



# Stereocontrolled Thio-Claisen Rearrangement of S-Allylic Ketene Aminothioacetals by an Hydroxysubstituted Adjacent Stereogenic Centre.

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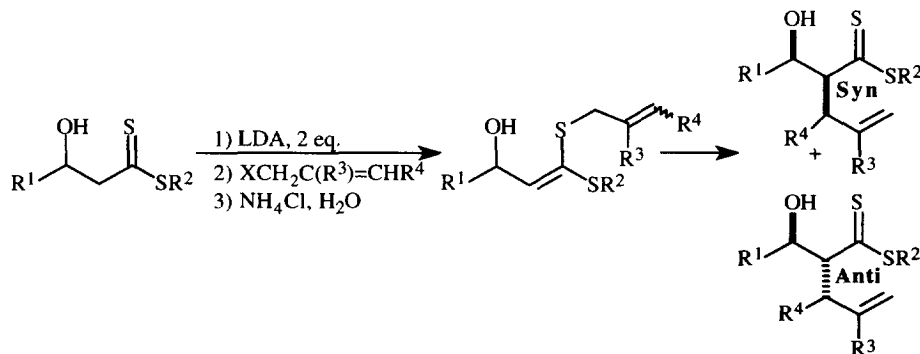
**Abstract:** (Z)-S-allylic ketene aminothioacetals were prepared from N,N-Dimethyl  $\beta$ -hydroxythioamides 2-8 by deprotonation with LDA ( 2 eq.) at  $-78^{\circ}\text{C}$  followed by S-alkylation with allylic bromide. Rearrangement of these compounds occurred easily at room temperature affording major syn N,N-dimethyl  $\beta$ -hydroxy  $\alpha$ -allylic thioamides 9-21 with a syn/anti ratio of 80/20 to 98/2. The syn configuration of the major diastereoisomer was confirmed by an univocal synthesis of syn thioamides 9 and 11. The structure assignments were confirmed by empirical  $^{13}\text{C}$  NMR rules. The observed induction is well supported by a proposed transition state model. © 1997 Elsevier Science Ltd.

## Introduction

Claisen rearrangement<sup>1</sup> and its variant, Ireland-Claisen rearrangement<sup>2</sup> have been widely used for controlling the stereochemistry of new formed stereogenic centres. The high stereochemistry control of this reaction is a consequence of a high ordered transition state: a cyclic chair like transition state<sup>3</sup> with the ensued stereospecificity and 1,3 or 1,4-asymmetric inductions as it has been reported.<sup>4</sup>

External induction by a stereogenic centre appended to the hetero-1,5-hexadienic framework has been also exemplified and has allowed an efficient stereochemistry control over two and even three contiguous stereogenic centres.<sup>5-7</sup>

Recently, in our group,<sup>8</sup> we showed that thio-Claisen rearrangement performed with S-allylic ketene dithioacetals derived from  $\beta$ -hydroxydithioesters occurred more easily than with oxygen analogues. A major  $\alpha,\beta$ -syn diastereoisomer is always formed independently of the ketene double bond geometry (scheme 1). It is an unprecedented result.

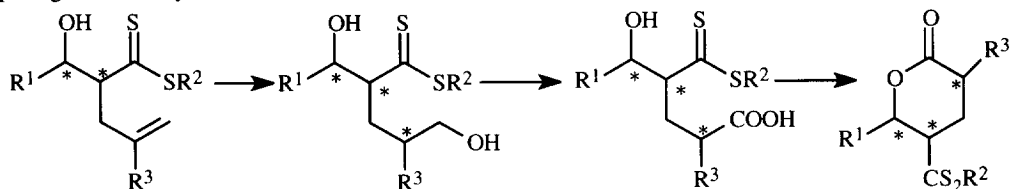


Scheme 1

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A similar result has been pointed out recently in sulfur chemistry by using a sulfinyl group instead of the hydroxysubstituted stereogenic centre.<sup>9</sup> Excellent diastereoisomeric excess in favour of syn diastereoisomer were then observed.

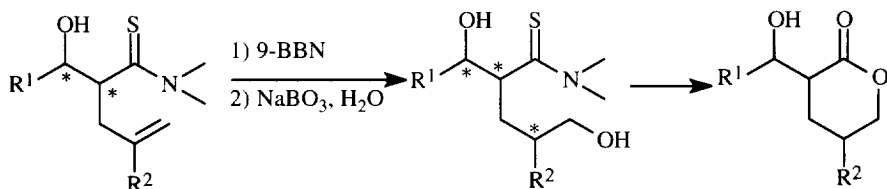
Following this result, we envisioned the conversion of the terminal double bond of the rearranged products into a terminal alcohol or acid in the aim to obtain a ring by lactonization with the secondary alcohol, opening thus the way to natural lactones such as invictolide<sup>10</sup> (scheme 2).



Scheme 2

Such a conversion may start with the hydroboration of the terminal double bond without alteration of the sulfur functionality and needs a high level of diastereoselectivity in the case of  $R^3 \neq H$ . The required diastereoselection may come from a chelating effect of the hydroborating reagent eventually by the hydroxyl group or the sulfur function or a steric effect as it has been reported by Evans.<sup>11</sup> It appeared after careful examination in the literature that dithioester function may be reduced by  $BH_3Me_2S$  only at high temperature.<sup>12</sup> As hydroboration reaction is usually done at low temperature, we then tested an hydroboration model reaction on a methyl 4-pentenedithioate and observed that even at low temperature the reaction was not chemoselective. A mixture of several products were formed (thiols and dithioesters and hemithioacetals).

