Stereospecific Nucleophilic Addition Reactions to Olefins. Addition of Thiols to α,β-Unsaturated Carboxylic Acid Derivatives[1]

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Stereospecific nucleophilic addition of thiols to derivatives of α,β-unsaturated carboxylic acids is described. The additions are carried out at room temperature in the presence of a catalytic amount of lithium thiolate and an excess of thiol as a proton source. Erythro and threo adducts are obtained with high diastereoselectivity from *E* and *Z* olefins, respectively. This anti addition suggests that the enolate generated by nucleophilic addition undergoes rapid protonation prior to conformational change in the intermediate.

Introduction

Nucleophilic addition reactions[2,3] such as Michael addition are one of the most important reactions in organic chemistry and biochemistry. There are many aspects of nucleophilic additions to olefins that are not well understood, particularly the stereochemistry of the reaction in acyclic systems.

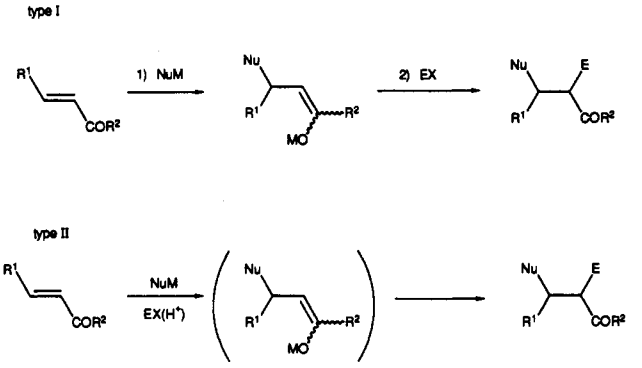
Nucleophilic addition reactions such as Michael addition can be classified into two types (Scheme I).

The type I reaction consists of two processes. Initial conjugate addition of a nucleophile, NuM, to the Michael acceptor forms a conjugate enolate, which is then trapped by addition of an appropriate electrophile, EX, to form the final adduct. The diastereoselectivity in this stepwise addition reaction has been studied by several groups.[4-9] On the other hand, type II reactions are carried out by treating the substrate with a nucleophile in the presence of an electrophile, e.g., under protic conditions. The stereochemistry of the type II reaction has not been fully understood because acyclic trisubstituted olefins have never been employed as substrates and because stereocontrol in the nucleophilic addition has not been expected to be successful, particularly in acyclic systems.

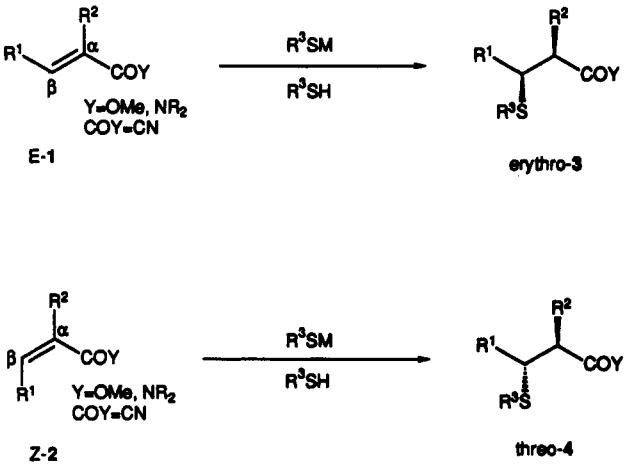
We found that nucleophilic addition of thiols[9] to olefins proceeds stereospecifically and with high stereoselectivity via a type II reaction.[10] The addition of thiols to *E* and *Z* α,β-unsaturated carboxylic acid derivatives **1** and **2** in the presence of excess thiol as a proton source gave erythro and threo adducts **3** and **4**, respectively, with high diastereoselectivity, even at room temperature, as a result of anti addition (Scheme II).

Contrary to the reaction mechanism[4-9] proposed for type I reactions, the newly discovered stereospecific type II reaction in protic solvent proceeds via rapid protonation of the enolate formed by attack of the nucleophile (RSLi).

Scheme I



Scheme II



Results and Discussion

Stereospecific Addition Reaction to Olefins. (i) Esters (Table I). We first examined the addition of thiophenol to trisubstituted olefinic esters (Scheme III), as summarized in Table I.

Methyl tiglate (**5a**) was treated with thiophenol in the presence of lithium thiophenoxide to give a mixture of two adducts **7a** and **8a** in 90% yield with a ratio of 91:9 (entry 1). Encouraged by the high selectivity, we varied the amounts of thiophenol and lithium thiophenoxide and the reaction temperature. When 0.1 equiv of lithium thiophenoxide and 10 equiv of thiophenol were used (standard

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(1) Preliminary communication: Miyata, O.; Shinada, T.; Ninomiya, I.; Naito, T. *Chem. Pharm. Bull.* **1989**, *37*, 3158-3160.
(2) (a) March, J. *Advanced Organic Chemistry*, 3rd ed; John Wiley and Sons, Inc.: New York, 1985; pp 657-666, 711-712. (b) Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Organic Reactions*; Blatt, A. H., Ed.; John Wiley and Sons, Inc.: New York, 1959; Vol. 10, pp 179-555. (c) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin, Inc.: Menlo Park, CA, 1972; pp 595-628.
(3) Michael, A. *J. Prakt. Chem.* **1887**, *35*, 349.
(4) Fleming, I.; Hill, J. H.; Parker, D.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1985**, 318-321.
(5) Tomioka, K.; Kawasaki, H.; Koga, K. *Tetrahedron Lett.* **1985**, *26*, 3027-3034.
(6) Yamamoto, Y.; Yamada, J.; Ueyama, T. *J. Am. Chem. Soc.* **1987**, *109*, 5820-5822.
(7) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438-2440.

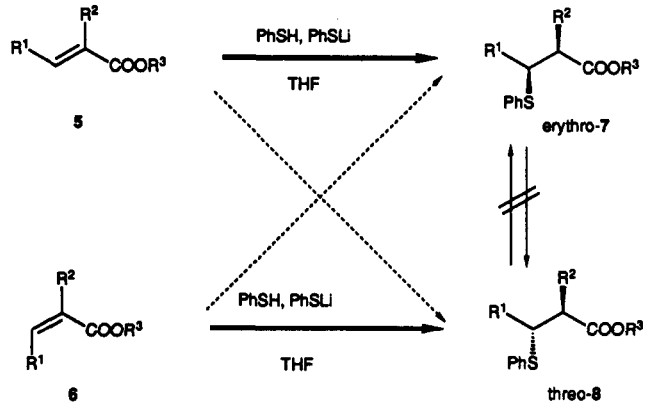
0022-3263/91/1956-6556$02.50/0

Table I. Addition Reaction of Thiophenol to α,β-Unsaturated Esters

entry	substrate	PhSLi, equiv	PhSH, equiv	temp, °C	time, h	yield, %	ratio[a] 7:8
1	**5a**	3	3	20	1.5	90	91:9
2	**5a**	0.1	10	20	2	99	96:4
3	**5a**	0.1	1.2	20	2	95	94:6
4	**5a**	0.1	10	0	6	59	96:4
5	**5a**		10	20	24	0	
6	**5a**	Et_3N	3	20	24	53	93:7
7	**5a**	1.2	MeOH	20	2	0	
8	**5a**	1.2		20	2	0	
9	**5b**	0.1	10	20	2	85	87:13
10	**5c**	0.1	10	20	2	95	85:15
11	**5d**	0.1	10	20	24	99	81:19
12	**5e**	0.1	10	20	24	25	57:43[b]
13	**5f**	3	3	20	0.5	85	38:62
14	**5f**	0.1	10	20	0.5	87	84:16
15	**5f**	0.1	10	0	1	94	92:8
16	**5f**	0.1	10	−78	3	60	90:10
17	**5g**	0.1	10	0	1	90	80:20
18	**5g**	0.1	10	−20	3	63	92:8
19	**6a**	0.1	10	20	2	85	14:86
20	**6a**	0.1	1.2	20	2	84	19:81
21	**6a**	0.1	100	20	2	78	14:86
22	**6a**	1.2		20	2	0	*c*
23	**6b**	0.1	10	20	2	61	17:83
24	**6c**	0.1	10	20	2	86	28:72
25	**6d**	0.1	10	20	24	82	66:34
26	**6f**	0.1	10	0	1	99	14:86
27	**6g**	0.1	10	−20	3	87	14:86
28	**5a**	PhSNa (0.1)	10	20	2.5	87	93:7
29	**6a**	PhSNa (0.1)	10	20	2.5	83	22:78

[a] Determined by 200- or 500-MHz ^1H NMR. [b] Stereochemistries of **7e** and **8e** have not been established. [c] Isomerization of **6a** to **5a** was observed.

