 6.82 (s, 1H, mesityl), 6.90 (s, 1H, mesityl); IR (neat) 1730, 1605, 1455, 1390, 1255, 1100, 1020, 860, 625; HRMS calcd for $C_{25}H_{41}O_4S$ (M+1) 437.2726, found 437.2740; Crystal data: chemical formula $C_{25}H_{40}O_4S_1$; formula weight 436.7; crystal system monoclinic; space group $P2_1/n$; Z=4; a=28.372(8), b=6.290(2), c=13.705(4) Å; β=92.48(2)°; V=2443.0(1) Å^3; D_c=1.19 g cm^{-3}; R=0.074; R_w=0.094 (used 3630 reflections).

6-[[1-(Mesitylthio)ethyl]cyclohexyl]-5-methoxy-2,2-dimethyl-3-hexanone (20h) ^{1}H NMR ($CDCl_3$,270 MHz) 0.94 (d, 3×0.22H, J = 7, CH_3CH), 0.97 (d, 3×0.78H, J = 7, CH_3CH), 1.15 (s, 9×0.22H, C(CH_3)$_3$), 1.16 (s, 9×0.78H, C(CH_3)$_3$), 1.35-1.82 (m, 12H, CH_2C(CH_2)$_5$), 2.25 (s, 3H, mesityl), 2.50 (s, 6H, mesityl), 2.57 (dd, 1H, J = 17, 7, CHHCO), 2.84 (dd, 1H, J = 17, 5, CHHCO), 3.265 (s, 3×0.78H, CH_3O), 3.273 (s, 3×0.22H, CH_3O), 3.43-3.50 (m, 1H, MesSCH), 3.83-3.91 (m, 0.22H, MeOCH), 3.92-4.02 (m, 0.78H, MeOCH), 6.91 (s, 2H, mesityl) IR (neat) 1705, 1605, 1460, 1370, 1080, 850, 735 HRMS calcd for $C_{26}H_{42}O_2S$ 418.2906, found 418.2893.

2-[[1-[1-(Mesitylthio)ethyl]-1-methoxy]ethyl]cyclohexanone (20i) Less polar diastereomers (mixture of *anti* isomers) ^{1}H NMR ($CDCl_3$,270 MHz) 0.97 (d, 3×0.10H, J = 7, CH_3CH), 0.99 (d, 3×0.90H, J = 7, CH_3CH), 1.26-2.62 (m, 20H, methylenes), 2.25 (s, 3H, mesityl), 2.50 (s, 6H, mesityl), 2.64-2.74 (m, 1H, COC*H*), 3.23 (s, 3H, CH_3O), 3.45 (pseudo q, 1H, J = 7, MesSC*H*), 3.79-3.88 (m, 0.10H, MeOC*H*), 3.94-4.03 (m, 0.90H, MeOC*H*), 6.91 (s, 2H, mesityl) IR (neat) 1710, 1605, 1455, 1080, 910, 850, 735 HRMS calcd for $C_{26}H_{40}O_2S$ 416.2749, found 416.2716. More polar diastereomers (mixture of *syn*isomers) ^{1}H NMR ($CDCl_3$,270 MHz) 0.96 (d, 3×0.12H, J = 7, CH_3CH), 0.97 (d, 3×0.88H, J = 7, CH_3CH), 1.35-2.43 (m, 21H, methylenes, COC*H*), 2.26 (s, 3H, mesityl), 2.49 (s, 6×0.88H, mesityl), 2.51 (s, 6×0.12H, mesityl), 3.27 (s, 3×0.88H, CH_3O), 3.29 (s, 3×0.12H, CH_3O), 3.40-3.48 (m, 1H, MesSC*H*), 4.05-4.10 (m, 0.12H, MeOC*H*), 4.10-4.15 (m, 0.88H, MeOC*H*), 6.91 (s, 2H, mesityl) IR (neat) 1710, 1600, 1450, 1375, 1105, 910, 850, 735 HRMS calcd for $C_{26}H_{40}O_2S$ 416.2749, found 416.2723.

Methyl 4-[1-[1-(mesitylthio)ethyl]]cyclohexyl-3-methoxybutyrate (20j) ^{1}H NMR ($CDCl_3$,270 MHz) 0.96 (d, 3H, J = 7, CH_3CH), 1.41-1.83 (m, 12H, $CH_2C(CH_2)_5$), 2.26 (s, 3H, mesityl), 2.43 (dd, 1H, J = 15, 7, C*H*HCO), 2.50 (s, 6H, mesityl), 2.68 (dd, 1H, J = 15, 5, CH*H*CO), 3.31 (s, 3H, CH_3O), 3.42 (q, 1H, J = 7, MesSC*H*), 3.70 (s, 3H, $COOCH_3$), 3.86-3.95 (m, 1H, MeOC*H*), 6.92 (s, 2H, mesityl) IR (neat) 1740, 1605, 1440, 1460, 1375, 1100, 850, 735 HRMS calcd for $C_{23}H_{36}O_3S$ 392.2386, found 392.2378.