We turned then, our attention, to the same reaction with the similar unsaturated backbone bearing a *N,N*-dimethylthioamide instead of a dithioester function. It is known that such thioamides are not reduced by an hydroborating agent as 9-BBN<sup>13a,b</sup> (Scheme 3).

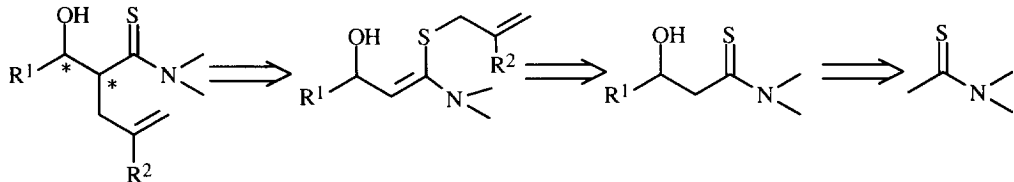


Scheme 3

## RESULTS

In this paper we report the synthesis of the required  $\beta$ -hydroxy  $\delta$ -unsaturated  $N,N$ -dimethylthioamides which will allow us in a next study to carry out successfully our initial goal.

According to the retrosynthetic scheme (scheme 4), the requisite unsaturated thioamides may be prepared by a thio-Claisen rearrangement of *S*-allylic ketene aminothioacetals, derived from  $\beta$ -hydroxythioamides, themselves available by an aldol reaction of  $N,N$ -dimethyl thioacetamide with appropriate aldehydes.



Scheme 4

Aldol reaction with thioamides have been already described by several groups who have studied the diastereoselectivity and the enantioselectivity of this reaction.<sup>14</sup>

The required  $\beta$ -hydroxy- $N,N$ -dimethylthioamides **2-8** were easily prepared according to a known procedure<sup>14</sup> from  $N,N$ -dimethylthioamide **1** and various aldehydes. One of them bears a stereogenic centre  $\alpha$  to the carbonyl function. In this particular case a 80/20 ratio of syn/anti diastereoisomer was formed and isolated as a partially separable mixture<sup>15</sup> (see table 1).

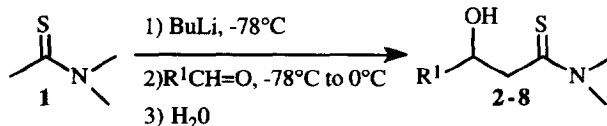


Table 1: Aldol synthesis

Entry	R <sup>1</sup>	Yield*	Aldol
1	CH <sub>3</sub> **	83%	2
2	CH <sub>3</sub> CH <sub>2</sub>	70%	3
3	(CH <sub>3</sub> ) <sub>2</sub> CH **	81%	4
4	(CH <sub>3</sub> ) <sub>3</sub> C **	75%	5
5	C <sub>6</sub> H <sub>5</sub> ***	85%	6
6	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	70%	7
7	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )	90%	8a-b
Syn / anti : 80 / 20			

\*yield: after purification by chromatography

\*\*briefly described by Cinquini and coworkers.<sup>16</sup>\*\*\*briefly described by Goasdoué and coworkers.<sup>14</sup>

These β-hydroxy-N,N-dimethylthioamides were then better deprotonated with two equivalents of LDA at -40°C to form a chelated dianion of Z configuration. Alkylation of these dianions by allylic halides occurred exclusively as expected<sup>17</sup> on the sulfur site to give the corresponding Z α-hydroxy S-allylic ketene dimethylamino thioacetals (the N,N-dimethyl <sup>1</sup>H NMR signal appears as a single singlet at 2.7 and only one).

Such S-allylic ketene aminothioacetals are prone to rearrange by a [3,3] sigmatropic shift into δ-unsaturated thioamides.<sup>5a,13</sup> Nevertheless asymmetric induction by an external asymmetric centre has never been reported with such S-allylic ketene dimethylamino thioacetals formed from thioamides.

Indeed, this rearrangement of the formed α-hydroxy S-allylic ketene aminothioacetal underwent at room temperature in 12 to 72 hours. In every case the major diastereoisomer is detected in a 80/20 to 98/2 ratio (see table 2). The diastereoisomeric ratio was determined by <sup>13</sup>C and <sup>1</sup>H NMR (integration measurement of N-dimethyl shifts for example).

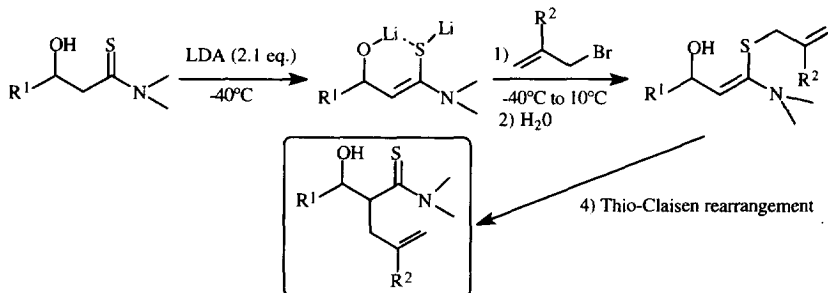


Table 2: Diastereoselectivity of the thio-Claisen rearrangement of Z-aminothioacetals

