Asymmetric Thio-Claisen Rearrangement Induced by an Enantiopure Alkylsulfinyl Group. Unusual Preference for a Boat Transition State in the Acyclic Series

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Received July 20, 2001

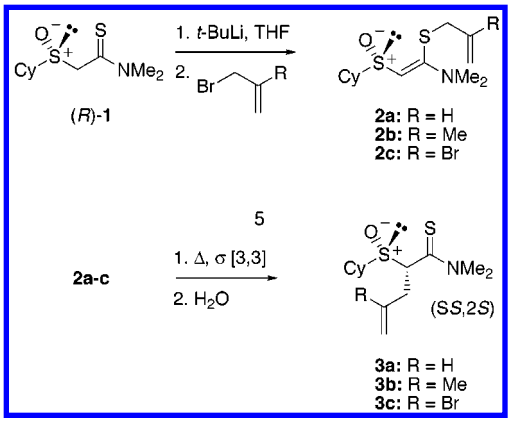
Ketene aminothioacetals **2a**−**c** and **5a**−**b** bearing an enantiopure vinylic alkylsulfinyl substituent were readily prepared from (*R*)-2-cyclohexylsulfinyl-*N*,*N*-dimethylethanethioamide **1** with full control of the geometry of their double bonds. They underwent a Claisen rearrangement upon heating at THF reflux to afford α-sulfinyl γ-unsaturated thioamides **3a**−**c** and **6a**−**b**. With all substrates the asymmetric induction of the sulfinyl group was excellent. The determination of the absolute configurations of thioamides **3a**−**c** and **6a**−**b** was achieved either by X-ray crystallographic analysis or by chemical correlation. The stereochemical course of this [3,3] sigmatropic transposition was explained by an electronic model. Interestingly the Claisen rearrangement of the (*ZE*)-cinnamyl substrates **5b** was shown to proceed through a boat transition state rather than a chair transition state; such a preference is quite unusual for acyclic systems.

Introduction

The Claisen rearrangement is well-established as an efficient method to achieve one of the main challenges for chemists, which is the stereoselective formation of carbon−carbon bonds in acyclic systems. Nevertheless only a few asymmetric variants of this [3,3] sigmatropic transposition involving a removable chiral auxiliary have been proposed so far.[1,2] We have recently reported the first examples of an asymmetric thio-Claisen rearrangement mediated by racemic alkylsulfinyl groups.[3] The control of the relative stereochemistry was excellent, and a model was proposed to explain the stereochemical course.

This reaction gave access to α-sulfinyl γ-unsaturated dithioesters, and in view of the limited number of known methods[4−6] allowing the highly selective allylation of carbonyl α-alkylsulfinyl compounds we wished to extend it to the enantiopure series. We chose to examine the thioamide series rather than the dithioester one because thioamides are usually more stable and crystallize more easily. For this purpose we developed an efficient asymmetric synthesis of the precursor of the Claisen rearrangement substrates **2** (Scheme 1), 2-cyclohexylsulfinyl-*N*,*N*-dimethylethanethioamide (*R*)-**1** from diacetone-D-glucose (Scheme 2), a cheap and accessible source of chirality.[7] We report here the first examples of asymmetric thio-Claisen rearrangements directed by an enantiopure alkylsulfinyl group and the efficient construction of molecules bearing two to three asymmetric centers. The full assignment of the molecular structures by X-ray crystallographic analysis or chemical correlation is described. We show that the stereochemical course of this reaction performed in the acyclic series unexpectedly switches in one example from the generally admitted pseudocyclic chair transition state to the boat transition state.

Scheme 1



Results and Discussion

Access to Thioamides Possessing Two Asymmetric Centers. The substrates of the rearrangement **2** were easily obtained by deprotonation of (*R*)-**1** (98% ee) with *tert*-butyllithium and subsequent allylation at the

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10.1021/jo015956m CCC: $20.00 © 2001 American Chemical Society
Published on Web 10/25/2001

Scheme 2

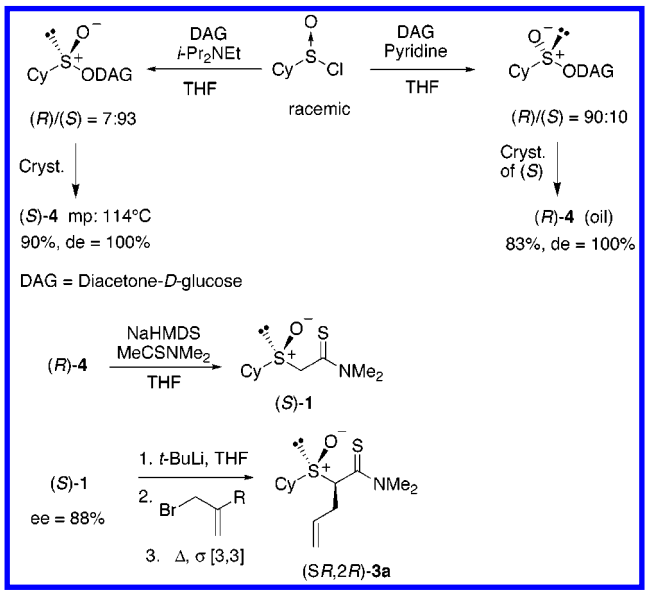

Table 1. Claisen Rearrangement of Compounds (S*S*,2*S*)-2a−c According to Scheme 1

entry	2	R	*T* (°C)	time	3	dr[a] (%)	yield (%)
1	**2a**	H	20	3 d	**3a**	96:4	60
2	**2a**	H	66	0.5 h	**3a**	95:5[b]	78
3	**2b**	Me	20	8 d	**3b**	>98:2	51
4	**2b**	Me	66	2 h	**3b**	100:0	76
5	**2c**	Br	20	5 d	**3c**	95:5	56
6	**2c**	Br	66	0.5 h	**3c**	96:4	58

[a] The diastereomeric ratio was measured by ^{1}H NMR analysis by integration of the signals of the diastereomeric proton. [b] Crystallization (ethyl acetate/pentane) afforded isomerically pure **3a** (100:0 dr).

sulfur atom of the resulting enethiolate (Scheme 1).[8] All our attempts to deprotonate **1** with other bases failed, while LDA was efficient with the analogous dithioesters.[3] The nature of the base is thus crucial, and this is quite surprising as the sulfinyl group should enhance the acidity of the α-located protons. Some precedents can be found in the literature with related systems.[9]

The *cis*-deprotonation[8,10] of **1** was exclusively observed, and as the alkylation of enethiolates is known to proceed with complete retention of configuration,[11,12] only the (*Z*)-isomer of ketene aminothioacetals **2a**−**c** was formed. It is worthy to note that, in the dithioester series, the enethiolate isomeric ratio was about 90:10 in favor of the (*Z*)-isomer.[3] The Claisen rearrangement of ketene aminothioacetals **2a**−**c** was slow at room temperature (Table 1, entries 1, 3, and 5) and even slower than in the dithioester series (less than 2 days). However, while dithioesters underwent some decomposition upon heating, the analogous thioamides proved to be stable at reflux of THF. We were then able to shorten drastically the rearrangement time of **2a**−**c** from several days to less than 2 h. Compounds **2a**−**c** are rather sensitive toward hydrolysis, which gives the amide analogue of **1**. To prevent such a transformation, **2a**−**c** should not be isolated. The reaction was thus carried out in one pot, and a significant increase in the yields of rearranged products up to 78% was observed (Table 1). Thioamides **3a**−**c** were obtained with an excellent diastereoselectivity (up to 100:0) with no variation related to the temperature. In all cases, the ^{1}H NMR signals of the proton linked to the stereogenic carbon center of the major isomer were shifted toward lower δ values. The enantiomeric excess of **3a** (96% ee) was determined by HPLC analysis (Daicel AD column) as identical to that of the precursor (*R*)-**1** (98% ee), demonstrating that the stereopurity of the sulfinyl group was preserved.