Scheme III



conditions) at room temperature, **5a** afforded the erythro adduct **7a** with high diastereoselectivity in quantitative yield (entry 2). Interestingly, high diastereoselectivity was observed at room temperature, in contrast to known diastereoselective reactions[4-9] which occur at −25 to −100 °C. Use of triethylamine as a base gave adduct **7a**, also with high diastereoselectivity but in only moderate yield (entry 6). In the absence of either lithium thiophenoxide or thiophenol, the reaction failed to give the adduct (entries 5, 7, 8). Similarly, methyl β-ethyl-, β-*n*-propyl-, and β-phenylmethacrylates (**5b,c,d**) underwent diastereoselective addition of thiophenol to give the erythro adducts **7b**, **7c**, and **7d** as major products (entries 9–11). However, when a bulky substituent such as *tert*-butyl was present at the R^1 position (**5e**), the stereoselectivity was markedly diminished, giving a 1:1 mixture of **7e** and **8e** in poor yield (entry 12).

The addition reaction was then applied to the *E* ethylidene lactones **5f,g**. The erythro products **7f,g** were obtained with high selectivity using 0.1 equiv of lithium thiophenoxide and 10 equiv of thiophenol (entries 14, 15, 17, 18). Lowering the temperature (−20 to 0 °C) improved the selectivity (92:8) (entries 15, 18).

In order to clarify the relationship between the stereostructures of the products and the configuration of the double bond in the substrate, we turned our attention to the corresponding *Z* esters.

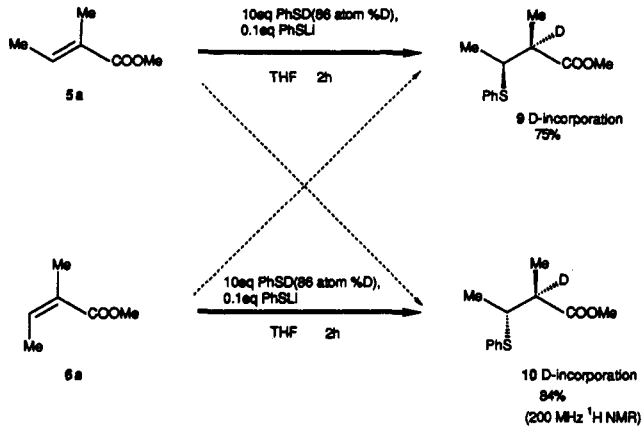
If the addition of thiophenol proceeds as in known conjugate additions[4-9] of type I, the erythro adduct **7** should form from the *Z* esters. Under the standard conditions, the *Z* esters **6a–c** and the *Z* lactones **6f,g** gave preferentially the threo adducts **8a–c** and **8f,g**, respectively, with high diastereoselectivity (entries 19, 23, 24, 26, 27). The ratio of the erythro and threo adducts **7a** and **8a** is independent of the concentration of thiophenol (entries 19–21). However, in the absence of thiophenol, *Z* ester **6a** did not give **7a** and **8a** but the isomerized *E* olefin **5a** (entry 22). Addition to the *Z* cinnamic ester derivative **6d** gave the expected threo adduct **8d** as the minor product (entry 25).

(8) McGarvey, G. J.; Williams, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 1435–1437.

(9) Although the sulfur atom centered nucleophile is well-known as an efficient Michael donor, little has been published about the stereochemistry of the reaction, particularly in simple acyclic systems. On the stereoselective addition reaction of thiols to nitro olefins in the type I reaction: (a) Kamimura, A.; Sasatani, H.; Hashimoto, T.; Kawai, T.; Hori, K.; Ono, N. *J. Org. Chem.* **1990**, *55*, 2437–2442. (b) Hori, K.; Higuchi, S.; Kamimura, A. *J. Org. Chem.* **1990**, *55*, 5900–5905.

(10) Recently, Mohrig et al. have reported on the stereochemistry of the addition of 2-methyl-2-propanethiol-*d* to ethyl crotonate in ethanol. However, their results are remarkably different from ours because their reaction is not stereospecific but stereoselective. Mohrig, J. R.; Fu, S. S.; King, R. W.; Warnet, R.; Gustafson, G. *J. Am. Chem. Soc.* **1990**, *112*, 3665–3667.

Scheme IV



Sodium can be used as the countercation. Treatment of the *E* and *Z* olefins **5a** and **6a** with thiophenol in the presence of sodium thiophenoxide gave **7a** and **8a** as the major products, respectively (entries 28, 29). Similar erythro:threo ratios observed in the presence of lithium and sodium thiophenoxides showed that the nature of the countercation does not affect selectivity.

Equilibration between **7** and **8** was not observed under the reaction conditions. **7** and **8** are the kinetic products, and the reaction proceeds by anti addition.

The reactions of **5a** and **6a** in the presence of deuterium thiophenoxide[11] gave the deuterated erythro and threo adducts **9** and **10**, respectively (Scheme IV). This result showed that the thiol is the proton source.

(ii) Nitriles (Table II). The reactions of the *E* and *Z* nitriles **13** and **14** are stereospecific and highly diastereoselective (entries 3 and 4).

(iii) Carboxamides (Table II). Carboxamides are less reactive Michael acceptors with thiophenol. A high temperature (110 °C) was required for successful addition to the *E* carboxamides **17**, **23**, and **27**. Interestingly, all olefins reacted with high diastereoselectivity even at the high temperature (110 °C) (entries 5, 9, 11). The isomeric *Z* amide **18** also preferentially underwent anti addition (entry 7), but with lower selectivity than that of the *E* amide **17**. The reactions of *Z* carboxamides **24** and **28** exhibited no stereoselectivity (entries 10, 13), in a striking contrast to *E* isomers **23** and **27**.

In order to explain the poor diastereoselectivity of the *Z* carboxamides **18** and **28**, we examined the stability of the products and substrates to equilibration. Under the reaction conditions, no equilibration was observed between erythro and threo adducts **19** and **20**, or **29** and **30**. On the other hand, *Z* carboxamides **18** and **28** isomerized[12] to the stable *E* carboxamides **17** and **27** upon heating at 100 °C in the presence of thiophenol. No isomerization of *Z* carboxamide **24** was observed under the same conditions. These results suggest that the addition of thiophenol to the *Z* carboxamides **18** and **28** competes with thermal radical isomerization[12] to the *E* congeners. Consequently, it is not clear whether the addition proceeds in a stereospecific manner.

In order to solve this problem, we investigated the addition of benzyl mercaptan, which added stereospecifically to esters **5a** and **6a** (entries 1, 2). Since benzyl mercaptan is a better nucleophile[13] than thiophenol, it was expected that the addition of benzyl mercaptan would proceed at a temperature low enough[12] to avoid the undesired isomerization of the substrate. The addition of benzyl mercaptan to *Z* carboxamide **18** proceeded smoothly even at 0 °C to afford the threo adduct **22** in good yield and with high diastereoselectivity, while the corresponding *E* isomer **17** afforded exclusively the erythro adduct **21** under the same conditions (entries 6, 8). Similarly, the ethylidene lactams **27** and **28** underwent smooth nucleophilic addition of benzyl mercaptan to give the respective adducts **31** and **32** in good yields and with high diastereoselectivity (entries 12, 14).

Scope and Limitations. In order to establish the generality of the stereospecific nucleophilic addition reaction, we investigated the reactions of α,β-unsaturated imides and dehydroamino esters. Imides reacted nondiastereospecifically and afforded stereoselectively the same erythro adduct. Stereospecificity was observed in the addition of thiophenol to dehydroamino esters, but benzyl mercaptan added stereoselectively, giving the threo adduct as the major product from either *Z* or *E* substrates.

(i) Imides (Table II). The addition of thiophenol to the *E* and *Z* imides **33** and **34** yielded predominantly the same erythro adduct **35** (entries 15, 16). Similarly, when benzyl mercaptan was used as a nucleophile, both *E* and *Z* imides **33** and **34** gave stereoselectively the same erythro thioester **37**, formed by displacement of the oxazolidinone moiety (entries 17, 18).

(ii) Dehydroamino Esters (Table II). At room temperature, the *Z* dehydroamino ester **39** gave stereoselectively the threo adduct **42** while the *E* ester **40** gave a 1:1 mixture of two adducts, **41** and **42** (entries 19, 22). At −40 °C, the *Z* and *E* esters **39** and **40** gave the threo and erythro adducts **42** and **41**, respectively, as the major products in good yields (entries 20, 23). The temperature dependence would be reasonably explained by the fact that the unstable *E* dehydroamino ester **40** was readily isomerized[14] to the stable *Z* congener **39** in the presence of thiophenol at temperatures from 0 °C to room temperature. Interestingly, the addition of benzyl mercaptan to esters **39** and **40** gave the same threo adduct **44** even at temperatures from −20 to −50 °C, thus exhibiting high threo selectivity (entries 21, 24). No isomerization[14] of the *E* ester **40** to the *Z* isomer **39** was observed in the presence of benzyl mercaptan even at room temperature. Additionally, no equilibration of the diastereomeric pairs (**41** ⇄ **42**, **43** ⇄ **44**) was observed under the reaction conditions at low temperature.