Typical procedure for the aldol reaction of aldehyde 21 with a silylated carbon nucleophile To a mixture of **21a** (80.4 mg, 0.340 mmol) and 1-methoxy-2-methyl-1-trimethylsilyloxypropene **2** (74.3 mg, 0.426 mmol) in 5 ml of dry dichloromethane was added a dichloromethane solution of triphenylmethyl hexachloroantimonate (0.12 mol·dm^{-3}, 0.50 ml, 0.061 mmol) at -78 °C under an argon atmosphere, and the reaction mixture was stirred for 45 min at that temperature. After an aqueous work up, the organic materials were extracted with dichloromethane (2×10 ml). The combined organic layers were dried, concentrated under reduced pressure, and purified by silica-gel thin layer chromatography (eluent: ethyl acetate/hexane = 1/10) to give methyl 3-hydroxy-6-mesitylthio-2,2-dimethylheptanoate (**22a**) (98.7 mg, 86%). The 270 MHz ^{1}H NMR spectral and capillary gas chromatographic analyses showed a diastereomer ratio of 81:19. ^{1}H NMR ($CDCl_3$, 270 MHz) 1.12-1.20 (m, 9H, C(CH_3)CH_3, CH_3CH), 1.25-1.91 (m, 5H, methylenes, O*H*), 2.25 (s, 3H, mesityl), 2.48 (s, 6H, mesityl), 2.99 (dt, 1H, J = 7, MesSC*H*), 3.53-3.64 (m, 1H, HOC*H*), 3.69 (s, 3×0.67H, $COOCH_3$), 3.70 (s, 3×0.33H, $COOCH_3$), 6.92 (s, 2H, mesityl); IR (neat) 3500 (br), 1725, 1275, 1140, 850, 735; HRMS calcd for $C_{19}H_{30}O_3S$ 338.1916, found 338.1935.

5-Hydroxy-8-mesitylthio-2,2-dimethyl-3-nonanone (22b) ^{1}H NMR ($CDCl_3$, 270 MHz) 1.13 (s, 9H, C(CH_3)$_3$), 1.13-1.16 (m, 3H, CH_3CH), 1.53-1.78 (m, 4H, methylenes), 2.25 (s, 3H, mesityl), 2.47 (s, 6×0.6H, mesityl), 2.49 (s, 6×0.4H, mesityl), 2.52 (dd, 0.40H, J = 18, 9, C*H*HCO), 2.53 (dd, 0.60H, J = 18, 9, C*H*HCO), 2.67 (dd, 0.40H, J = 18, 3, CH*H*CO), 2.68 (dd, 0.60H, J = 18, 3, CH*H*CO), 2.91-3.03 (m, 1H, MesSC*H*), 3.23 (s, 1H, O*H*), 3.91-4.15 (m, 1H, HOC*H*), 6.92 (s, 2H, mesityl); IR (neat) 3500 (br), 1705, 1605, 1465, 1370, 1060, 850; HRMS calcd for $C_{20}H_{32}O_2S$ 350.2280, found 350.2267.

Methyl 3-hydroxy-6-mesitylthio-2,2-dimethyloctanoate (22d) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.96 (t, 3×0.09H, J = 7, CH_3CH_2), 0.97 (t, 3×0.91H, J = 7, CH_3CH_2), 1.15 (s, 3×0.91H, C(CH_3)CH_3), 1.17 (s, 3×0.09H, C(CH_3)CH_3), 1.18 (s, 3×0.91H, C(CH_3)CH_3), 1.19 (s, 3×0.09H, C(CH_3)CH_3), 1.23-1.96 (m, 6H, methylenes), 2.25 (s, 3H, mesityl), 2.38-2.43 (m, 1H, O*H*), 2.48 (s, 6×0.09H, mesityl), 2.49 (s, 6×0.91H, mesityl), 2.82-2.89 (m, 1H, MesSC*H*), 3.50-3.58 (m, 1H, HOC*H*), 3.69 (s, 3×0.91H, $COOCH_3$), 3.70 (s, 3×0.09H, $COOCH_3$), 6.91 (s, 2H, mesityl); IR (neat) 3520 (br), 1730, 1605, 1470, 1380, 1275, 1140, 1080, 915, 855, 740; HRMS calcd for $C_{20}H_{32}O_3S$ 352.2072, found 352.2066.