The (S*S*,2*S*) configuration of **3a** was established by X-ray crystallographic analysis. The same configuration was assigned to thioamides **3b**−**c** according to similar trends observed in the proton NMR spectra.

We also selectively prepared the (S*R*,2*R*) enantiomer of **3a** (dr = 91:9) from the (*S*) enantiomer of **1** (88% ee), which was available from the same source of chirality, diacetone-D-glucose (DAG). Indeed, the reaction of racemic cyclohexanesulfinyl chloride[13] with DAG led to either diastereomer of DAG cyclohexanesulfinate **4** according to the nature of the base employed in agreement with the methodology described by Alcudia.[14] While (*S*)-DAG cyclohexanesulfinate **4** was selectively obtained[7] with *N*,*N*-diisopropylethylamine, the (*R*)-isomer of **4** was preferentially formed with pyridine (Scheme 2). Similarly both (S*S*,2*S*) and (S*R*,2*R*) enantiomers of molecules **3b**−**c** are easily accessible. Moreover we have recently reported[15] that the aminolysis of (S*S**,2*S**)-α-sulfinyl-γ-unsaturated dithioesters by dimethylamine proceeded under dynamic kinetic control and led to the corresponding (S*S**,2*R**)-thioamides with inversion of configuration at the asymmetric carbon center. Consequently all four isomers of molecules **3** can be selectively synthesized.

Access to Thioamides Possessing Three Asymmetric Centers. To apply our method to the synthesis of natural biologically active compounds, we wished to extend it to the formation of thioamides possessing three contiguous asymmetric centers. We have shown previously that the deprotonation of **1** was stereoselective and that the alkylation of the resulting enethiolate proceeded with full retention of configuration. Therefore, by using isomerically pure allylic halides or mesylates, the geometry of both double bonds of the Claisen rearrangement substrates **5a**−**b** could be controlled. This fulfillment is quite important as the configuration of the double bonds involved in the [3,3] sigmatropic transposition is known[16,17] to be crucial for the stereochemistry of the newly formed asymmetric centers. This feature has been often exploited in synthesis.[18−21]

The enolate of (*R*)-**1** was thus treated with isomerically pure or enriched crotyl and cinnamyl allylic reagents[22−24] to afford (*ZZ*)- and (*ZE*)-**5a**−**b** quantitatively (Scheme 3).

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Scheme 3

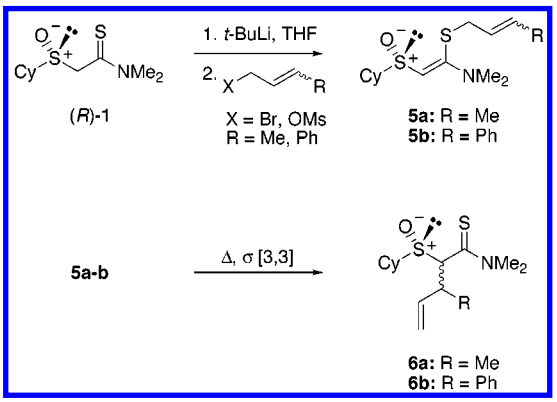


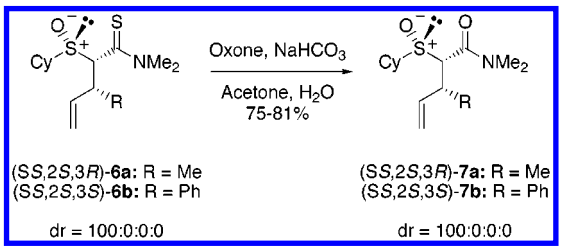
Table 2. Claisen Rearrangement of Compounds 5a−b According to Scheme 3

entry	5[a]	R	(*ZE*)/(*ZZ*)[b]	*T* (°C)	time	6	yield (%)	dr[c]
1	**(*ZE*)−5a**	Me	86:14	20	4 wks	**6a**	43	15:85:0:0
2	**(*ZE*)−5a**	Me	95:5	66	2 h	**6a**	64	18:82:0:0
3	**(*ZZ*)−5a**	Me	0:100	66	2.5 h	**6a**	53	100:0:0:0
4	**(*ZE*)−5b**	Ph	100:0	20	3 wks	**6b**	30	70:30:0:0
5	**(*ZE*)−5b**	Ph	100:0	66	4 h	**6b**	53	90:10:0:0
6	**(*ZZ*)−5b**	Ph	4:96	66	5 h	**6b**	45	100:0:0:0

[a] The (*ZE*) configuration of **5a**−**b** refers to the (*Z*)-configuration of the enethiolate moiety and the (*E*)-configuration of the allylic moiety. [b] The (*ZE*)/(*ZZ*) ratio was determined by ^{1}H NMR analysis by integration of the signals of the vinylic proton of the enethiolate moiety. [c] The diastereomeric ratio was measured by ^{1}H NMR analysis by integration of the signals of the proton linked to the carbon located α to the cyclohexylsulfinyl group and those of the methyl groups of the thioamide function.

The Claisen rearrangement of **5a**−**b** was very slow at room temperature, but as in the case of substrates **2a**−**c**, it could be accelerated by heating at THF reflux (Table 2). The transposition was slower in the cinnamyl series (entries 4−6) than in the crotyl series (entries 1−3) probably as a result of the loss of conjugation between the phenyl group and the double bond of the allylic moiety in the course of the rearrangement. The obtained yields were relatively modest (45−64%) since the full conversion of the ketene aminothioacetals **5a**−**b** into the thioamides **6a**−**b** could not be achieved even by prolonging the heating time. Nevertheless the results were excellent in terms of stereoselectivity since only one or two diastereomers out of the four possible ones were formed (Table 2). A single isomer of **6a**−**b** was isolated in the case of the (*ZZ*)-substrates **5a**−**b**. The isomeric purity of the major product of the rearrangement of (*ZE*)-substrates **5a** and **5b** was 64% and 80%, respectively. A variation of the isomeric ratio of **6b** according to the temperature was observed (entries 4 and 5) and is due to some decomposition of the minor isomer at THF reflux. Not only the configuration of the allylic double bond but also the nature of the allylic substituent had an influence on the stereochemical course of the rearrangement. Indeed, while the (*ZE*)- and (*ZZ*)-**5a** substrates led to distinct isomers of **6a** as major products (entries 2 and 3) the corresponding **5b** substrates gave access to the same major isomer of **6b** (entries 5 and 6). According to ^{1}H and ^{13}C NMR analysis, the structure of the minor isomer of **6a** arising from the rearrangement of the (*ZE*)-**5a** substrate was that of the product of the (*ZZ*)-**5a** substrate.