Stereochemical Rationalization. Most of the *E* and *Z* α,β-unsaturated esters, amides, and nitriles afforded the erythro and threo adducts, respectively, with high diastereoselectivity. Since the reaction proceeds smoothly in the presence of a catalytic amount of lithium thiophenoxide and an excess of thiophenol, the stereochemistry would be explained by anti addition of thiols due to rapid protonation of the conjugate enolates (Scheme V).

Nucleophilic addition of lithium thiolate to the *E* and *Z* olefins forms transient enolates A and B, which are protonated rapidly from the face opposite the SR^3 group because of the stereoelectronic effect of the SR^3 group.

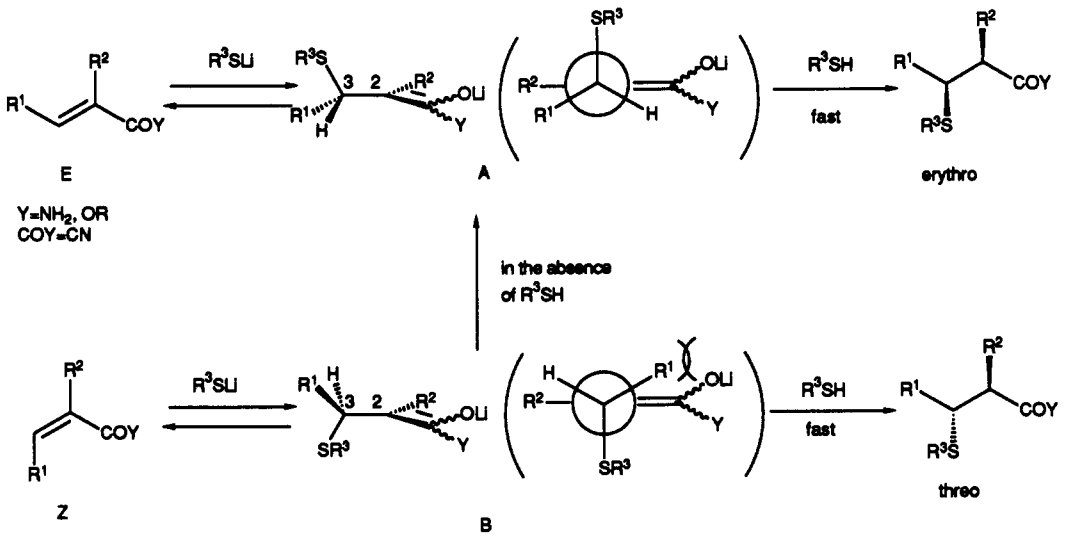
(11) Lambert, J. B.; Clikeman, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 4203–4211.

(12) Cis–trans isomerization of olefins catalyzed by a thiyl radical generated from either thiophenol or diphenyl disulfide is well-known. (a) Walling, C.; Helmreich, W. *J. Am. Chem. Soc.* **1959**, *81*, 1144–1148. (b) Moussebois, C.; Dale, J. *J. Chem. Soc. C* **1966**, 260–264. (c) Miyata, O.; Shinada, T.; Ninomiya, I.; Naito, T. *Synthesis* **1990**, 1123–1125.

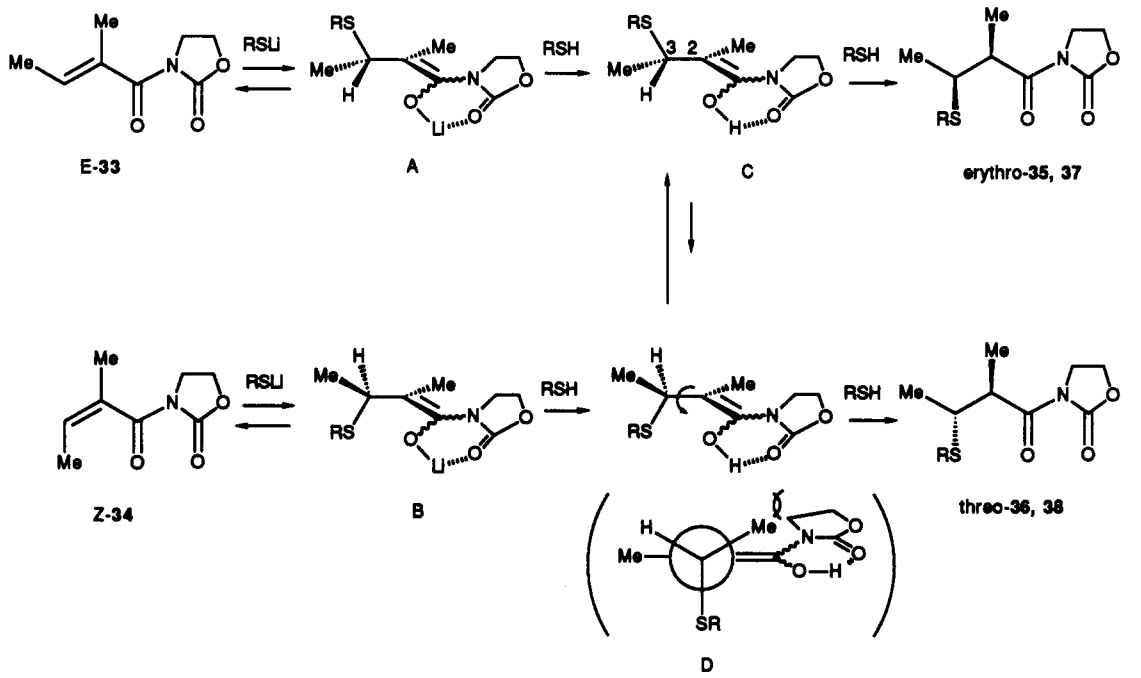
(13) Kreevoy, M. M.; Harper, E. T.; Duvall, R. E.; Wilgus, H. S., III; Ditsch, L. T. *J. Am. Chem. Soc.* **1960**, *82*, 4899–4902.

(14) The isomerization of the *E* dehydroamino ester to the stable *Z* isomer with thiophenol would proceed through imine–enamine tautomerization catalyzed by the acidic thiophenol. On the other hand, no isomerization would be observed in the presence of benzyl mercaptan, which is a weaker acid than thiophenol.

Scheme V



Scheme VI



Protonation of enolate ions at the α-carbon is known[15] to proceed very fast, and thus conformational change of enolate B to A owing to rotation around the C_2–C_3 bond is improbable in the presence of a large amount of thiol as proton source. Ab initio molecular orbital calculations[16] of a model compound ($HSCH_2CH{=}COH(O^-)$) for the intermediate enolates, using the Gaussian-80 program with the STO-3G basis set, has provided positive support for our proposed mechanism. The C_2 carbon in the enolate double bond is appreciably pyramidalized (Figure 1).

The pyramidalization[17] would be brought about by the stereoelectronic effect of the neighboring sulfur group and may be responsible for anti addition of the proton at the C_2 carbon. Recently, Kamimura and co-workers[9] have reported that stereoselective addition of alcohols and thiols to *E* nitro olefins is explained by the endo alkoxy effect. Rapid protonation is compatible with the observation that treatment of *Z* olefin **6a** with lithium thiophenoxide in the absence of thiophenol gave the completely isomerized *E* olefin **5a** (entry 22 in Table I). In the absence of thiol, enolate B, formed by addition of lithium thiolate to the *Z* olefin, is isomerized by rotation around the C_2–C_3 bond. Thiolate anion is eliminated from the resulting conformation A to give the stable *E* olefin.

The exceptional result that the erythro adduct **7d** is obtained in greater amount than threo adduct **8d** (66:34) (entry 25, Table I) would be explained by steric hindrance

(15) Recently, Kresge's group has measured the rates of protonation of ketone enols and enolate ions in aqueous buffer solutions and has indicated that the rate constants for protonation of enolate ions are 10^6–10^9 M^{-1} s^{-1} and that carbon protonation of the enolate ions proceeds very rapidly. On the other hand, carbon protonation of the corresponding enols is slower by a factor of 10^6–10^9 compared to the corresponding enolate ions. Chiang, Y.; Kresge, A. J.; Santaballa, J. A.; Wirz, J. *J. Am. Chem. Soc.* **1988**, *110*, 5506–5510. Capon, B.; Zucco, C. *J. Am. Chem. Soc.* **1982**, *104*, 7567–7572.

(16) We thank the Computer Center, Institute for Molecular Science, for the use of the HITAC M-680H computer.

(17) Recently, a novel idea relating stereoselectivity to pyramidalization of sp^2 carbon has been proposed. (a) Seebach, D.; Zimmermann, J.; Gysel, V.; Ziegler, R.; Ha, T.-K. *J. Am. Chem. Soc.* **1988**, *110*, 4763–4772. (b) Katagiri, N.; Watanabe, N.; Sakai, J.; Kawai, T.; Kaneko, C. *Tetrahedron Lett.* **1990**, *31*, 4633–4636.