Methyl 3-hydroxy-6-mesitylthio-2,2,7-trimethyloctanoate (22e) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.92 (d, 3×0.91H, J = 7, isopropyl), 0.94 (d, 3×0.09H, J = 7, isopropyl), 1.02 (d, 3×0.09H, J = 7, isopropyl), 1.03 (d, 3×0.91H, J = 7, isopropyl), 1.14 (s, 3×0.91H, C(CH_3)CH_3), 1.15 (s, 3×0.09H, C(CH_3)CH_3), 1.16 (s, 3×0.91H, C(CH_3)CH_3), 1.17 (s, 3×0.09H, C(CH_3)CH_3), 1.56-1.80 (m, 4H, methylenes), 1.90-1.99 (m, 1H, isopropyl), 2.25 (s, 3H, mesityl), 2.39-2.44 (m, 1H, O*H*), 2.49 (s, 6H, mesityl), 2.76-2.82 (m, 1H, MesSC*H*), 3.48-3.57 (m, 1H, HOC*H*), 3.69 (s, 3×0.91H, $COOCH_3$), 3.70 (s, 3×0.09H, $COOCH_3$), 6.90 (s, 2H, mesityl); IR (neat) 3520 (br), 1730, 1465, 1275, 1145, 910, 855, 740; HRMS calcd for $C_{21}H_{34}O_3S$ 366.2229, found 366.2205.

Methyl 3-hydroxy-6-mesitylthio-2,2,5,5-tetramethylheptanoate (22f) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.96 (d, 3×0.28H, J = 7, CH_3CH), 0.99 (d, 3×0.72H, J = 7, CH_3CH), 1.10 (s, 3×0.28H, $CH_2C(CH_3)CH_3$), 1.11 (s, 3×0.28H, $CH_2C(CH_3)CH_3$), 1.13 (s, 3×0.28H, $CH_2C(CH_3)CH_3$), 1.167 (s, 3×0.72H, $CH_2C(CH_3)CH_3$), 1.175 (s, 3×0.28H, COC(CH_3)CH_3), 1.188 (s, 3×0.28H, COC(CH_3)CH_3), 1.194 (s, 3×0.72H, COC(CH_3)CH_3), 1.21 (s, 3×0.72H, COC(CH_3)CH_3), 1.51-1.61 (m, 2H, CH_2CH), 2.26 (s, 3H, mesityl), 2.35 (d, 0.72H, J = 7, O*H*), 2.47 (s, 6×0.28H, mesityl), 2.48 (s, 6×0.72H, mesityl), 2.57 (d,

0.28H, J = 7, O*H*), 3.04 (q, 0.72H, J = 7, MesSC*H*), 3.11 (q, 0.28H, J = 7, MesSC*H*), 3.70 (s, 3×0.28H, COOCH_3), 3.71 (s, 3×0.72H, COOCH_3), 3.84-3.92 (m, 1H, HOC*H*), 6.92 (s, 2H, mesityl); IR (neat) 3525 (br), 1720, 1465, 1275, 1135, 910, 855, 735; HRMS calcd for $C_{21}H_{34}O_3S$ 366.2229, found 366.2210.

Methyl 3-hydroxy-4-[1-[1-(mesitylthio)ethyl]cyclohexyl]-2,2-dimethylbutyrate (22g) ^{1}H NMR ($CDCl_3$, 270 MHz) 0.95 (d, 3×0.34H, J = 7, CH_3CH), 0.99 (d, 3×0.66H, J = 7, CH_3CH), 1.23 (s, 6H, C(CH_3)CH_3), 1.41-1.81 (m, 12H, methylenes), 2.26 (s, 3H, mesityl), 2.49 (s, 6H, mesityl), 2.56 (d, 0.66H, J = 7, O*H*), 2.91 (d, 0.34H, J = 7, O*H*), 3.47-3.52 (m, 1H, MesSC*H*), 3.705 (s, 3×0.34H, COOCH_3), 3.715 (s, 3×0.66H, COOCH_3), 3.88-4.04 (m, 1H, HOC*H*), 6.92 (s, 2H, mesityl) IR (neat) 3475 (br), 1720, 1600, 1455, 1375, 1270, 1140, 1075, 910, 850, 735 HRMS calcd for $C_{24}H_{38}O_3S$ 406.2542, found 406.2550.

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