Scheme 4



Determination of the Absolute Configurations of Thioamides 6a−b. It was not possible to obtain crystals suitable for X-ray analysis of the isomerically pure thioamides **6a**−**b** obtained from the Claisen rearrangement of (*ZZ*)-**5a**−**b**. They were then converted into the corresponding amides **7a**−**b** with dimethyldioxirane,[25] which was formed in situ from oxone and acetone (Scheme 4). The reaction proceeded readily at 0 °C without loss of stereopurity. By a careful addition of oxone further oxidation such as the transformation of the sulfinyl moiety to the sulfone function was prevented. The X-ray crystallographic analysis of amides **7a**−**b** allowed us to assign the (S*S*,2*S*,3*R*) and (S*S*,2*S*,3*S*) configuration to thioamides **6a** and **6b**, respectively. By contrast, the Claisen rearrangement of (*ZE*)-**5a** led to a mixture of two diastereoisomers of **6a** (Table 2), which could not be separated either by flash chromatography through silica gel or by crystallization, even after their transformation into the corresponding amides. The structure of the minor isomer was known as it corresponded to the unique product of the Claisen rearrangement of the (*ZZ*)-**5a** substrate. The identification of the major isomer was then attempted by chemical correlation.

The strategy was to reduce first the sulfinyl moiety of both isomers to have access to molecules bearing only two asymmetric centers. The resulting thioamides could be either enantiomers or diastereomers. In the first case, as the configuration at the sulfur atom was known, the full assignment would be made. In the second case, the removal of two asymmetric centers by reduction of the carbon−sulfur bond of both isomers would be necessary. Using HPLC analysis, we expected to be able to resolve whether the reduction product was a single molecule or an enantiomeric mixture. The same strategy could serve for the determination of the structure of the minor isomer of thioamide **6b** arising from the Claisen rearrangement of (*ZE*)-**5b** (Table 2). We first investigated the selective reduction of the sulfinyl moiety of molecules **6a**−**b**. Many methods exist for the conversion of sulfoxides into sulfides.[26] After a short screening of reducing agents, P_4S_{10} proved to be the most convenient one for the selective transformation of **6a**−**b** and **3a** into thioamides **8a**−**c** (Scheme 5).[27] The reaction proceeded readily at room temperature in CH_2Cl_2 within 0.5−1 h and the isolated yields ranged from 59% to 86%. The conversion of thioamides **6a**−**b** bearing the unknown isomer as minor component (same dr 90:10:0:0) led to thioamides **8a** and **8b** as diastereomeric mixtures (dr 90:10 and 84:

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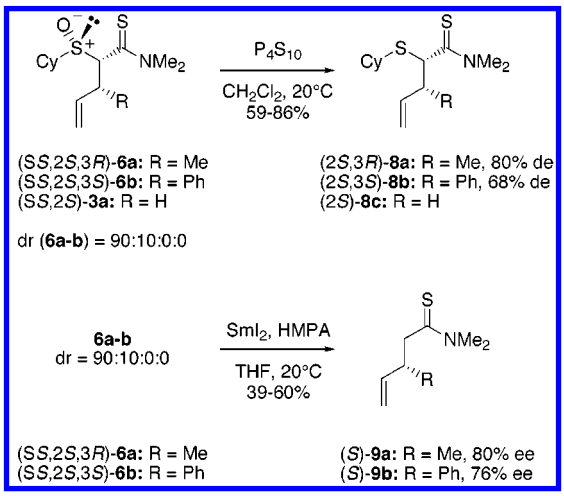
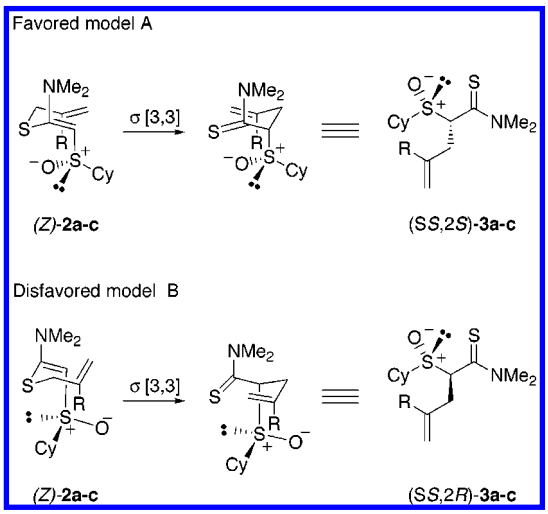
Scheme 5



16, respectively, according to proton NMR analysis). Thus the (S*S*,2*R*,3*S*) and (S*S*,2*R*,3*R*) respective configurations for thioamides **6a** and **6b** should not be considered. To discriminate between the two last possible structures, the determination of the absolute configuration of carbon 3 was necessary and required the reduction of the carbon−sulfur bond. We first prepared the racemic reference[28] compounds **9a** and **9b** by aminolysis of the corresponding dithioesters[29,30] with dimethylamine and found the best conditions for the separation of their enantiomers on HPLC (Daicel AD column). The electron-transfer system SmI_2-THF−HMPA has been reported to be quite efficient for the mild reduction of sulfoxides.[31,32] Therefore we attempted such a reaction with **6a** and **6b** (same dr 90:10:0:0) and obtained thioamides **9a**−**b** as enantiomer mixtures with respective unoptimized yields of 60 and 39% (Scheme 5). The enantiomeric ratio of compounds **9a** and **9b** was determined by HPLC analysis as 90:10 and 88:12, respectively. According to the results of both reactions (P_4S_{10} and SmI_2), we were able to assign the (S*S*,2*S*,3*S*) configuration to the major isomer of **6a** obtained from the Claisen rearrangement of (*ZE*)-**5a** and the (S*S*,2*S*,3*R*) configuration to the minor isomer of **6b** arising from the rearrangement of (*ZE*)-**5b**.

Stereochemical Course of the Claisen Rearrangement of 2 and 5. We have demonstrated that the cyclohexylsulfinyl group was a quite efficient chiral inducer in the Claisen rearrangement of ketene aminothioacetals **2** and **5**. To explain the high level of selectivity of this reaction, we suggest that it proceeds under orbital control and that the steric control is not significant. Such a model has been previously proposed for the Claisen rearrangement in the racemic dithioester series.[3] A pseudo-cyclic chair transition state is usually described for [3,3] sigmatropic transpositions in the acyclic series.[16,33−34] To optimize the electronic transfer, the best donor substituent of the sulfinyl group, the lone

Scheme 6



pair, is oriented *anti* to the electrophilic attack of the allylic chain. Two transition states deriving from conformers A and B are then possible (Scheme 6), and they only differ in the orientation of the oxygen atom and the cyclohexyl group. Model B where the cyclohexyl group, the bulkier substituent,[35] is located at the *inside* position is sterically disfavored in comparison to model A where the cyclohexyl group is oriented at the *outside* position. Moreover, in model A the oxygen atom of the sulfinyl group occupies the *inside* position, which is a stabilizing electronic factor.[4] Model A is thus more favorable than model B, and it gives access to the major diastereoisomer of (S*S*,2*S*) configuration in agreement with the experimental results.

The stereochemical course of the Claisen rearrangement of the (*ZZ*)-**5a**−**b** substrates that afforded only one isomer of thioamides **6a**−**b** can be described by the same pseudo-cyclic chair model A leading to the (S*S*,2*S*,3*R*)-isomer of **6a** and the (S*S*,2*S*,3*S*)-isomer of **6b** (scheme in Supporting Information).