Table II. Addition Reaction of Thiophenol and Benzyl Mercaptan to α,β-Unsaturated Carboxylic Acid Derivatives[a]

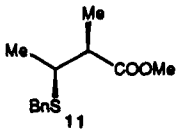
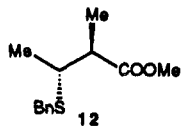
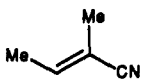
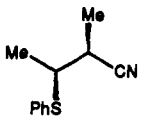
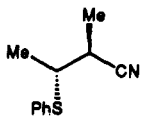
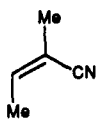
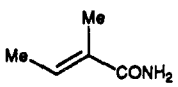
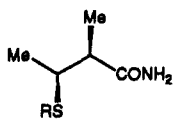
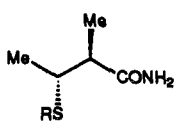
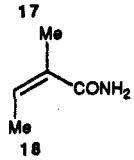
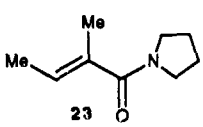
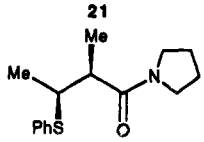
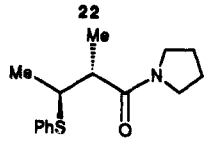
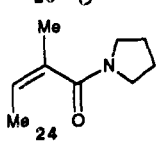
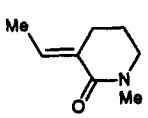
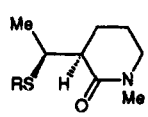
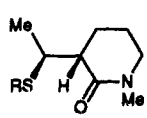
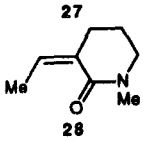
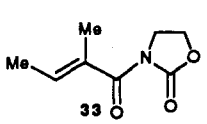
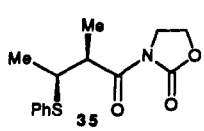
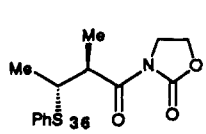
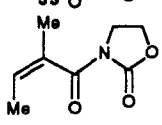
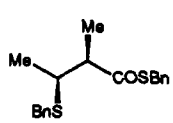
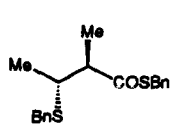
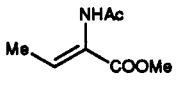
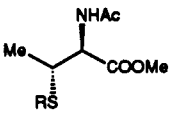
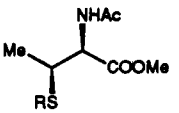
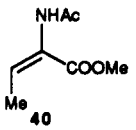
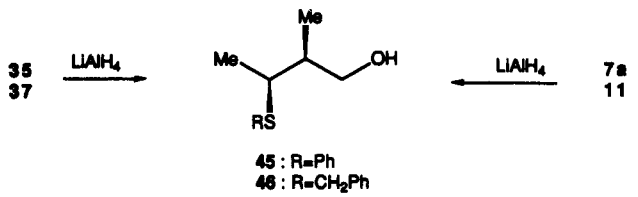
entry	substrate	temp, °C	time, h	products: erythro	products: threo	yield, %	ratio e:t[b]
1	**5a**	0	0.5	 **11**	 **12**	98	98: 2
2	**6a**	0	0.5	**11**	**12**	98	10:90
3	 **13**	20	2	 **15**	 **16**	92	96: 4
4	 **14**	20	2	**15**	**16**	95	13:87
5	 **17**	110	2	 **19**:R=Ph	 **20**:R=Ph	93	95: 5
6	**17**	0	1	**21**:R=CH_2Ph	**22**:R=CH_2Ph	94	99: 1
7	 **18**	110	2	**19**	**20**	92	25:75
8	**18**	0	1	**21**	**22**	88	16:84
9	 **23**	110	8	 **25**	 **26**	49	96: 4
10	 **24**	110	8	**25**	**26**	trace	50:50
11	 **27**	110	3	 **29**:R=Ph	 **30**:R=Ph	99	99: 1
12	**27**	10	14	**31**:R=CH_2Ph	**32**:R=CH_2Ph	98	98: 2
13	 **28**	110	3	**29**	**30**	89	46:54
14	**28**	10	14	**31**	**32**	98	13:87
15	 **33**	0	1	 **35**	 **36**	87	91: 9
16	 **34**	0	1	**35**	**36**	88	89:11
17	**33**	-30	1	 **37**	 **38**	92	88:12
18	**34**	-30	1	**37**	**38**	90	85:15

Table II (Continued)

entry	substrate	temp, °C	time, h	products: erythro	products: threo	yield, %	ratio e:t[b]
							
19	39	20	1	41:R=Ph	42:R=Ph	97	15:85
20	39	-40	1	41	42	97	11:89
21	39	-20	1	43:R=CH_2Ph	44:R=CH_2Ph	98	10:90
22	 40	20	1	41	42	96	50:50
23	40	-40	1	41	42	96	74:26
24	40	-50	1	43	44	97	20:80

[a] All reactions were carried out by treatment with 0.1 equiv of PhSLi (or $PhCH_2SLi$) and 10 equiv of PhSH (or $PhCH_2SH$) (standard conditions). [b] Ratio of erythro (e) to threo (t).

Scheme VII



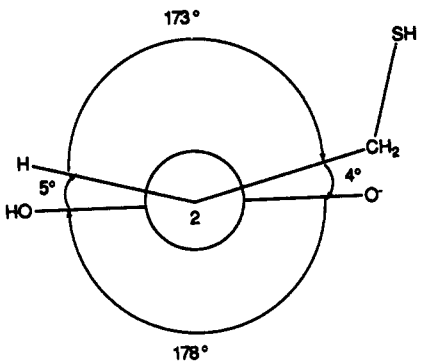


Figure 1. Pyramidalization at the unsaturated carbons in the intermediate enolate model, $HSCH_2CH{=}COH(O^-)$.

of the bulky phenyl group, which interferes with protonation of intermediate B. Therefore, rotation around the C_2–C_3 bond occurs to give the more stable conformer A, which is then protonated to afford the erythro adduct **7d** as the main product.

Addition of thiophenol and benzyl mercaptan to imides **33** and **34** yielded the same erythro adducts **35** and **37** irrespective of *E* or *Z* configuration. Since equilibration between the *E* and *Z* imides **33** and **34** was not observed on treatment with either thiophenol or benzyl mercaptan at 0 °C, adducts **35** and **37** would be formed kinetically. This result can be explained as follows (Scheme VI).

Enolates A and B, formed from **33** and **34**, are smoothly protonated to give the respective enols C and D, which are stabilized by hydrogen bonding between the enol and the carbonyl group in the oxazolidinone moiety. Since subsequent protonation of enols C and D is known[15] to proceed slowly compared with protonation of the enolates generated from esters, amides, and nitriles, the sterically hindered unstable conformation D has enough time to convert to the more stable conformer C by rotation around the C_2–C_3 bond. Subsequently, carbon protonation of the more stable conformer C gives **35** and **37** from either *E* or *Z* imide **33** or **34**.

Structure Determination

The structures of the adducts were established from the results of syn elimination reactions of the corresponding sulfoxides, which gave the corresponding *Z* and *E* olefins. Heating the sulfoxides of the erythro adducts, neat or in boiling toluene, gave predominantly the *Z* olefins in good yields. Similarly, the threo adducts were converted regioselectively into the *E* isomers. The structures of **43** and **44** were confirmed by NMR spectra and established unambiguously by single-crystal X-ray analysis of **43**. The structures of **35** and **37** were established by reduction with lithium aluminum hydride to afford alcohols **45** and **46**, which were identical with samples prepared by reduction of **7a** and **11** with the same reagent (Scheme VII).