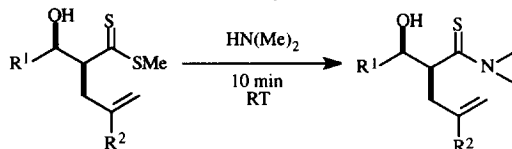
Entry	R <sup>1</sup>	R <sup>2</sup>	Yield*	Syn / Anti** Ratio	Thioamide
1	CH <sub>3</sub>	H	55%	80 / 20	9
2	CH <sub>3</sub> CH <sub>2</sub>	H	70%	85 / 15	10
3	(CH <sub>3</sub> ) <sub>2</sub> CH	H	61%	93 / 7	11
4	(CH <sub>3</sub> ) <sub>3</sub> C	H	30%	>98 / 2	12
5	C <sub>6</sub> H <sub>5</sub>	H	40%	80 / 20	13
6	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	H	75%	90 / 10	14
7	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> ) syn 8a	H	31%	>95 / 5	15
7'	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> ) anti 8b	H	31%	>95 / 5	15
8	CH <sub>3</sub>	CH <sub>3</sub>	52%	80 / 20	16
9	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub>	60%	85 / 15	17
10	(CH <sub>3</sub> ) <sub>2</sub> CH	CH <sub>3</sub>	56%	85 / 15	18
11	(CH <sub>3</sub> ) <sub>3</sub> C	CH <sub>3</sub>	56%	>98 / 2	19
13	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	CH <sub>3</sub>	55%	95 / 5	20
14	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> ) syn 8a	CH <sub>3</sub>	45%	>95 / 5	21

(\*yield: after purification ; \*\*Syn/Anti Ratio was determined by <sup>1</sup>H and <sup>13</sup>C NMR)

As shown in the table, the diastereoisomeric excess increases with the steric hindrance (see entries 1-4 and 8-11). When  $R^1 = \text{benzyl}$ , an improvement of the diastereoselectivity (entries 6, 7, 13 and 14) is evidenced, a possible  $\pi$ -stacking<sup>18</sup> effect may account for this increase.

Configuration determination of the major diastereoisomer which may exist as a syn or anti diastereoisomer was clearly assigned by chemical correlation.

A known syn  $\beta$ -hydroxy- $\delta$ -unsaturated dithioester ( $R^1 = \text{CH}_3$  or  $i\text{Pr}$ ) prepared according to our precedent works<sup>8a</sup> was converted into the corresponding syn  $N,N$ -dimethylthioamide by a non epimerizing aminolysis reaction with  $N,N$ -dimethylamine (scheme 5).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of these thioamides were identical to those of the major thioamides **9** and **11** formed by thio-Claisen rearrangement.



Scheme 5

This assignment of syn configuration to the major rearranged thioamides **9** and **11** was extended to the thioamides **10** and **12-21**. It was confirmed by careful examination of  $^{13}\text{C}$  NMR spectra of each diastereoisomer. Some empirical rules concerning the  $^{13}\text{C}$  NMR chemical shift values may be set up (see table 3). These rules are slightly different from those reported for esters and dithioesters analogues.<sup>8a,19</sup> Moreover the Anti minor configuration has been confirmed: the thioamide **10b Anti** has been cyclized into a trans- $\beta$ -lactone whose coupling constant  $J_{\text{H}\text{C}_2\text{H}\text{C}_3}$  is 4 Hz (a trans coupling constant). This result will be described in a next publication.

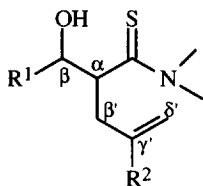
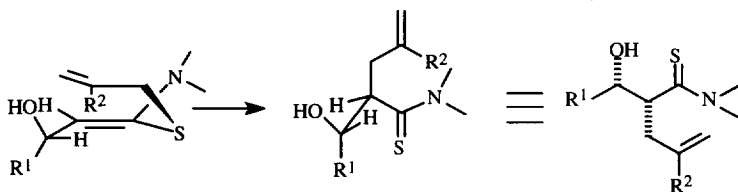


Table 3: Chemical shift rules

N°	Chemical Shift
1	$\delta(\text{C}\beta' \text{ syn}) < \delta(\text{C}\beta' \text{ anti})$
2	$\delta(\text{C}\gamma' \text{ syn}) > \delta(\text{C}\gamma' \text{ anti})$
3	$\delta(\text{C}\delta' \text{ syn}) < \delta(\text{C}\delta' \text{ anti})$
4	$\delta(\text{C}\beta \text{ syn}) < \delta(\text{C}\beta \text{ anti})$
5	$\delta(\text{C}\alpha \text{ syn}) < \delta(\text{C}\alpha \text{ anti})$

Formation of a major syn diastereoisomer may be interpreted, with the model we proposed in our previous studies of the same rearrangement of S-allylic ketene dithioacetals issued from  $\beta$ -hydroxydithioesters. In the pseudo cyclic transition state, the external stereogenic centre adopts a conformation similar to that of the Houk model<sup>20</sup> and confirmed by Kahn and Hehre<sup>21</sup>: H lies in inside position,  $R^1$  in outside position and the OH perpendicular to the ketene plan. The formation of C-C bond occurs on the more electronic rich face of the ketene (considered as the nucleophile) that is syn to the hydroxy group (see model below).



Scheme 6

From this model based on electronic effect, the formation of syn diastereoisomer is favoured. As the size of  $R^1$  group increases, the steric effect may amplify this trend (see entries 1-4 and 8-11 of the table). If  $R^1 = \text{PhCH}_2$  or  $\text{PhCH-Me}$ , the formation of the syn diastereoisomer is favoured because of a possible  $\pi$ -stacking interaction. The phenyl ring lies underneath the ketene plan and then prevents a bottom side C-C bond formation (see entries 6, 7, 13 and 14).

#### CONCLUSION :

Various S-allylic ketene aminothioacetals prepared as single Z-diastereoisomers from thioamides (**2-8a,b**) rearranged easily at room temperature, involving a sigmatropic-[3,3]-pathway, into a major syn  $\beta$ -hydroxy  $\delta$ -unsaturated thioamides (**9-21**). The external stereocontrol is governed by stereoelectronic effects with, in some instance, an additional steric effect and consequently an enhanced diastereoselectivity.