Similarly, in the case of the (*ZE*)-crotyl substrate **5a** such a chair conformation is preferential, although the selectivity is lowered probably because of the increase of steric hindrance within the molecule (scheme in Supporting Information). By contrast the pseudo-cyclic chair conformation is less suitable in the case of (*ZE*)-**5b** as a result of the disfavorable steric interaction between the phenyl substituent and the cyclohexyl group. This interaction is less pronounced in the pseudo-boat conformation, which is then more favorable, and the (S*S*,2*S*,3*S*) isomer of **6b** is formed preferentially (Scheme 7). Such a switch in selectivity is quite unusual in acyclic systems where boat transition states are usually higher in energy. The known examples of pseudo-cyclic boat transition states mostly involve substrates whose allyl bonds are included in a ring,[36] and only a few specific cases have been reported in the acyclic series.[37−39]

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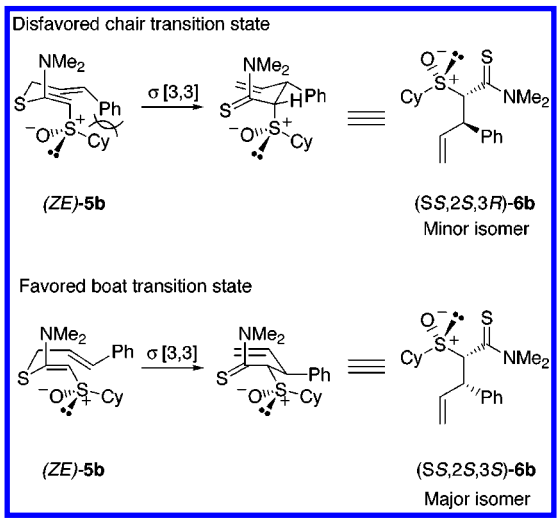
Scheme 7



Conclusion

The stereocontrolled thio-Claisen rearrangement mediated by a cyclohexylsulfinyl group afforded diastereo- and enantioenriched α-sulfinyl γ-unsaturated thiocarbonyl compounds possessing two or three contiguous asymmetric centers. Excellent diastereoselectivities were achieved by the ability of the cyclohexylsulfinyl group as chiral auxiliary and by the full control of the geometry of the double bonds of the Claisen rearrangement substrates **2** and **5**. Excellent enantioselectivities were obtained using diacetone-D-glucose, an easily available and inexpensive source of chirality. Moreover diacetone-D-glucose gave selective access to both enantiomers of the substrates **2** and **5**. Thus our method allows the control of both relative and absolute stereochemistries in acyclic series. It can be considered as an alternative to the palladium-catalyzed regio- and stereoselective allylation reaction.[40−42] Indeed, while this reaction has proven high efficiency in the preparation of enantiopure phenyl-substituted allyl compounds, it is not optimal for the synthesis of the methyl analogues.[43] Quite unexpectedly, the thio-Claisen rearrangement was stereodiverging in the crotyl series and stereoconverging in the cinnamyl series. The stereochemical course of this reaction was mostly explained by a pseudocyclic chair transition state, but an unusual switch to a boat transition state was observed with the (*ZE*)-cinnamyl substrates **5b**.

The Claisen rearrangement products **3a**−**c** and **6a**−**b** are stable molecules bearing several important functional groups that can be selectively modified without altering the diastereopurity. A large diversity of transformations are possible and give access to versatile synthons. For example the reduction of compounds **6a**−**b** and **3a** with P_4S_{10} afforded new α-sulfanyl γ-unsaturated thioamides **8a**−**c**, while the oxidation of **6a**−**b** by dimethyldioxirane led to the corresponding amides **7a**−**b**. Compounds **6a**−**b** are also precursors of enantioenriched pent-4-enethioamides **9a**−**b** bearing an asymmetric center in β-position. Further transformation of compounds **3** and **6** is in course with the aim of synthesizing biologically active compounds.

Experimental Section

Solvents were dried immediately prior use. Dry THF was distilled from sodium/benzophenone under N_2. Commercial reagents were used directly as received. All reactions were monitored by TLC carried out on analytical silica gel TLC plates purchased from Merck silica gel and visualized with UV light and iodine. Preparative flash liquid chromatography was performed with Merck 60 silica gel (63−200 μm) in the eluting solvents indicating below. ^{1}H NMR spectra were recorded on 250 and 400 MHz spectrometers. ^{13}C NMR spectra were determined with the same spectrometers operating with broad band ^{1}H decoupling. Elemental analyses were performed by the Service Central d'Analyse of CNRS at Vernaison or by the "Service d'Analyse de l'ICSN" at Gif sur Yvette for C, H, N, and O or by LCMT for C, H, S, N, and O. Melting points are uncorrected.

Cyclohexanesulfinyl chloride was prepared from cyclohexanethiol according to the literature.[13] It was obtained in 94% yield after distillation [bp (°C/mm) 65−66/0.075 (lit.[13] 62−64/0.07)].

(*S*)-**4** was obtained according to our previous procedure[7] from diacetone-D-glucose and *i*-Pr_2NEt. (*R*)-**1** was prepared[7] from (*S*)-**4** with 91% yield and 98% ee (using 0.33 equiv of *N*,*N*-dimethylethanethioamide instead of 0.25).

Thioamides 3a−c. Only the signals of the minor isomer that were clearly identified are given. The (S*S*,2*S*) configuration of both **3b** and the major isomer of **3c** was deduced from that of the major isomer of **3a**.

(S*S*,2*S*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethylpent-4-enethioamide (3a). Typical Procedure. (*R*)-**1** (107 mg, 0.46 mmol) was diluted in freshly distilled THF (3 mL), and a 1.64 M solution of *t*-BuLi in pentane (285 μL, 0.47 mmol) was slowly added at −40 °C under nitrogen. After 1 h of stirring at −40 °C and 15 min at 0 °C allyl bromide (45 μL, 0.52 mmol) was added at −40 °C, and the reaction mixture was allowed to warm to room temperature over 1.5 h. The reaction mixture was heated at THF reflux for 0.5 h and then cooled to 0 °C before hydrolysis (5 mL). The aqueous phase was acidified with diluted sulfuric acid and extracted with CH_2Cl_2 (5 mL, three times); the combined organic layers were washed with water (5 mL), dried over $MgSO_4$, and then concentrated to dryness for analysis. Flash chromatography on silica gel (ethyl acetate) afforded 98 mg (78% yield, dr 95:5) of **3a** as a pale yellow solid. Crystallization (ethyl acetate/pentane) afforded isomerically pure **3a** (100% de). Its (S*S*,2*S*) configuration was assigned by X-ray crystallographic analysis. Its enantiopurity (96% ee) was measured by HPLC on a Chiralpack AD Daicel column (*n*-hexane/*i*-PrOH 96:4, λ = 280.9 nm). Mp 76 °C; $[\alpha]^{26}_D$ −396 (*c* = 1.02, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−2.15 (m, 10H), 2.84 (tt, *J* = 3.8 Hz, *J* = 12.0 Hz, 1H), 3.05−3.15 (m, 2H), 3.36 (s, 3H), 3.48 (s, 3H), 4.13 (dd, *J* = 6.2 Hz, *J* = 8.5 Hz, 1H), 5.08−5.30 (m, 2H), 5.67−5.85 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 22.6, 25.5, 25.6, 26.2, 28.7, 36.8, 42.3, 44.2, 54.7, 68.3, 119.6, 133.0, 196.9; IR (KBr) ν = 3072, 2932, 2854, 2362, 1518, 1450, 1396, 1266, 1142, 1036, 918 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 274 (MH^+, 1), 247 (2), 190 (1), 108 (21), 83 (56), 55 (100), 45 (42). Anal. Calcd for $C_{13}H_{23}NOS_2$: C, 57.12; H, 8.49; N, 5.13; O, 5.86; S, 23.41. Found: C, 56.99; H, 8.55; N, 5.18; O, 6.03; S, 23.35. ^{1}H NMR signals of the (S*S*,2*R*) minor isomer (250 MHz, $CDCl_3$) δ 3.44 (s, 3H), 3.56 (s, 3H), 4.51 (dd, *J* = 3.6 Hz, *J* = 10.3 Hz, 1H), 5.29−5.47 (m, 2H), 5.85−6.03 (m, 1H).