Experimental Section[18]

Starting Materials. Compounds **5a**, **6a**, and **13** were purchased from Tokyo Kasei Kogyo Co. Ltd., Japan. Compounds **5b**[19] and **5d**[20] were prepared by esterification of the corresponding carboxylic acids. Compounds **5c**,[21] **5e**,[19] **5f**,[22] **5g**,[22] **6f**,[22] **6g**,[22] **27**,[23] **28**,[23] **39**,[25] and **40**[25] were prepared according to reported procedures. Compounds **33** and **34** were prepared by applying the reported procedure[24] to tigloyl and angeloyl chlorides with 2-oxazolidinone. Compounds **6b**,[19] **6c**,[21] **6d**,[20] and **14**[26] were prepared by oxidation of **7b**, **7c**, **7d**, and **15**, respectively, followed by syn elimination of the resulting sulfoxides as described later. Compounds **17**[27]

(18) General information for the Experimental Section has been recently reported: Naito, T.; Miyata, O.; Kida, N.; Namoto, K.; Ninomiya, I. *Chem. Pharm. Bull.* **1990**, *38*, 2419–2423.
(19) Kirstle, T. H.; Mandanas, B. Y. *J. Chem. Soc., Chem. Commun.* **1968**, 1699–1700.
(20) Bottin-Strzalko, T. *Tetrahedron* **1973**, *29*, 4199–4204.
(21) Tanikaga, R.; Miyashita, K.; Ono, N.; Kaji, A. *Synthesis* **1982**, 131–132.
(22) Ksander, G. M.; McMurry, J. E.; Johnson, M. *J. Org. Chem.* **1977**, *42*, 1180–1185.
(23) Lee, D. L.; Morron, C. J.; Rapoport, H. *J. Org. Chem.* **1974**, *39*, 893–902.

and **23** were prepared by treatment of tigloyl chloride with the corresponding amines. Compounds **18**[28] and **24** were prepared by treatment of angeloyl chloride[29] with the corresponding amine.

(*E*)-2-Methyl-2-butenamide (17): colorless crystals, mp 78–79 °C (Et_2O) (lit.[27] mp 76–77 °C); IR 3544, 3420, 1674, 1640 cm^{-1}; ^1H NMR δ 6.56 (br q, J = 7 Hz, 1 H), 6.06 (br s, 2 H), 1.86 (s, 3 H), 1.79 (d, J = 7 Hz, 3 H); HRMS calcd for C_5H_9NO 99.0683, found 99.0685.

(*Z*)-2-Methyl-2-butenamide (18): colorless crystals, mp 119–120 °C (Et_2O) (lit.[28] mp 121.5–122.5 °C); IR 3540, 3412, 1674, 1644 cm^{-1}; ^1H NMR δ 6.20 (br s, 1 H), 5.76 (qq, J = 7, 1.5 Hz, 1 H), 5.68 (br s, 1 H), 1.91 (br s, 3 H), 1.90 (dq, J = 7, 1.5 Hz, 3 H); HRMS calcd for C_5H_9NO 99.0683, found 99.0675.

(*E*)-1-(2-Methyl-1-oxo-2-buten-1-yl)pyrrolidine (23): oil; IR 1600 cm^{-1}; ^1H NMR δ 5.78 (qq, J = 7, 1.5 Hz, 1 H), 3.48 (br t, J = 7 Hz, 4 H), 1.90 (m, 4 H), 1.83 (m, 3 H), 1.71 (dq, J = 7, 1.5 Hz, 3 H); HRMS calcd for $C_9H_{15}NO$ 153.1153, found 153.1160.

(*Z*)-1-(2-Methyl-1-oxo-2-buten-1-yl)pyrrolidine (24): oil; IR 1606 cm^{-1}; ^1H NMR δ 5.43 (qq, J = 7, 1.5 Hz, 1 H), 3.48 (m, 4 H), 1.94 (m, 4 H), 1.88 (m, 3 H), 1.62 (dq, J = 7, 1.5 Hz, 3 H); HRMS calcd for $C_9H_{15}NO$ 153.1153, found 153.1155.

(*E*)-3-(2-Methyl-1-oxo-2-buten-1-yl)-2-oxazolidinone (33): oil; IR 1786, 1678 cm^{-1}; ^1H NMR δ 6.22 (qq, J = 7, 1.5 Hz, 1 H), 4.47 (t, J = 7 Hz, 2 H), 4.05 (t, J = 7 Hz, 2 H), 1.92 (quint, J = 1.5 Hz, 3 H), 1.82 (dq, J = 7, 1.5 Hz, 3 H); HRMS calcd for $C_8H_{11}NO_3$ 169.0738, found 169.0750.

(*Z*)-3-(2-Methyl-1-oxo-2-buten-1-yl)-2-oxazolidinone (34): oil; IR 1790, 1686 cm^{-1}; ^1H NMR δ 5.68 (qq, J = 7 Hz, 1.5, 1 H), 4.49 (t, J = 7 Hz, 2 H), 4.12 (t, J = 7 Hz, 2 H), 1.95 (quint, J = 1.5 Hz, 3 H), 1.64 (dq, J = 7, 1.5 Hz, 3 H); HRMS calcd for $C_8H_{11}NO_3$ 169.0738, found 169.0713.

Addition of Thiols to α,β-Unsaturated Carboxylic Acid Derivatives: General Procedure (Standard Conditions). Thiophenol or benzyl mercaptan (10 mmol) was added with stirring at 0 °C to a solution of butyllithium (10% solution in hexane) (0.064 mL, 0.1 mmol) in THF (5 mL) to give a solution of a 100:1 mixture of the thiols and lithium thiolate. To the resulting solution was added a solution of α,β-unsaturated carboxylic acid derivatives (1 mmol) in THF (5 mL). After stirring at the temperature shown in the corresponding table, the mixture was made alkaline by addition of 5% aqueous NaOH and extracted with CH_2Cl_2. The extract was dried and evaporated to give a residue, which was purified by MCC (medium-pressure column chromatography) to give a diastereomeric mixture of adducts. The ratio of erythro to threo adducts was determined by 200- or 500-MHz ^1H NMR.

***erythro*- and *threo*-2-Methyl-3-(phenylthio)butanoic Acid Methyl Esters (7a and 8a).** *erythro*-**7a**/*threo*-**8a** = 96:4: oil; IR 1730 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_2S$ 224.0869, found 224.0858. *erythro*-**7a**/*threo*-**8a** = 14:86: oil, IR 1728 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_2S$ 224.0869, found 224.0852. ^1H NMR (**7a**): δ 7.46 (m, 2 H), 7.32 (m, 3 H), 3.64 (s, 3 H), 3.48 (quint, J = 7 Hz, 1 H), 2.63 (quint, J = 7 Hz, 1 H), 1.32 (d, J = 7 Hz, 6 H). ^1H NMR (**8a**): δ 7.47 (m, 2 H), 7.32 (m, 3 H), 3.71 (s, 3 H), 3.64 (quint, J = 7 Hz, 1 H), 2.68 (quint, J = 7 Hz, 1 H), 1.25 (d, J = 7 Hz, 3 H), 1.22 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-(phenylthio)pentanoic Acid Methyl Esters (7b and 8b).** *erythro*-**7b**/*threo*-**8b** = 87:13: oil; IR 1730 cm^{-1}; HRMS calcd for $C_{13}H_{18}O_2S$ 238.1026, found 238.1016. *erythro*-**7b**/*threo*-**8b** = 17:83: oil; IR 1728 cm^{-1}; HRMS calcd for $C_{13}H_{18}O_2S$ 238.1026, found 238.1016. ^1H NMR (**7b**): δ 7.47 (m, 2 H), 7.30 (m, 3 H), 3.56 (s, 3 H), 3.38 (q, J = 7 Hz, 1 H), 2.75 (quint, J = 7 Hz, 1 H), 1.66 (br quint, J = 7 Hz, 2 H), 1.29 (d, J = 7 Hz, 3 H), 1.08 (t, J = 7 Hz, 3 H). ^1H NMR (**8b**): δ 7.46 (m, 2 H), 7.30 (m, 3 H), 3.68 (s, 3 H), 3.41 (m, 1 H), 2.72 (quint, J = 7 Hz, 1 H), 1.80–1.40 (m, 2 H), 1.23 (d, J = 7 Hz, 3 H), 1.08 (t, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-(phenylthio)hexanoic Acid Ethyl Esters (7c and 8c).** *erythro*-**7c**/*threo*-**8c** = 85:15: oil; IR 1726 cm^{-1}; HRMS calcd for $C_{15}H_{22}O_2S$ 266.1338, found 266.1325. *erythro*-**7c**/*threo*-**8c** = 28:72: oil; IR 1724 cm^{-1}; HRMS calcd for $C_{15}H_{22}O_2S$ 266.1338, found 266.1338. ^1H NMR (**7c**): δ 7.46 (m, 2 H), 7.40–7.20 (m, 3 H), 4.03 (m, 2 H), 3.47 (br q, J = 7 Hz, 1 H), 2.70 (quint, J = 7 Hz, 1 H), 1.70–1.40 (m, 4 H), 1.28 (d, J = 7 Hz, 3 H), 1.18 (t, J = 7 Hz, 3 H), 0.92 (br t, J = 7 Hz, 3 H). ^1H NMR (**8c**): δ 7.46 (m, 2 H), 7.40–7.20 (m, 3 H), 4.15 (m, 2 H), 3.50 (m, 1 H), 2.70 (quint, J = 7 Hz, 1 H), 1.70–1.40 (m, 4 H), 1.26 (t, J = 7 Hz, 3 H), 1.23 (d, J = 7 Hz, 3 H), 0.92 (br t, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-phenyl-3-(phenylthio)-propionic Acid Methyl Esters (7d and 8d).** *erythro*-**7d**/*threo*-**8d** = 81:19: oil; IR 1732 cm^{-1}; HRMS calcd for $C_{17}H_{18}O_2S$ 286.1026, found 286.1017. *erythro*-**7d**/*threo*-**8d** = 66:34: oil; IR 1732 cm^{-1}; HRMS calcd for $C_{17}H_{18}O_2S$ 286.1026, found 286.1028. ^1H NMR (**7d**): δ 7.22 (m, 10 H), 4.43 (d, J = 9 Hz, 1 H), 3.47 (s, 3 H), 3.02 (dq, J = 9, 7 Hz, 1 H), 1.43 (d, J = 7 Hz, 3 H). ^1H NMR (**8d**): δ 7.22 (m, 10 H), 4.36 (d, J = 10 Hz, 1 H), 3.77 (s, 3 H), 3.02 (dq, J = 10, 7 Hz, 1 H), 1.03 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-2,4,4-Trimethyl-3-(phenylthio)pentanoic Acid Ethyl Esters (7e and 8e).** *erythro*-**7e**/*threo*-**8e** = 57:43 or 43:57: oil; IR 1726 cm^{-1}; ^1H NMR δ 7.46 (m, 2 H), 7.40–7.11 (m, 3 H), 4.16–4.02 (m, 2 H), 3.69 (d, J = 4 Hz, 0.5 H), 3.17 (d, J = 4 Hz, 0.5 H), 3.00 (m, 1 H), 1.41 (d, J = 7 Hz, 1.5 H), 1.35 (d, J = 7 Hz, 1.5 H), 1.27 (t, J = 7 Hz, 1.5 H), 1.10 (t, J = 7 Hz, 1.5 H), 1.11 (s, 4.5 H), 1.08 (s, 4.5 H); HRMS calcd for $C_{16}H_{24}O_2S$ 280.1496, found 280.1498.