Some works are in progress to perform the same rearrangement starting from enantiopure  $\beta$ -hydroxythioamides easily available.<sup>16</sup> Transformation of the terminal double bond bearing a prostereogenic

centre into a terminal alcohol is now under way. In addition we have already obtained, as in scheme 3, a separable 80/20 mixture of the diastereoisomeric corresponding diols from thioamides **10a** and **10b**. The structure determination of the major diastereoisomer is under progress. Corresponding  $\delta$ -lactone has been then formed by action of methyl iodide and hydrolysis. These last results will be reported in a next publication.

## EXPERIMENTAL SECTION

### General

All reactions were run under a positive nitrogen pressure. THF was distilled over sodium benzophenone ketyl. The chromatography columns were prepared with a suspension of silica gel 60 Merck in the eluting solvent: a mixture of petroleum ether and ethyl acetate in the ratio indicated.  $^1\text{H}$  NMR 250 MHz and  $^{13}\text{C}$  NMR 62.5 MHz spectra were run on a BRUCKER AC 250. The products were dissolved in  $\text{CDCl}_3$  + TMS. Reported data are quoted in order: chemical shift in ppm, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant, number of H, assignment. IR absorption spectra were run on a PERKIN ELMER PC FT-IR instrument. Mass spectra were obtained at 70 eV with a NERMAG R10 RH spectrometer and the data tabulated as m/e and relative intensities. Elemental analyses were performed by "Service Central d'Analyse of CNRS" at Vernaion. The results are described as percentage.

### General Procedure for Aldol Reaction between N,N-dimethylthioacetamide and Aldehydes.

To a solution of N,N-dimethylthioacetamide (10 mmol) in THF (50 ml), under nitrogen was added dropwise at  $-78^\circ\text{C}$  a solution of n-butyllithium in THF (6.6 ml of a 1.6 M solution). After stirring for 1 h., the corresponding aldehyde (10.5 mmol) was added at  $-78^\circ\text{C}$ . Then the temperature was risen up at  $10^\circ\text{C}$  in 1.5 h. The mixture was then quenched with water and extracted with ether. The extract was washed with brine, dried over  $\text{MgSO}_4$ , filtrated and concentrated *in vacuo*. The products were purified by chromatography on silicagel.

#### N,N-dimethyl-3-hydroxybutanethioamide **2**

From the reaction between N,N-dimethylthioacetamide and ethanal. Purification by chromatography (petroleum ether / ethyl acetate: 40 / 60) gives a yellow powder in 83 % yield. m.p. =  $41^\circ\text{C}$ .

$\delta\text{H}$  1.28 (d, 6.4 Hz, 3 H,  $\text{CH}_3$ ), 2.52-2.75 (m, 2 H,  $\text{CH}_2\text{C}=\text{S}$ ), 3.32 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 4.3-4.4 (m, 1H,  $\text{CHOH}$ ), 4.42 (s, 1H,  $\text{OH}$ );  $\delta\text{C}$  22.3 ( $\text{CH}_3$ ), 41.7 and 44.4 ( $\text{NCH}_3$ ), 49.6 ( $\text{CH}_2\text{C}=\text{S}$ ), 65.6 ( $\text{CHOH}$ ), 201.5 ( $\text{C}=\text{S}$ ); IR (KBr) ( $\text{cm}^{-1}$ ): 3350 ( $\nu$  O-H), 2966, 2928, 2892 ( $\nu$  C-H), 1140 ( $\nu$  C-O), 1398 ( $\delta$  O-H); M/e % : **147** (100),  $\text{M}^+$ ; 132 (17), ( $\text{M}^+ - \text{CH}_3$ ) $^+$ ; 114 (71),  $\text{CH}=\text{CHC}=\text{SN}(\text{CH}_3)_2^+$ ; 103 (48),  $\text{CH}_3\text{CH}(\text{OH})\text{C}=\text{S}^+$ ; 88 (65),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 70 (95),  $\text{CH}=\text{CHC}=\text{S}$ ; 57 (46),  $\text{CH}_3\text{C}=\text{OCH}_2^+$ ; 45 (65),  $\text{CH}_3\text{CH}(\text{OH})^+$ ; 44 (71),  $\text{N}(\text{CH}_3)_2^+$ ; 43 (33),  $\text{CH}_3\text{C}=\text{O}^+$ ; 41 (25),  $\text{CH}_3\text{CH}=\text{CH}^+$ .

Anal.: Calcd. for  $\text{C}_6\text{H}_{13}\text{NOS}$ : C, 48.95; H, 8.90; N, 9.51; S, 21.77. Found: C, 48.92; H, 9.16; N, 9.21; S, 21.93.

#### N,N-dimethyl-3-hydroxypentanethioamide **3**

From the reaction between N,N-dimethylthioacetamide and propanal. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a yellow oil in 70 % yield.

$\delta\text{H}$  1.01 (t, 7.6 Hz, 3H,  $\text{CH}_3$ ), 1.44-1.72 (m, 2H,  $\text{CH}_3\text{-CH}_2$ ), 2.54-2.78 (m, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 3.32 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 4.06-4.16 (m, 1H,  $\text{CHOH}$ ), 4.25 (d, 2.74 Hz, 1H,  $\text{OH}$ );  $\delta\text{C}$  10.2 ( $\text{CH}_3$ ), 29.4 ( $\text{CH}_3\text{CH}_2$ ), 41.7 and 44.4 ( $\text{NCH}_3$ ), 48.0 ( $\text{CH}_2\text{C}=\text{S}$ ), 70.9 ( $\text{CHOH}$ ), 201.7 ( $\text{C}=\text{S}$ ); IR (NaCl) ( $\text{cm}^{-1}$ ): 3404 ( $\nu$  O-H), 2962, 2932, 2878 ( $\nu$  C-H), 1110 ( $\nu$  C-O), 1394 ( $\delta$  O-H); M/e % : **161** (100),  $\text{M}^+$ ; 103 (8),  $\text{CH}_3\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 72 (10),  $\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}_2^+$ ; 70 (29),  $\text{CH}=\text{CHC}=\text{S}^+$ ; 55 (16),  $\text{CH}=\text{CHCH}_2\text{CH}_3^+$ ; 44 (30),  $\text{N}(\text{CH}_3)_2^+$ .