(S*S*,2*S*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-4-methylpent-4-enethioamide (3b). Prepared from (*R*)-**1** (765 mg, 3.28 mmol) and methallyl iodide (664 mg, 3.65 mmol). Flash chromatography on silica gel (ethyl acetate) afforded 713 mg (76% yield, dr 100:0) of **3b** as a yellow oil. The enantiopurity (90% ee) of a sample of **3b** (de 86%) was measured by HPLC on a Chiralpack AD Daicel column (hexane/*i*-PrOH 95:5, λ =

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280.9 nm). $[\alpha]^{21}_D$ −262 (c = 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.15−2.00 (m, 10H), 1.79 (s, 3H), 2.84 (tt, J = 2.3 Hz, J = 7.4 Hz, 1H), 2.98−3.15 (m, 2H), 3.35 (s, 3H), 3.47 (s, 3H), 4.17 (dd, J = 2.1 Hz, J = 6.8 Hz, 1H), 4.84 (s, 1H), 4.87 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_22.6, 25.3, 25.4, 26.0, 28.6, 23.2, 39.8, 42.0, 44.1, 54.5, 67.9, 114.9 141.1, 197.3; IR (NaCl) ν 3076, 2932, 2854, 2362, 1518, 1450, 1394, 1036 cm^{-1}; MS (70 eV, EI) m/z (%) 288 (MH^+, 1), 258 (4), 156 (84), 88 (51), 83 (61), 55 (100), 41 (90). Anal. Calcd for $C_{14}H_{25}NOS_2$: C, 58.51; H, 8.77; N, 4.88; S,22.27. Found: C, 58.62; H, 8.70; N,4.91; S, 22.03.

(S*S*,2*S*)-4-Bromo-2-cyclohexylsulfinyl-*N*,*N*-dimethylpent-4-enethioamide (3c). Prepared from (*R*)-**1** (100 mg, 0.43 mmol) and 2,3-dibromopropene (65 μL, 0.5 mmol). Flash chromatography on silica gel (ethyl acetate) afforded 87 mg (58% yield, dr 96:4) of **3c** as a solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−2.06 (m, 10H), 2.64−2.84 (m, 1H), 3.30−3.68 (m, 2H), 3.48 (s, 3H), 3.49 (s, 3H), 4.44 (dd, J = 3.2 Hz, J = 10.8 Hz, 1H), 5.48 (s, 1H), 5.78 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 23.3, 25.6, 25.7, 26.3, 28.9, 42.9, 44.5, 44.7, 55.6, 66.7, 121.8, 128.5, 196.0; IR (NaCl) ν 3444, 3096, 2932, 2854, 1628, 1518, 1450, 1416, 1394, 1302, 1272, 1042, 994, 894, 612 cm^{-1}; MS (70 eV, EI) m/z (%) 352 (MH^+, 1), 272 (3), 230 (19), 140 (75), 83 (100), 55 (1), 44 (1); HRMS found 351.03257, $C_{13}H_{22}NOS_2$-Br (M^+) requires 351.03276; ^{1}H NMR signals of the (2*R*,S*S*) minor isomer (250 MHz, $CDCl_3$) δ 3.51 (s, 3H), 4.94 (dd, J = 3.0 Hz, J = 9.9 Hz, 1H); ^{13}C NMR signals of the minor isomer (62.9 MHz, $CDCl_3$) δ 22.6, 25.7, 26.4, 28.6, 42.1, 46.0, 55.7, 63.0, 121.7, 128.3.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranosyl (*R*)-Cyclohexanesulfinate (4). To a cooled (−50 °C) solution of freshly distilled cyclohexanesulfinyl chloride (7.00 g, 42 mmol, 1.6 equiv) in 25 mL of anhydrous THF was added dropwise and with vigorous stirring a mixture of diacetone-D-glucose (6.83 g, 26.3 mmol, 1 equiv) and pyridine (2.60 mL, 31.5 mmol, 1.2 equiv) in dry THF (20 mL). The reaction mixture was stirred at −50 °C for 2.5 h and then quenched with water (100 mL). The aqueous layer was extracted with ethyl acetate (70 mL, three times). The combined organic extracts were successively washed with 5% aq HCl (100 mL), 2% aq $NaHCO_3$ (100 mL), and brine (100 mL), dried over $MgSO_4$, and concentrated to dryness to afford the crude sulfinate (11.10 g) as a colorless oil. The diastereomeric ratio was determined by ^{1}H NMR analysis: (*R*)/(*S*) = 90/10. (*R*)-**4** was isolated as a colorless oil (8.49 g, 83% yield) after crystallization of (*S*)-**4** from ethyl acetate/petroleum ether 1/4. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.30, 1.32, 1.42 and 1.50 (4 s, 12 H), 1.18−2.06 (m, 10 H), 2.65 (m, 1 H), 3.94−3.98 (m, 2 H), 4.10−4.18 (m, 2 H), 4.71 (d, J = 1.7 Hz, 1H), 4.80 (d, J = 3.5 Hz, 1H), 5.91 (d, J = 3.5 Hz, 1H).

(*S*)-2-(Cyclohexylsulfinyl)-*N*,*N*-dimethylethanethioamide (1). To a cooled (−78 °C) solution of *N*,*N*-dimethylethanethioamide (1.86 g, 18 mmol, 3 equiv) in dry THF (22 mL) was added dropwise a 2 M solution of NaHMDS in THF (8.7 mL, 17.4 mmol, 2.9 equiv). The reaction mixture was stirred at −78 °C for 1 h, and then a solution of (*R*)-**4** (2.34 g, 6 mmol, 1 equiv) in dry THF (15 mL) was added dropwise. The reaction was monitored by thin-layer chromatography. It was complete after 1.5 h and quenched by addition of a H_2O/THF (1/4) mixture at −78 °C. The reaction mixture was worked up by addition of diluted aq H_2SO_4 solution (pH 1), followed by extraction with CH_2Cl_2 (50 mL, four times). The combined organic layers were washed with brine, dried over $MgSO_4$, and then concentrated to dryness. Purification by column chromatography (silica gel, ethyl acetate then 10% MeOH) afforded 1.33 g (95% yield) of the (*S*)-enantiomer of **1** as a white solid (mp 82 °C). Its enantiopurity (88% ee) was measured by HPLC on a Chiralpack AD Daicel column (*n*-hexane/*i*-PrOH 90:10, λ = 280.9 nm). The ^{1}H and ^{13}C NMR data are identical to those previously reported[7] for (*R*)-**1**.