***erythro*- and *threo*-4,5-Dihydro-3-(1-(phenylthio)-ethyl)-2(3*H*)-furanones (7f and 8f).** The diastereomers **7f** and **8f** were separated by MCC (silica gel, Et_2O/*n*-hexane = 2:1). **7f**: oil; IR 1772 cm^{-1}; ^1H NMR δ 7.56 (m, 2 H), 7.32 (m, 3 H), 4.46 (ddd, J = 9, 8, 4.5 Hz, 1 H), 4.28 (td, J = 9, 8 Hz, 1 H), 3.67 (qd, J = 7, 5 Hz, 1 H), 2.83 (ddd, J = 10, 9, 5 Hz, 1 H), 2.22 (m, 2 H), 1.49 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{12}H_{14}O_2S$ 222.0713, found 222.0703. **8f**: oil; IR 1768 cm^{-1}; ^1H NMR δ 7.46–7.30 (m, 5 H), 4.38 (ddd, J = 9, 7, 4 Hz, 1 H), 4.20 (td, J = 9, 8 Hz, 1 H), 3.90 (qd, J = 7, 3.5 Hz, 1 H), 2.88 (ddd, J = 11, 9, 3.5 Hz, 1 H), 2.32 (m, 1 H), 2.28 (m, 1 H), 1.28 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{12}H_{14}O_2S$ 222.0713, found 222.0711.

***erythro*- and *threo*-Tetrahydro-3-(1-(phenylthio)-ethyl)-2*H*-pyran-2-ones (7g and 8g).** The diastereomers **7g** and **8g** were separated by MCC (silica gel, Et_2O/*n*-hexane = 2:1). **7g**: oil; IR 1728 cm^{-1}; ^1H NMR δ 7.52 (m, 2 H), 7.30 (m, 3 H), 4.36 (m, 2 H), 3.97 (qd, J = 7, 4 Hz, 1 H), 2.78 (ddd, J = 11, 7, 4 Hz, 1 H), 2.16 (m, 1 H), 1.96–1.88 (m, 3 H), 1.42 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{13}H_{16}O_2S$ 236.0870, found 236.0885. **8g**: oil; IR 1726 cm^{-1}; ^1H NMR δ 7.50–7.30 (m, 5 H), 4.30 (m, 2 H), 4.18 (qd, J = 7, 3 Hz, 1 H), 2.72 (ddd, J = 11, 7, 3 Hz, 1 H), 2.23 (m, 1 H), 1.96–1.70 (m, 3 H), 1.37 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{13}H_{16}O_2S$ 236.0870, found 236.0867.

***erythro*- and *threo*-2-Methyl-3-((phenylmethyl)thio)butanoic Acid Methyl Esters (11 and 12).** *erythro*-**11**/*threo*-**12** = 98:2: oil; IR 1730 cm^{-1}; HRMS calcd for $C_{13}H_{18}O_2S$ 238.1025, found 238.1024. *erythro*-**11**/*threo*-**12** = 10:90: oil; IR 1728 cm^{-1}; HRMS calcd for $C_{13}H_{18}O_2S$ 238.1025, found 238.1017. ^1H NMR (**11**): δ 7.40–7.20 (m, 5 H), 3.76 and 3.74 (AB q, J = 13 Hz, 2 H), 3.65 (s, 3 H), 2.98 (quint, J = 7 Hz, 1 H), 2.59 (quint, J = 7 Hz, 1 H), 1.30 (d, J = 7 Hz, 3 H), 1.22 (d, J = 7 Hz, 3 H). ^1H NMR (**12**): δ 7.32 (m, 5 H), 3.77 (s, 2 H), 3.68 (s, 3 H), 3.06 (quint, J = 7 Hz, 1 H), 2.67 (quint, J = 7 Hz, 1 H), 1.21 (d, J = 7 Hz, 3 H), 1.18 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-(phenylthio)butyronitriles (15 and 16).** *erythro*-**15**/*threo*-**16** = 96:4: oil; IR 2240 cm^{-1}; HRMS calcd for $C_{11}H_{13}NS$ 191.0768, found 191.0773. *erythro*-**15**/*threo*-**16** = 13:87: oil; IR 2240 cm^{-1}; calcd for $C_{11}H_{13}NS$ 191.0768, found 191.0772. ^1H NMR (**15**): δ 7.48 (m, 2 H), 7.36 (m, 3 H), 3.48 (qd, J = 7, 4 Hz, 1 H), 2.80 (qd, J = 7, 4 Hz, 1 H), 1.42 (d, J = 7 Hz, 3 H), 1.39 (d, J = 7 Hz, 3 H). ^1H NMR (**16**): δ 7.50 (m, 2 H), 7.37 (m, 3 H), 3.19 (qd, J = 7, 5 Hz, 1 H), 2.81

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(qd, J = 7, 5 Hz, 1 H), 1.44 (d, J = 7 Hz, 3 H), 1.36 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-(phenylthio)butanamides (19 and 20).** The diastereomers **19** and **20** were separated by recrystallization with Et_2O/*n*-hexane/MeOH. **19**: colorless crystals, mp 117–118 °C; IR 3536, 3412, 1680 cm^{-1}; ^1H NMR δ 7.46 (m, 2 H), 7.34 (m, 3 H), 5.92 (br s, 1 H), 5.64 (br s, 1 H), 3.43 (quint, J = 7 Hz, 1 H), 2.47 (quint, J = 7 Hz, 1 H), 1.36 (d, J = 7 Hz, 1 H), 1.32 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{11}H_{15}NOS$ 209.0873, found 209.0872. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 62.93; H, 7.20; N, 6.40. **20**: colorless crystals, mp 146–147 °C (Et_2O/*n*-hexane/MeOH); IR 3536, 3412, 1680 cm^{-1}; ^1H NMR δ 7.46 (m, 2 H), 7.32 (m, 3 H), 5.80 (br s, 2 H), 3.63 (quint, J = 7 Hz, 1 H), 2.48 (quint, J = 7 Hz, 1 H), 1.29 (d, J = 7 Hz, 3 H), 1.25 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{11}H_{15}NOS$ 209.0873, found 209.0877. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.28; H, 7.24; N, 6.64.