Anal.: Calcd. for  $\text{C}_7\text{H}_{15}\text{NOS}$ : C, 52.14; H, 9.38; N, 8.69; S, 19.88. Found: C, 52.32; H, 9.51; N, 8.67; S, 19.99.

#### N,N-dimethyl-3-hydroxy-4-methyl-pentanethioamide **4**

From the reaction between N,N-dimethylthioacetamide and 2-methylpropanal. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a yellow oil in 81 % yield.

$\delta\text{H}$  0.98 (d, 6.71 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.00 (d, 6.71 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.79 (oct, 6.71 Hz, 1H,  $(\text{CH}_3)_2\text{CH}$ ), 2.58-2.81 (m, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 3.33 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 3.91-3.99 (m, 1H,  $\text{CHOH}$ ), 4.09 (d, 2.75 Hz, 1H,  $\text{OH}$ );  $\delta\text{C}$  18.0 and 18.7 ( $\text{CH}_3$ ), 33.4 ( $(\text{CH}_3)_2\text{CH}$ ), 41.8 and 44.6 ( $\text{NCH}_3$ ), 45.6 ( $\text{CH}_2\text{C}=\text{S}$ ), 74.3 ( $\text{CHOH}$ ), 202.2 ( $\text{C}=\text{S}$ ); IR (NaCl) ( $\text{cm}^{-1}$ ): 3408 ( $\nu$  O-H), 2958, 2934, 2874 ( $\nu$  C-H), 1116 ( $\nu$  C-O), 1394 ( $\delta$  O-H); M/e % : **175** (100),  $\text{M}^+$ ; 161 (6),  $(\text{CH}_3)_2\text{CH-CH}(\text{OH})\text{CH}_2\text{C}=\text{SNCH}_3^+$ ; 157 (16),  $(\text{CH}_3)_2\text{CHCH}=\text{CH}_2\text{C}=\text{SNCH}_3^+$ ; 70 (29),  $\text{CH}=\text{CHC}=\text{S}^+$ ; 44 (4),  $\text{N}(\text{CH}_3)_2^+$ ; 43 (5),  $(\text{CH}_3)_2\text{CH}^+$ .

Anal.: calcd. for  $\text{C}_8\text{H}_{17}\text{NOS}$ : C, 54.82; H, 9.78; N, 7.99; S, 18.29. Found: C, 54.62; H, 9.90; N, 7.56; S, 17.63.

**N,N-dimethyl-3-hydroxy-4,4-dimethyl-pentanethioamide 5**

From the reaction between N,N-dimethylthioacetamide and 2, 2-dimethylpropanal. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a pale yellow oil in 75 % yield.

$\delta_{\text{H}}$  0.97 (s, 9H,  $\text{CH}_3$ ), 2.58-2.68 and 2.84-2.9 (m, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 3.33 (s, 3H,  $\text{NCH}_3$ ), 3.52 (s, 3H,  $\text{NCH}_3$ ), 3.77-3.83 (m, 1H,  $\text{CHOH}$ ), 3.94 (d, 2.74 Hz, 1H,  $\text{OH}$ );  $\delta_{\text{C}}$  26 [ $(\text{CH}_3)_3\text{C}$ ], 34.7 [ $(\text{CH}_3)_3\text{C}$ ], 41.9 and 44.7 ( $\text{NCH}_3$ ), 43.8 ( $\text{CH}_2\text{C}=\text{S}$ ), 77.2 ( $\text{CHOH}$ ), 202.5 ( $\text{C}=\text{S}$ ); IR (NaCl) ( $\text{cm}^{-1}$ ): 3406 (v O-H), 2956, 2906, 2870 (v C-H), 1118 (v C-O), 1396 (8 O-H); M/e %: 189 (34),  $\text{M}^+$ ; 132 (22),  $\text{CH}(\text{OH})\text{CH}_2\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 88 (71),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 71 (49),  $\text{CH}_2=\text{CHC}=\text{S}^+$ ; 70 (92),  $\text{CH}=\text{CHC}=\text{S}^+$ ; 58 (56),  $\text{CH}_2\text{C}=\text{S}^+$ ; 57 (99),  $(\text{CH}_3)_3\text{C}^+$ ; 44 (84),  $\text{N}(\text{CH}_3)_2^+$ ; 41 (100),  $\text{CH}_3\text{C}=\text{CH}_2^+$ .

Anal.: calcd. for  $\text{C}_9\text{H}_{19}\text{NOS}$ : C, 57.10; H, 10.12; N, 7.40; S, 16.93. Found: C, 56.99; H, 10.18; N, 7.18; S, 16.87.

**N,N-dimethyl-3-hydroxy-3-phenylpropanethioamide 6**

From the reaction between N,N-dimethylthioacetamide and benzaldehyde. Purification by recrystallisation (ethyl ether / petroleum ether) gives white crystals in 85% yield. m.p. = 60°C.