(S*R*,2*R*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethylpent-4-enethioamide (3a). (*S*)-**1** (233 mg, 1 mmol) was diluted in freshly distilled THF (2 mL), and a 1.5 M solution of *t*-BuLi in pentane (670 μL, 1 mmol) was slowly added at −40 °C under nitrogen. After 50 min of stirring at −40 °C and 45 min at −5 °C, allyl bromide (95 μL, 1,1 mmol) was added at −40 °C, and the reaction mixture was allowed to warm to room temperature over 1.75 h. The reaction mixture was heated at THF reflux for 0.5 h and then cooled to 0 °C before hydrolysis (10 mL). The aqueous phase was acidified with diluted sulfuric acid and extracted with CH_2Cl_2 (10 mL, three times). The combined organic layers were washed with water (10 mL), dried over $MgSO_4$, and then concentrated to dryness to afford 264 mg of crude product as orange oil. Flash chromatography on silica gel (ethyl acetate) afforded 221 mg (81% yield, dr 91:9) of (S*R*,2*R*)-**3a** as a pale yellow oil. A second flash chromatography and a crystallization (ethyl acetate/petroleum ether 1/4) were necessary to obtain isomerically pure **3a** (>99% de). Its enantiopurity (>99% ee) was measured by HPLC on a Chiralpack AD Daicel column (*n*-hexane/*i*-PrOH 96:4, λ = 280.9 nm). $[\alpha]^{26}_D$ +321 (c = 1, $CHCl_3$).). The ^{1}H and ^{13}C NMR data are identical to those previously reported for (S*S*,2*S*)-**3a**.

(S*S*,2*S*,3*S*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-3-methylpent-4-enethioamide (6a). Typical Procedure. (*R*)-**1** (99 mg, 0.42 mmol) was diluted in freshly distilled THF (3 mL), and a 1.5 M solution of *t*-BuLi in pentane (300 μL, 0.45 mmol) was slowly added at −40 °C under nitrogen. After the reaction had been stirred for 1 h at −40 °C and for 15 min at 0 °C, a solution of (*E*)-4-bromobut-2-ene (61 mg, 0.52 mmol) diluted in THF (1 mL) was then added at −40 °C, and the reaction mixture was allowed to warm to room temperature over 1.5 h. The reaction mixture was heated at THF reflux for 2 h and then hydrolyzed (5 mL) at 0 °C. The aqueous phase was acidified with diluted sulfuric acid and extracted with CH_2Cl_2 (5 mL, 3 times). The combined organic layers were washed with water, dried over $MgSO_4$, and then concentrated to dryness for analysis. Flash chromatography on silica gel (ethyl acetate) afforded 79 mg (64% yield, dr 18:82:0:0) of **6a** as a yellow solid: mp 64 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.01−2.01 (m, 10H), 1.31 (d, J = 6.9 Hz, 3H), 2.96 (tt, J = 3.8 Hz, J = 11.9 Hz, 1H), 3.22−3.36 (m, 1H), 3.39 (s, 3H), 3.49 (s, 3H), 4.14 (d, J = 6.4 Hz, 1H), 5.02−5.32 (m, 2H), 5.80−6.04 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 17.5, 22.9, 25.7, 25.8, 26.4, 28.9, 40.5, 42.9, 44.3, 55.1, 71.7, 116.7, 140.3, 202.3; IR (KBr) ν 3078, 2930, 2854, 2362, 1508, 1040 cm^{-1}; MS (70 eV, EI) m/z (%) 287 (M^+, 13), 198 (11), 171 (16), 97 (18), 83 (36), 69 (71), 55 (100), 43 (99). Anal. Calcd for $C_{14}H_{25}NOS_2$: C, 58.51; H, 8.77; N, 4.88; S, 22.27. Found: C, 58.39; H, 8.81; N, 5.28; S, 22.53.

(S*S*,2*S*,3*R*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-3-methylpent-4-enethioamide (6a). Obtained from (*R*)-**1** (310 mg, 1.34 mmol) and (*Z*)-4-bromobut-2-ene (235 mg, 1.74 mmol). Flash chromatography on silica gel (ethyl acetate) afforded 202 mg (53% yield, dr 100:0:0:0) of **6a** as a yellow solid. Its (S*S*,2*S*,3*R*) configuration was deduced from that of the corresponding amide **7a**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.02−2.00 (m, 10H), 1.38 (d, J = 6.6 Hz, 3H), 2.91−3.06 (m, 1H), 3.27−3.45 (m, 1H), 3.38 (s, 3H), 3.46 (s, 3H), 3.98 (d, J = 6.2 Hz, 1H), 5.07 (d, J = 10.2 Hz, 1H), 5.17 (d, J = 17.1 Hz, 1H), 5.84−6.02 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 18.1, 22.8, 25.7, 25.8, 26.4, 28.7, 42.0, 42.7, 44.1, 55.3, 72.7, 116.4, 139.6, 196.1. Further characterization of **6a** was made on the corresponding amide **7a**.

(S*S*,2*S*,3*S*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-3-phenylpent-4-enethioamide (6b). Obtained from (*R*)-**1** (157 mg, 0.67 mmol) and (*Z*)-3-phenylprop-2-enyl methane sulfonate (156 mg, 0.74 mmol). Flash chromatography on silica gel (ethyl acetate) afforded 106 mg (45% yield, dr 100:0:0:0) of **6b** as a solid. Its (S*S*,2*S*,3*S*) configuration was deduced from that of the corresponding amide **7b**: mp 91 °C; $[\alpha]^{19}_D$ −140 (c = 0.98, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−2.15 (m, 10H), 2.44 (s, 3H), 2.88 (tt, J = 3.7 Hz, J = 12.0 Hz, 1H), 3.32 (s, 3H), 4.27 (d, J = 5.3 Hz, 1H), 4.35 (dd, J = 5.3 Hz, J = 7.9 Hz, 1H), 5.34 (d, J = 10.0 Hz, 1H), 5.40 (d, J = 16.9 Hz, 1H), 6.84 (ddd, J = 7.9 Hz, J = 10.0 Hz, J = 16.9 Hz, 1H), 7.15−7.50 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 22.7, 25.5, 25.6, 26.2, 28.7, 41.2, 43.6, 49.7, 54.3, 72.3, 118.6, 127.7, 128.7, 129.0, 134.9, 140.8, 193.6; IR (NaCl) ν 3426, 3030, 2930, 2854, 1512, 1450, 1392, 1274, 1114, 1030, 990, 742, 702 cm^{-1}; MS (70 eV, EI) m/z (%) 349 (M^+, 0.8), 265 (1), 249 (3), 218 (100), 184 (68), 127 (30),

115 (37), 88 (70), 83 (55), 55 (96), 44 (62); HMRS found 350.1622, $C_{19}H_{28}NOS_2$ (MH^+) requires 350.1612.

This reaction was also carried out with (*R*)-**1** (171 mg, 0.73 mmol) and (*Z*)-3-bromo-1-phenylpropene (164 mg, 0.83 mmol) and afforded 102 mg (40% yield, dr 100:0:0:0) of **6b**.