***erythro*- and *threo*-1-(2-Methyl-1-oxo-3-(phenylthio)butyl)pyrrolidines (25 and 26).** *erythro*-**25**/*threo*-**26** = 96:4: oil; IR 1620 cm^{-1}; HRMS calcd for $C_{15}H_{21}NOS$ 263.1343, found 263.1348. ^1H NMR (**25**): δ 7.44 (m, 2 H), 7.30 (m, 3 H), 3.48 (t, J = 7 Hz, 2 H), 3.44 (m, 1 H), 3.42 (t, J = 7 Hz, 2 H), 2.62 (dq, J = 10, 7 Hz, 1 H), 1.88 (m, 4 H), 1.35 (d, J = 7 Hz, 3 H), 1.29 (d, J = 7 Hz, 3 H). ^1H NMR (**26**): δ 1.18 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-1-Methyl-3-(1-(phenylthio)ethyl)-2-piperidinones (29 and 30).** The diastereomers **29** and **30** were separated by MCC (silica gel, AcOEt). **29**: oil; IR 1630 cm^{-1}; ^1H NMR δ 7.55 (m, 2 H), 7.48 (m, 3 H), 4.24 (qd, J = 7, 3 Hz, 1 H), 3.37 (td, J = 11, 5 Hz, 1 H), 3.22 (br d, J = 11 Hz, 1 H), 2.90 (s, 3 H), 2.57 (m, 1 H), 2.10–1.70 (m, 4 H), 1.37 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{14}H_{19}NOS$ 249.1186, found 249.1195. **30**: oil; IR 1626 cm^{-1}; ^1H NMR δ 7.42 (m, 2 H), 7.24 (m, 3 H), 4.34 (qd, J = 7, 3 Hz, 1 H), 3.30 (td, J = 12, 5 Hz, 1 H), 3.18 (br d, J = 12 Hz, 1 H), 2.88 (s, 3 H), 2.52 (m, 1 H), 2.10 (m, 1 H), 1.80 (m, 1 H), 1.65 (m, 2 H), 1.17 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{14}H_{19}NOS$ 249.1186, found 249.1184.

***erythro*- and *threo*-2-Methyl-3-((phenylmethyl)thio)butanamides (21 and 22).** *erythro*-**21**/*threo*-**22** = 99:1: colorless crystals, mp 102.5–103.5 °C (Et_2O/*n*-hexane/MeOH); IR 3538, 3496, 1678 cm^{-1}; HRMS calcd for $C_{12}H_{17}NOS$ 223.1029, found 223.1011. Anal. Calcd for $C_{12}H_{17}NOS$: C, 64.54; H, 7.67; N, 6.27. Found: C, 64.41; H, 7.58; N, 6.06. *erythro*-**21**/*threo*-**22** = 16:84: oil; IR 3536, 3518, 1678 cm^{-1}; HRMS calcd for $C_{12}H_{17}NOS$ 223.1029, found 223.1036. ^1H NMR (**21**): δ 7.40–7.20 (m, 5 H), 6.02 (br s, 1 H), 5.86 (br s, 1 H), 3.83 and 3.72 (AB q, J = 13 Hz, 2 H), 2.88 (quint, J = 7 Hz, 1 H), 2.42 (quint, J = 7 Hz, 1 H), 1.28 (d, J = 7 Hz, 3 H), 1.20 (d, J = 7 Hz, 3 H). ^1H NMR (**22**): δ 7.40–7.20 (m, 5 H), 6.10 (br s, 2 H), 3.82 and 3.78 (AB q, J = 13 Hz, 2 H), 2.97 (quint, J = 7 Hz, 1 H), 2.40 (quint, J = 7 Hz, 1 H), 1.23 (d, J = 7 Hz, 3 H), 1.15 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-1-Methyl-3-(1-((phenylmethyl)thio)-ethyl)-2-piperidinones (31 and 32).** The diastereomers **31** and **32** were separated by MCC (silica gel, AcOEt). **31**: oil; IR 1628 cm^{-1}; ^1H NMR δ 7.40–7.20 (m, 5 H), 3.87 and 3.75 (AB q, J = 13 Hz, 2 H), 3.80 (qd, J = 7, 5 Hz, 1 H), 3.39 (br t, J = 10 Hz, 1 H), 3.20 (br d, J = 10 Hz, 1 H), 2.98 (s, 3 H), 2.48 (m, 1 H), 2.00–1.60 (m, 4 H), 1.11 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{15}H_{21}NOS$ 263.1343, found 263.1344. **32**: oil; IR 1624 cm^{-1}; ^1H NMR δ 7.30 (m, 5 H), 3.82 and 3.72 (AB q, J = 13 Hz, 2 H), 3.74 (m, 1 H), 3.30 (m, 2 H), 2.94 (s, 3 H), 2.72 (m, 1 H), 2.10–1.50 (m, 4 H), 1.14 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{15}H_{21}NOS$ 263.1343, found 263.1353.

***erythro*- and *threo*-3-(2-Methyl-1-oxo-3-(phenylthio)butyl)-2-oxazolidinones (35 and 36).** *erythro*-**35**/*threo*-**36** = 91:9: oil; IR 1778, 1700 cm^{-1}; HRMS calcd for $C_{14}H_{17}NO_3S$ 279.0956, found 279.0942. ^1H NMR (**35**): δ 7.46 (m, 2 H), 7.40–7.20 (m, 3 H), 4.40–4.18 (m, 2 H), 4.08–3.86 (m, 2 H), 3.76–3.60 (m, 2 H), 1.39 (d, J = 7 Hz, 3 H), 1.34 (d, J = 7 Hz, 3 H). ^1H NMR (**36**): δ 1.32 (d, J = 7 Hz, 3 H), 1.26 (d, J = 7 Hz, 3 H).

***erythro*- and *threo*-2-Methyl-3-((phenylmethyl)thio)butanethioic *S*-Acid Phenylmethyl Esters (37 and 38).** *erythro*-**37**/*threo*-**38** = 88:12: oil; IR 1680 cm^{-1}; HRMS calcd for $C_{19}H_{22}OS_2$ – $PhCH_2$ 239.0563, found: 239.0571. ^1H NMR (**37**): δ 7.32 (m, 10 H), 4.16 (s, 2 H), 3.74 (s, 2 H), 2.98 (br quint, J = 7 Hz, 1 H), 2.71 (br quint, J = 7 Hz, 1 H), 1.30 (d, J = 7 Hz, 3 H), 1.28 (d, J = 7 Hz, 3 H). ^1H NMR (**38**): δ 1.20, 1.17 (each d, J = 7 Hz, 3 H × 2).

***erythro*- and *threo*-2-(Acetylamino)-3-(phenylthio)butanoic Acid Methyl Esters (41 and 42).** The diastereomers **41** and **42** were separated by MCC (silica gel, CH_2Cl_2/Et_2O = 2:1). **41**: colorless crystals, mp 89–90 °C (Et_2O/*n*-hexane); IR 3440, 1738, 1678 cm^{-1}; ^1H NMR δ 7.49 (m, 2 H), 7.33 (m, 3 H), 6.34 (br d, J = 9 Hz, 1 H), 4.80 (dd, J = 9, 4 Hz, 1 H), 3.78 (s, 3 H), 3.67 (qd, J = 7, 4 Hz, 1 H), 1.92 (s, 3 H), 1.38 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{13}H_{17}NO_3S$ 267.0928, found 267.0936. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41; H, 6.41; N, 5.24. Found: C, 58.34; H, 6.36; N, 5.21. **42**: oil; IR 3436, 1744, 1678 cm^{-1}; ^1H NMR δ 7.48 (m, 2 H), 7.32 (m, 3 H), 6.34 (br d, J = 9 Hz, 1 H), 4.88 (dd, J = 9, 3 Hz, 1 H), 3.86 (qd, J = 7, 3 Hz, 1 H), 3.38 (s, 3 H), 2.08 (s, 3 H), 1.38 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{13}H_{17}NO_3S$ 267.0928, found 267.0938.

***erythro*- and *threo*-2-(Acetylamino)-3-((phenylmethyl)-thio)butanoic Acid Methyl Esters (43 and 44).** The diastereomers **43** and **44** were separated by MCC (silica gel, CH_2Cl_2/Et_2O = 2:1). **43**: colorless crystals, mp 74–75 °C (Et_2O/*n*-hexane/MeOH); IR 3440, 1740, 1678 cm^{-1}; ^1H NMR δ 7.37 (m, 5 H), 6.18 (br d, J = 9 Hz, 1 H), 4.90 (dd, J = 9, 4 Hz, 1 H), 3.85 and 3.72 (AB q, J = 13 Hz, 2 H), 3.76 (s, 3 H), 3.09 (qd, J = 7, 4 Hz, 1 H), 2.01 (s, 3 H), 1.26 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{14}H_{19}NO_3S$ 281.1085, found 281.1085. Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.80; N, 4.97. Found: C, 59.61; H, 6.85; N, 5.02. **44**: colorless crystals, mp 78–79 °C (Et_2O/*n*-hexane/MeOH); IR 3432, 1742, 1676 cm^{-1}; ^1H NMR δ 7.36 (m, 5 H), 6.26 (br d, J = 9 Hz, 1 H), 4.85 (dd, J = 9, 3 Hz, 1 H), 3.76 and 3.70 (AB q, J = 13 Hz, 2 H), 3.72 (s, 3 H), 3.32 (qd, J = 7, 3 Hz, 1 H), 2.07 (s, 3 H), 1.30 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{14}H_{19}NO_3S$ 281.1085, found 281.1066. Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.80; N, 4.97. Found: C, 59.96; H, 6.77; N, 5.10.