$\delta_{\text{H}}$  2.92 (d, 6.1 Hz, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 3.22 (s, 3H,  $\text{NCH}_3$ ), 3.52 (s, 3H,  $\text{NCH}_3$ ), 4.78 (d, 3.1 Hz, 1H,  $\text{OH}$ ), 5.3 (dt, 6.1 Hz and 3.1 Hz, 1H,  $\text{CHOH}$ ), 7.26-7.44 (m, 5H,  $\text{H}$  arom.);  $\delta_{\text{C}}$  41.8 and 44.5 ( $\text{NCH}_3$ ), 50.7 ( $\text{CH}_2\text{C}=\text{S}$ ), 72.0 ( $\text{CHOH}$ ), 126.0, 127.7 and 128.6 (o., m., p. aromat.  $\text{C}$ ), 143.1 (quatern. aromat.  $\text{C}$ ), 200.7 ( $\text{C}=\text{S}$ ); IR (NaCl) ( $\text{cm}^{-1}$ ): 3286 (v O-H), 3026 (v C-H aromat.), 2932, 2868 (v C-H), 1528 (v  $\text{C}=\text{C}$  aromat.), 1116 (v C-O), 1396 (8 O-H); M/e %: 209 (10),  $\text{M}^+$ ; 105 (50),  $\text{C}_6\text{H}_5\text{C}=\text{O}^+$ ; 88 (59),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 77 (88),  $\text{C}_6\text{H}_5^+$ ; 70 (83),  $\text{CH}=\text{CHC}=\text{S}^+$ ; 44 (100),  $\text{N}(\text{CH}_3)_2^+$ .

Anal.: calcd. for  $\text{C}_{11}\text{H}_{15}\text{NOS}$ : C, 63.12; H, 7.22; N, 6.69; S, 15.32. Found: C, 63.36; H, 7.27; N, 6.86; S, 15.48.

**N,N-dimethyl-3-hydroxy-4-phenylbutanethioamide 7**

From the reaction between N,N-dimethylthioacetamide and phenylethanal. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a pale yellow oil in 70 % yield.

$\delta_{\text{H}}$  2.54-3.06 (m, 4H,  $\text{Ph-CH}_2$  and  $\text{CH}_2\text{C}=\text{S}$ ), 3.17 (s, 3H,  $\text{NCH}_3$ ), 3.46 (s, 3H,  $\text{NCH}_3$ ), 4.38 (d, 3.3 Hz, 1H,  $\text{OH}$ ), 4.4-4.47 (m, 1H,  $\text{CHOH}$ ), 7.19-7.33 (m, 5H,  $\text{H}$  arom.);  $\delta_{\text{C}}$  41.7 and 44.4 ( $\text{NCH}_3$ ), 42.8 ( $\text{Ph-CH}_2$ ), 47.3 ( $\text{CH}_2\text{C}=\text{S}$ ), 70.9 ( $\text{CHOH}$ ), 126.6, 128.6 and 129.5 (o., m., p. aromat.  $\text{C}$ ), 138.3 (quatern. aromat.  $\text{C}$ ), 201.3 ( $\text{C}=\text{S}$ ); IR (NaCl) ( $\text{cm}^{-1}$ ): 3386 (v O-H), 3060, 3026, 3000 (v C-H aromat.), 2932, (v C-H), 1602, 1522 (v  $\text{C}=\text{C}$  aromat.), 1120 (v C-O), 1394 (8 O-H); M/e %: 223 (8),  $\text{M}^+$ ; 205 (17),  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}=\text{CH}_2\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 187 (100); 157 (52,8); 103 (8,6),  $\text{C}_6\text{H}_5\text{CH}=\text{CH}^+$ ; 91 (5),  $\text{C}_6\text{H}_5\text{CH}_2^+$ ; 88 (5),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 45 (8).

Anal.: calcd. for  $\text{C}_{12}\text{H}_{17}\text{NOS}$ : C, 64.54; H, 7.67; N, 6.27; S, 14.36. Found: C, 63.25; H, 7.42; N, 6.81; S, 14.31.

**N,N-dimethyl-3-hydroxy-4-phenylpentanethioamide 8**

From the reaction between N,N-dimethylthioacetamide and 2-Phenyl-2-methylethanal. Separation by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a colorless oil in 90 % yield. Syn / Anti ratio 80 / 20.

**syn isomer 8a:**  $\delta_{\text{H}}$  1.42 (d, 6.9 Hz, 3H,  $\text{CH}_3$ ), 2.41-2.61 (m, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 2.78-2.89 (m, 1H,  $\text{CHCH}_3$ ), 3.00 (s, 3H,  $\text{NCH}_3$ ), 3.43 (s, 3H,  $\text{NCH}_3$ ), 4.14-4.2 (m, 1H,  $\text{CHOH}$ ), 4.53 (d, 3.1 Hz, 1H,  $\text{OH}$ ), 7.2-7.33 (m, 5H,  $\text{H}$  arom.);  $\delta_{\text{C}}$  18.5 ( $\text{CH}_3$ ), 41.5 and 44.4 ( $\text{NCH}_3$ ), 46 ( $\text{CHCH}_3$ ), 46.5 ( $\text{CH}_2\text{C}=\text{S}$ ), 74.3 ( $\text{CHOH}$ ), 126.6, 127.9 and 128.7 (o., m., p. aromat.  $\text{C}$ ), 144.5 (quatern. aromat.  $\text{C}$ ), 201.6 ( $\text{C}=\text{S}$ ).