The same (S*S*,2*S*,3*S*) isomer of **6b** was also obtained from (*R*)-**1** (100 mg, 0.43 mmol) and (*E*)-3-bromo-1-phenylpropene (96 mg, 0.49 mmol). Flash chromatography on silica gel (ethyl acetate) afforded 80 mg (53% yield, dr 90:10:0:0) of **6b**. Only the signals of the (S*S*,2*S*,3*R*) minor isomer that were clearly identified are given: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.73 (s, 3H, NMe), 3.23 (s, 3H, NMe); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.4 (NMe), 43.9 (NMe), 75.0 (SOCH), 117.6 (CH_2=).

(S*S*,2*S*,3*R*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-3-methylpent-4-enamide (7a). Typical Procedure. (S*S*,2*S*,3*R*)-**6a** (93 mg, 0.32 mmol) was diluted in acetone (4.5 mL). Sodium bicarbonate (107 mg, 1.26 mmol) and water (450 μL) were added, and the mixture was stirred at 0 °C. Then 0.5 equiv of oxone (100 mg, 0.16 mmol) was first added. After 15 min of stirring, 0.25 equiv of oxone was added every 15 min (4 × 50 mg, 0.32 mmol). Water (5 mL) was then added. The aqueous phase was extracted with ethyl acetate (5 mL, three times). The combined organic layers were dried over $MgSO_4$ and then concentrated to dryness to afford 66 mg (75% yield, dr 100:0:0:0) of a white solid. Its (S*S*,2*S*,3*R*) configuration was assigned by X-ray crystallographic analysis after crystallization (ethyl acetate/petroleum ether): mp 95 °C; $[\alpha]^{19}_D$ −160 (c = 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−2.05 (m, 10H), 1.30 (d, J = 7.0 Hz, 3H), 2.60−2.75 (m, 1H), 2.98−3.20 (m, 1H), 2.98 (s, 3H), 3.11(s, 3H), 3.82 (d, J = 6.3 Hz, 1H), 5.10 (d, J = 10.5 Hz, 1H), 5.17 (d, J = 17.1 Hz, 1H), 5.84−5.99 (m, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 18.5, 23.1, 25.4, 25.5, 26.0, 28.2, 35.7, 38.4, 38.5, 55.8, 66.4, 116.1, 139.0, 167.5; IR (KBr) ν 3222, 3070, 2924, 2854, 1620, 1496, 1456, 1404, 1258, 1128, 1044, 992, 910, 518, 456 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 272 (MH^+, 2), 214 (2), 189 (33), 172 (4), 141 (45), 134 (100), 126 (53), 105 (18), 72 (57), 55 (41), 44 (21).

(S*S*,2*S*,3*S*)-2-Cyclohexylsulfinyl-*N*,*N*-dimethyl-3-phenylpent-4-enamide (7b). Obtained from (S*S*,2*S*,3*S*)-**6b** (116 mg, 0.33 mmol) as white crystals (90 mg, 81% yield, dr 100:0:0:0). Its (S*S*,2*S*,3*S*) configuration was assigned by X-ray crystallographic analysis after crystallization (ethyl acetate/petroleum ether): mp 130 °C; $[\alpha]^{21}_D$ −92 (c = 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−2.05 (m, 10H), 2.30 (s, 3H), 2.48−2.62 (m, 1H), 2.86 (s, 3H), 4.03 (d, J = 5.4 Hz, 1H), 4.24 (dd, J = 5.4 Hz, J = 9.3 Hz, 1H), 5.32 (d, J = 10.0 Hz, 1H), 5.34 (d, J = 17.1 Hz, 1H), 6.51 (ddd, J = 9.3 Hz, J = 10.0 Hz, J = 17.1 Hz, 1H), 7.15−7.40 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 23.1, 25.5, 26.0, 28.2, 35.5, 37.2, 48.2, 55.5, 66.3, 119.1, 127.5, 128.2, 129.0, 134.9, 140.9, 166.7; IR (KBr) ν 2984, 2954, 2930, 2852, 1628, 1492, 1452, 1414, 1400, 1256, 1178, 1128, 1108, 1040, 994, 928, 758, 702, 602, 512 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 334 (MH^+, 1), 251 (7), 234 (1), 214 (2), 203 (8), 201 (8), 189 (3), 157 (7), 141 (2), 134 (100), 105 (15), 72 (30), 55 (18). Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.17; N, 4.20; S, 9.60. Found: C, 68.60; H, 8.22; N, 4.59; S, 9.91.

Compounds 8a−c. Conformational changes of the molecule within the NMR time scale resulted in broad signals. The ^{1}H NMR signal of C*H*R for **8a**−**b** (R = Me, Ph) was hidden by the NC*H*$_3$ signals.

(2*S*,3*R*)-2-Cyclohexylsulfanyl-*N*,*N*-dimethyl-3-methylpent-4-enethioamide (8a). Typical Procedure. P_4S_{10} (117 mg, 0.26 mmol) was added slowly to a stirred solution of (S*S*,2*S*,3*R*)-**6a** (dr 90:10:0:0, 150 mg, 0.52 mmol) in CH_2Cl_2 (4 mL) at room temperature. The reaction was monitored by TLC. After 45 min, the CH_2Cl_2 layer was separated, and the residual inorganic reagent was shaken with water (2 mL) and CH_2Cl_2 (3 mL, three times). The combined organic extracts were washed once with water (5 mL) and evaporated to dryness. Flash chromatography on silica gel (CH_2Cl_2) afforded 113 mg (80% yield) of **8a** as a yellow oil. The diastereomeric ratio was determined by ^{1}H NMR analysis: (2*S*,3*R*)/(2*S*,3*S*) 90:10; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20−2.02 (m, 10H), 1.28 (d, J = 6.6 Hz, 3H), 2.91 (m, 1H), 3.39 (s, 3H), 3.45 (s, 3H), 4.01 (br s, 1H), 4.95−5.08 (m, 2H), 5.76−5.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 25.6, 26.0, 26.02, 33.7, 34.5, 42.2, 43.2, 44.6, 45.4, 114.7, 140.7, 202.5; IR (NaCl) ν 3076, 2928, 2852, 1638, 1516, 1448, 1390, 1276, 1146, 1096, 1068, 996, 918 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 271 (M^+, 1), 255 (0.8), 236 (1), 216 (30), 208 (23), 193 (87), 188 (99), 157 (95), 156 (100), 142 (33), 88 (24), 83 (13), 55 (82), 41 (47); HRMS found 271.1463, $C_{14}H_{25}NS_2$ (M^+) requires 271.1428. Anal. Calcd for $C_{14}H_{25}NS_2$: C, 61.94; H, 9.28; N, 5.16; S, 23.62. Found: C, 61.87; H, 9.43; N, 5.55; S, 23.51. ^{1}H NMR signals of the (2*S*,3*S*) minor isomer (400 MHz, $CDCl_3$) δ 1.06 (d, J = 6.6 Hz, 3H), 3.44 (s, 3H), 3.51 (s, 3H); ^{13}C NMR signals of the (2*S*,3*S*) minor isomer (100 MHz, $CDCl_3$) δ 115.4, 141.1.