Isomerization of *Z* Ester 6a to *E* Isomer 5a. Thiophenol (0.13 mL, 1.2 mmol) was added to a solution of butyllithium (10% solution in hexane) (0.77 mL, 1.2 mmol) in THF (5 mL) with stirring at 0 °C. To the resulting solution was added a solution of **6a** (114 mg, 1 mmol) in THF (5 mL), and the reaction mixture was stirred at room temperature for 3 h. After the usual workup and purification of the crude product by MCC, **5a** was obtained in 93% yield. **5a** was identical with an authentic sample, which was commercially available.

Reaction with Sodium Thiophenoxide. Thiophenol (1.04 mL, 10 mmol) was added to a suspension of sodium hydride (60% dispersion in oil) (4 mg, 0.1 mmol) in THF (5 mL) with stirring at 0 °C for 2 h. To the resulting solution was added a solution of **5a** or **6a** (114 mg, 1 mmol) in THF (5 mL), and the mixture was stirred at room temperature for 24 h. After the usual workup and purification of the crude product by MCC, a mixture of **7a** and **8a** was obtained with the ratios shown in Table I.

Equilibration between Erythro and Threo Adducts. The erythro adduct **7a** (*erythro*-**7a**/*threo*-**8a** = 96:4) (45 mg, 0.2 mmol) was added with stirring at 0 °C to a solution of a 100:1 mixture of thiophenol (2 mmol) and lithium thiophenoxide (0.02 mmol) in THF (3 mL). After stirring at room temperature for 3 h, the mixture was made alkaline by addition of 5% aqueous NaOH and extracted with CH_2Cl_2. The extract was dried and evaporated to give a residue, which was purified by MCC to give a mixture of the erytho and threo adducts **7a** and **8a** with an unchangeable ratio in 98% yield. Similarly, when the threo adduct **8a** (*erythro*-**7a**/*threo*-**8a** = 14:86) was treated under the same conditions, the ratio of the erythro and threo adducts was unchangeable. Furthermore, no equilibration between other erythro and threo adducts was observed under the reaction conditions.

Reaction with Deuterium Thiophenoxide. According to the general procedure, the addition reaction of deuterium thiophenoxide (86 atom % D),[11] prepared from thiophenol and deuterium oxide, to **5a** and **6a** afforded the deuteriated erythro and threo adducts **9** and **10**, respectively. **9**: oil; ^1H NMR δ 7.48 (m, 2 H), 7.31 (m, 3 H), 3.64 (s, 3 H), 3.48 (q, J = 7 Hz, 1 H), 1.33 (d, J = 7 Hz, 3 H), 1.32 (s, 3 H); HRMS calcd for $C_{12}H_{15}DO_2S$ 225.0932, found 225.0939. **10**: oil; ^1H NMR δ 7.48 (m, 2 H), 7.31 (m, 3 H), 3.71 (s, 3 H), 3.64 (q, J = 7 Hz, 1 H), 1.25 (d, J = 7 Hz, 3 H), 1.22 (s, 3 H); HRMS calcd for $C_{12}H_{15}DO_2S$ 225.0932, found 225.0926.

Isomerization of *Z* Carboxamides 18, 24, and 28 to *E* Iso-

mers 17 and 27. A solution of the *Z* carboxamide (0.5 mmol) in THF (5 mL) and thiophenol (5 mmol) was refluxed for 6 h. After the usual workup and purification by MCC (silica gel, AcOEt), a mixture of the *Z* and *E* carboxamides was obtained in 95–98% yield. The *Z*:*E* ratio was determined by 200 MHz ^{1}H NMR. **18** was converted to a 74:26 mixture of **18** and **17**, and **28** was converted to a 37:63 mixture of **28** and **27**. No isomerization of the *Z* carboxamides was observed at room temperature under the same conditions.

Isomerization of *E* Dehydroamino Ester 40 to *Z* Isomer 39. A solution of the *E* dehydroamino ester **40** (79 mg, 0.5 mmol) and thiophenol (0.5 mL, 5 mmol) in THF (5 mL) was stirred at room temperature for 1 h. After the usual workup and purification by MCC (silica gel, AcOEt), the *Z* dehydroamino ester **39** (76 mg) was obtained in 98% yield. Similar treatment of **40** with thiophenol at 0 °C gave a 1:1 mixture of the *E* and *Z* dehydroamino esters **40** and **39**. The *Z* dehydroamino ester **39** was identical with an authentic sample[25] prepared by the reported procedure.

Conversion of Erythro Adducts to *Z* Olefins: Method A (for Erythro Adducts 7a–c, 11, and 15). A solution of oxone (330 mg) in water (5 mL) was added dropwise with stirring at 0 °C to a solution of the erythro adduct in methanol (5 mL). After stirring at 0 °C for 0.5 h, the mixture was extracted with CH_2Cl_2. The extract was dried and evaporated to give the sulfoxide, which without purification was heated neat at 150 °C for 1 h. The residue was distilled under reduced pressure to give the *Z* olefins in 72–79% yield in addition to the *E* isomers (8–10% yield) and the deconjugated olefins (5–8% yield). The *Z* olefins were identical with authentic samples,[19,21,26] which were commercially available or prepared by reported procedures.

Method B (for Erythro Adducts 7d, 7f, 7g, 19, 21, 25, and 41). The sulfoxide, prepared by oxidation of the sulfide with oxone as in method A, was heated in refluxing toluene for 2 h. After evaporation of solvent, the residue was purified by MCC to afford the *Z* olefins in 70–90% yield in addition to the *E* isomers (5–25% yield) and the deconjugated olefins (3% yield). The *Z* olefins were identical with authentic samples[20,22,25,28] prepared by reported procedures.

Method C (for Erythro Adducts 29 and 31). The sulfoxide, prepared similarly from the erythro adduct, was heated in refluxing toluene with a catalytic amount of triethylamine for 2 h. The usual workup afforded *Z* olefin **28** (65–69% yield) in addition to the deconjugated olefin (23–26% yield). *Z* olefin **28** was identical with an authentic sample[23] prepared by the reported procedure. In all cases, oxidation of the sulfides with *m*-CPBA also proceeded smoothly to obtain the corresponding sulfoxides.

Conversion of Threo Adducts to *E* Olefins. According to the procedure given for the erythro adducts, oxidation of the threo adducts followed by syn elimination of the resulting sulfoxide gave the *E* olefins as sole products in 93–95% yield. *E* olefins were identical with authentic samples,[19–28] which were commercially available or prepared by reported procedures.

Reduction of 35 and 37 with Lithium Aluminum Hydride. A solution of **35** (56 mg, 0.2 mmol) in anhydrous Et_2O was added dropwise to an ice-cooled, stirred solution of $LiAlH_4$ (8 mg) in anhydrous Et_2O. After stirring at 0 °C for 1 h, the usual workup afforded *erythro*-2-methyl-3-(phenylthio)butan-1-ol (**45**) (36 mg, 92%) as a pale yellow oil: IR 3624 cm^{-1}; ^{1}H NMR δ 7.46 (m, 2 H), 7.40 (m, 3 H), 3.81 (dd, J = 11, 7 Hz, 1 H), 3.61 (dd, J = 11, 7 Hz, 1 H), 3.51 (qd, J = 7, 4 Hz, 1 H), 2.00 (m, 1 H), 1.80 (br s, 1 H), 1.35 (d, J = 7 Hz, 3 H), 1.01 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{11}H_{16}OS$ 196.0921, found 196.0925. **45** was identical with the sample prepared by reduction of erythro adduct **7a** with $LiAlH_4$. According to the procedure given for the adduct **35**, reduction of **37** with $LiAlH_4$ afforded *erythro*-2-methyl-3-((phenylmethyl)thio)butan-1-ol (**46**) as a pale yellow oil in 91% yield: IR 3464 cm^{-1}; ^{1}H NMR δ 7.36 (m, 5 H), 3.80 and 3.72 (AB q, J = 13 Hz, 2 H), 3.62 (dd, J = 11, 7.5 Hz, 1 H), 3.46 (dd, J = 11, 5.5 Hz, 1 H), 2.85 (qd, J = 7, 3 Hz, 1 H), 1.86 (m, 1 H), 1.28 (d, J = 7 Hz, 3 H), 0.86 (d, J = 7 Hz, 3 H); HRMS calcd for $C_{12}H_{18}OS$ 210.1078, found 210.1092. **46** was identical with the sample prepared by reduction of the erythro adduct **11** with $LiAlH_4$.

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Supplementary Material Available: Experimental details for the X-ray crystal structure determination of **43**, ORTEP representations and crystal data tables of positional and anisotropic or isotropic thermal parameters and interatomic distances and angles for **43**, and ^{1}H NMR spectra for compounds **7a–g**, **8a–g**, **9–12**, **15–26**, **29–38**, and **41–46** (69 pages). Ordering information is given on any current masthead page.