**anti isomer 8b:**  $\delta_{\text{H}}$  1.38 (d, 7.2 Hz, 3H,  $\text{CH}_3$ ), 2.41-2.7 (m, 2H,  $\text{CH}_2\text{C}=\text{S}$ ), 2.78-2.89 (m, 1H,  $\text{CHCH}_3$ ), 3.11 (s, 3H,  $\text{NCH}_3$ ), 3.45 (s, 3H,  $\text{NCH}_3$ ), 3.99 (d, 2.2 Hz, 1H,  $\text{OH}$ ), 4.28-4.36 (m, 1H,  $\text{CHOH}$ ), 7.2-7.33 (m, 5H,  $\text{H}$  arom.);  $\delta_{\text{C}}$  16.6 ( $\text{CH}_3$ ), 41.7 and 44.6 ( $\text{NCH}_3$ ), 45 ( $\text{CHCH}_3$ ), 45.6 ( $\text{CH}_2\text{C}=\text{S}$ ), 74.1 ( $\text{CHOH}$ ), 126.7, 128.4 and 128.5 (o., m., p. aromat.  $\text{C}$ ), 143.3 (quatern. aromat.  $\text{C}$ ), 201.6 ( $\text{C}=\text{S}$ ).

IR (NaCl) ( $\text{cm}^{-1}$ ): 3338 (v O-H), 3082, 3056, 3026 (v C-H aromat.), 2964, 2930, 2094 (v C-H), 1600, 1494 (v  $\text{C}=\text{C}$  aromat.), 1126 (v C-O), 1394 (8 O-H); M/e %: 237 (11),  $\text{M}^+$ ; 219 (100),  $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{-CH}=\text{CH}_2\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 214 (67); 186 (47); 88 (4),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; 41 (5).

Anal.: calcd. for  $\text{C}_{13}\text{H}_{19}\text{NOS}$ : C, 65.78; H, 8.07; N, 5.9; S, 13.51. Found: C, 65.87; H, 8.19; N, 5.9; S, 13.68.

**General procedure for the Thio-Claisen rearrangement**

To a solution of LDA (2.1 eq.) in 20 ml of dry THF under nitrogen was added dropwise at  $-50^{\circ}\text{C}$  the corresponding  $\beta$ -hydroxythioamide (1 mmol). After stirring the solution between  $-40^{\circ}\text{C}$  and  $-60^{\circ}\text{C}$  for one hour, the corresponding allyl bromide (1.05 eq.) was added at  $-50^{\circ}\text{C}$ . And the temperature was risen up slowly at  $10^{\circ}\text{C}$ . The mixture was then quenched with water and extracted with ether. The extracts were washed with brine, dried over  $\text{MgSO}_4$  and left at room temperature for 12 to 24 h. After filtration and concentration in vacuo the products were purified by chromatography on silicagel.

**N,N-dimethyl-2-(1-hydroxyethyl)-4-pentenethioamide 9**

From the reaction between aldol **2** and allyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 40 / 60) gives a yellow oil in 55% yield. Syn / Anti ratio 80 / 20.

**syn isomer 9a:**  $\delta_{\text{H}}$  1.21 (d, 6.4 Hz, 3H,  $\text{CH}_3$ ), 2.49-2.77 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.02-3.09 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.32 (s, 3H,  $\text{NCH}_3$ ), 3.48 (s, 3H,  $\text{NCH}_3$ ), 3.93-4.03 (m, 1H,  $\text{CHOH}$ ), 4.35 (s, 1H, OH), 4.94-5.13 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.61-5.78 (m, 1H,  $\text{CH}=\text{CH}_2$ );  $\delta_{\text{C}}$  21.4 ( $\text{CH}_3$ ), 34.1 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.3 and 44.6 ( $\text{NCH}_3$ ), 53.4 ( $\text{CHC}=\text{S}$ ), 69.1 ( $\text{CHOH}$ ), 117.3 ( $\text{CH}=\text{CH}_2$ ), 136.0 ( $\text{CH}=\text{CH}_2$ ), 207.1 ( $\text{C}=\text{S}$ ).

**anti isomer 9b:**  $\delta_{\text{H}}$  1.17 (d, 6.11 Hz, 3H,  $\text{CH}_3$ ), 2.35-2.64 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3-3.08 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.29 (s, 3H,  $\text{NCH}_3$ ), 3.46 (s, 3H,  $\text{NCH}_3$ ), 3.89-4.04 (m, 1H,  $\text{CHOH}$ ), 3.92 (s, 1H, OH), 4.9-5.09 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.58-5.74 (m, 1H,  $\text{CH}=\text{CH}_2$ );  $\delta_{\text{C}}$  21.2 ( $\text{CH}_3$ ), 38.1 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.3 and 44.7 ( $\text{NCH}_3$ ), 54.6 ( $\text{CHC}=\text{S}$ ), 70.0 ( $\text{CHOH}$ ), 117.5 ( $\text{CH}=\text{CH}_2$ ), 135.2 ( $\text{CH}=\text{CH}_2$ ), 205.3 ( $\text{C}=\text{S}$ ).  
IR (NaCl) ( $\text{cm}^{-1}$ ): 3384 (v O-H), 3076 (v C-H ethylen.), 2972, 2930 (v C-H), 1640 (v C=C), 1124 (v C-O), 1394 ( $\delta$  O-H); M/e %: **187** (2),  $\text{M}^+$ ; 173 (11); 142 (17),  $\text{CH}_2=\text{CHCHC}=\text{SN}(\text{CH}_3)_2^+$ ; 97 (50),  $\text{CH}_2=\text{CHC}=\text{C}=\text{S}^+$ ; 88 (94),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; **45** (100),  $\text{CH}_3\text{CHOH}^+$ ; 44 (70),  $\text{N}(\text{CH}_3)_2^+$ ; 43 (87),  $\text{CH}_3\text{C}=\text{O}$ . Anal.: calcd. for  $\text{C}_9\text{H}_{17}\text{NOS}$ : C, 57.71; H, 9.15; N, 7.48; S, 17.12. Found: C, 56.49; H, 9.06; N, 7.29; S, 17.36.