(2*S*,3*S*)-2-Cyclohexylsulfanyl-*N*,*N*-dimethyl-3-phenylpent-4-enethioamide (8b). Obtained from (S*S*,2*S*,3*S*)-**6b** (dr 100:0:0:0, 237 mg, 0.68 mmol). Flash chromatography on silica gel (petroleum ether/ethyl acetate 8:2) afforded 134 mg (59% yield) of **8b** as a white solid: mp 120 °C; $[\alpha]^{18}_D$ −17 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91−1.61 (m, 10H), 1.77 (m, 1H), 3.45 (s, 3H), 3.46 (m, 1H), 3.49 (s, 3H), 4.30 (br s, 1H), 5.04−5.08 (m, 2H), 6.08 (br s, 1H), 7.26−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 26.06, 32.9, 34.7, 42.0, 43.7, 45.0, 53.9, 57.2, 117.4, 127.1, 128.4, 129.3, 138.2, 141.1, 202.4; IR (KBr) ν 3058, 3026, 2924, 2848, 2364, 1636, 1514, 1450, 1446, 1414, 1390, 1274, 1206, 1114, 998, 990, 770, 704, 668, 526 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 333 (M^+, 2), 250 (4), 219 (100), 204 (10), 186 (21), 134 (17), 128 (18), 117 (17), 88 (55), 55 (27), 44 (19); HRMS found 333.1574, $C_{19}H_{27}NS_2$ (M^+) requires 333.1585.

Starting from (S*S*,2*S*,3*S*)-**6b** (dr 90:10:0:0, 10 mg, 0.029 mmol), **8b** (7 mg, 73% yield) was obtained after flash chromatography (CH_2Cl_2). The diastereomeric ratio was determined by ^{1}H NMR analysis: (2*S*,3*S*)/(2*S*,3*R*) 84:16.

(*S*)-2-Cyclohexylsulfanyl-*N*,*N*-dimethylpent-4-enethioamide (8c). Obtained from (S*S*,2*S*)-**3a** (123 mg, 0.45 mmol). Flash chromatography on silica gel (CH_2Cl_2) afforded 100 mg (86% yield) of **8c** as a yellow oil: $[\alpha]^{18}_D$ −137 (c = 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27−1.98 (m, 10H), 2.62−2.69 (m, 1H), 2.97 (m, 1H), 3.07 (br s, 1H), 3.43 (s, 3H), 3.50 (s, 3H), 4.03 (br s, 1H), 5.03−5.14 (m, 2H), 5.76−5.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_25.6, 26.0, 26.1, 34.2, 34.7, 41.0, 41.8, 43.0, 45.30, 45.34, 117.4, 135.4, 202.0; IR (NaCl) ν 3074, 2928, 2850, 1638, 1508, 1448, 1390, 1276, 1140, 1088, 998, 918 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 257 (M^+, 1), 255 (1), 236 (0.4), 216 (1), 214 (3), 208 (2), 193 (7), 174 (28), 156 (10), 143 (100), 142 (100), 127 (13), 114 (12), 88 (12), 55 (34), 44 (74); HRMS found 257.1221, $C_{13}H_{23}NS_2$ (M^+) requires 257.1272.

(*S*)-*N*,*N*-Dimethyl-3-methylpent-4-enethioamide (9a).[28] **Typical Procedure.** To a solution of (S*S*,2*S*,3*R*)-**6a** (dr 90:10:0:0, 79 mg, 0.27 mmol) in HMPA (0.275 mL, 1.58 mmol) was added slowly a solution of SmI_2 (0.58 mmol) in THF [5.8 mL, freshly prepared from 1,2-diiodoethane (282 mg, 1 mmol) and samarium (301 mg, 2 mmol) in THF (10 mL)]. The resulting mixture was stirred at room temperature, and the reaction was monitored by TLC. After 1.5 h, the reaction mixture was hydrolyzed by addition of a 0.1 M aqueous solution of HCl (5 mL) and then extracted with ethyl acetate (5 mL, three times). The combined organic layers were washed with water (5 mL), a saturated aqueous solution of sodium thiosulfate (5 mL), and brine (5 mL), dried over $MgSO_4$, and concentrated to dryness. Flash chromatography on silica gel (petroleum ether/ethyl acetate 8:2) afforded 26 mg (60% yield) of **9a** as a colorless oil. The enantiomeric ratio of **9a** was determined by HPLC analysis on a Daicel Chiralpack AD column (*n*-hexane/*i*-PrOH 99:1, λ = 275.7 nm): (*S*)/(*R*) 90:10; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.12 (d, J = 6.5 Hz, 3H), 2.73−2.98 (m, 3H), 3.32 (s, 3H), 3.50 (s, 3H), 4.95−5.08 (m, 2H), 5.83 (ddd, J = 6.7 Hz, J = 10.3 Hz, J = 17.0 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.5, 38.3, 42.2, 44.8, 49.6, 113.6 142.6, 202.8; IR (NaCl) ν 3076, 2964, 2930, 2870, 1640, 1520, 1456, 1392, 1284, 1124, 1054, 998, 916, 854, 720, 676 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 157 (M^+, 100), 142 (71), 128 (13), 88 (55), 44 (56).

(*S*)-*N*,*N*-Dimethyl-3-phenylpent-4-enethioamide (9b). Obtained from (S*S*,2*S*,3*S*)-**6b** (dr 90:10:0:0, 50 mg, 0.14 mmol). After 2.5 h of stirring, the reaction was stopped, although it

was not complete. Flash chromatography on silica gel (petroleum ether/ethyl acetate 8:2) afforded 12 mg (39% yield) of **9b** as a yellow oil; 10 mg of starting material was recovered (dr 90:10:0:0, 20%). The enantiomeric ratio of **9b** was determined by HPLC analysis on a Daicel Chiralpack AD column (*n*-hexane/*i*-PrOH 98:2, $\lambda = 278.1$ nm): (*S*)/(*R*) 88:12; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.96 (s, 3H), 3.17 and 3.25 (AB of ABX, 2H, $J_{AB} = 12.7$ Hz, $J_{AX} = 8.0$ Hz, $J_{BX} = 6.9$ Hz), 3.39 (s, 3H), 4.15−4.21 (m, 1H), 5.08−5.15 (m, 2H), 6.12 (ddd, $J = 6.7$ Hz, $J = 10.4$ Hz, $J = 17.0$ Hz, 1H), 7.22−7.31 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 41.9, 44.8, 48.4, 49.9, 115.2 127.0, 128.0, 128.6, 140.1, 142.6, 202.1; IR (NaCl) ν 3080, 3060, 3026, 2974, 2932, 2360, 2340, 1636, 1600, 1520, 1452, 1392, 1284, 1072, 918, 758, 702 cm^{-1}; MS (70 eV, EI) *m*/*z* (%) 219 (M^+, 100), 204 (49), 186 (22), 158 (11), 131 (11), 115 (27), 105 (17), 88 (39), 70 (16), 68 (10), 44 (57); HRMS found 219.10809, $C_{13}H_{17}NS$ (M^+) requires 219.10816.

Acknowledgment. We gratefully acknowledge the CNRS and the "Région Basse-Normandie" for financial support to S.N., Margareth Lemarié for HPLC analysis of **9b,** and Pascale Gancel for technical assistance.

Supporting Information Available: Scheme for the rearrangement of keteneaminothioacetals (*ZZ*)-**5a**−**b** and (*ZE*)-**5a**. Experimental procedures and typical ^{1}H NMR data for aminoketenethioacetals **2a**−**c** and **5a**−**b**. X-ray crystallographic data for compounds **3a** and **7a**−**b** and HPLC isomer analyses of **9a**−**b**. This material is available free of charge via the Internet at http://pubs.acs.org. *Fax: +33 231 452 877.

JO015956M