**N,N-dimethyl-2-(1-hydroxypropyl)-4-pentenethioamide 10**

From the reaction between aldol **3** and allyl bromide. Separation by recrystallisation (ethyl ether / petroleum ether) gives a white solid in 70% yield. Syn / Anti ratio 85 / 15.

**syn isomer 10a:**  $\delta_{\text{H}}$  0.99 (t, 7.4 Hz, 3H,  $\text{CH}_3$ ), 1.41-1.68 (m, 2H,  $\text{CH}_2\text{CH}_2$ ), 2.47-2.57 and 2.7-2.8 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 2.95-3.19 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.34 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 3.66-3.71 (m, 1H,  $\text{CHOH}$ ), 4.42 (s, 1H, OH), 4.98 (dd, 10.1 Hz and 1.5 Hz, 1H,  $\text{CH}=\text{CH}_{\text{cis}}\text{H}$ ), 5.1 (dd, 17.1 Hz and 1.5 Hz, 1H,  $\text{CH}=\text{CH}_{\text{trans}}\text{H}$ ), 5.63-5.79 (m, 1H,  $\text{CH}=\text{CH}_2$ );  $\delta_{\text{C}}$  10.8 ( $\text{CH}_3$ ), 28 ( $\text{CH}_2\text{CH}_2$ ), 34.2 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.2 and 44.7 ( $\text{NCH}_3$ ), 51.8 ( $\text{CHC}=\text{S}$ ), 74.7 ( $\text{CHOH}$ ), 117.2 ( $\text{CH}=\text{CH}_2$ ), 136.1 ( $\text{CH}=\text{CH}_2$ ), 205.3 ( $\text{C}=\text{S}$ ).

**anti isomer 10b:**  $\delta_{\text{H}}$  1.00 (t, 7.3 Hz, 3H,  $\text{CH}_3$ ), 1.40-1.68 (m, 2H,  $\text{CH}_2\text{CH}_2$ ), 2.49-2.82 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.12-3.21 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.35 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 3.66-3.76 (m, 1H,  $\text{CHOH}$ ), 4.0 (d, 14.3 Hz, 1H, OH), 4.95-5.16 (m, 2H,  $\text{CH}=\text{CH}_2$ ), 5.63-5.81 (m, 1H,  $\text{CH}=\text{CH}_2$ );  $\delta_{\text{C}}$  10.7 ( $\text{CH}_3$ ), 28.2 ( $\text{CH}_2\text{CH}_2$ ), 38.2 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.1 and 44.5 ( $\text{NCH}_3$ ), 52.7 ( $\text{CHC}=\text{S}$ ), 75.0 ( $\text{CHOH}$ ), 117.5 ( $\text{CH}=\text{CH}_2$ ), 135.3 ( $\text{CH}=\text{CH}_2$ ), 206.1 ( $\text{C}=\text{S}$ ).  
IR (NaCl) ( $\text{cm}^{-1}$ ): 3384 (v O-H), 3076 (v C-H ethylen.), 2962, 2934, 2876 (v C-H), 1640 (v C=C), 1124 (v C-O), 1394 ( $\delta$  O-H); M/e %: **201** (3),  $\text{M}^+$ ; 186 (95), ( $\text{M}^+ - \text{CH}_3$ ) $^+$ ; 142 (32),  $\text{CH}_2=\text{CHCHC}=\text{SN}(\text{CH}_3)_2^+$ ; 97 (32),  $\text{CH}_2=\text{CHC}=\text{C}=\text{S}^+$ ; 88 (65),  $\text{C}=\text{SN}(\text{CH}_3)_2^+$ ; **44** (100),  $\text{N}(\text{CH}_3)_2^+$ . Anal.: calcd for  $\text{C}_{10}\text{H}_{19}\text{NOS}$ : C, 59.66; H, 9.51; N, 6.96; S, 15.92. Found: C, 59.67; H, 9.49; N, 7.18; S, 15.82.

**N,N-dimethyl-2-(1-hydroxy-2-methylpropyl)-4-pentenethioamide 11**

From the reaction between aldol **4** and allyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 61% yield. Syn / Anti ratio 93 / 7.

**syn isomer 11a:**  $\delta_{\text{H}}$  0.94 (d, 6.7 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.02 (d, 6.7 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.83 (oct, 6.7 Hz, 1H,  $(\text{CH}_3)_2\text{CH}$ ), 2.42-2.52 and 2.7-2.86 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.31-3.41 (m, 2H,  $\text{CHC}=\text{S}$  and  $\text{CHOH}$ ), 3.35 (s, 3H,  $\text{NCH}_3$ ), 3.52 (s, 3H,  $\text{NCH}_3$ ), 4.47 (d, 1.5 Hz, 1H, OH), 4.98 (dd, 10.1 Hz and 1.6 Hz, 1H,  $\text{CH}=\text{CH}_{\text{cis}}\text{H}$ ), 5.1 (dd, 17.1 Hz and 1.6 Hz, 1H,  $\text{CH}=\text{CH}_{\text{trans}}\text{H}$ ), 5.6-5.8 (m, 1H,  $\text{CH}=\text{CH}_2$ );  $\delta_{\text{C}}$  19.3 and 19.5 ( $\text{CH}_3\text{CH}$ ), 31.1 ( $\text{CH}_3\text{CH}$ ), 34.2 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.1 and 44.8 ( $\text{NCH}_3$ ), 49.2 ( $\text{CHC}=\text{S}$ ), 78.4 ( $\text{CHOH}$ ), 117.1 ( $\text{CH}=\text{CH}_2$ ), 136.2 ( $\text{CH}=\text{CH}_2$ ), 207.3 ( $\text{C}=\text{S}$ ).

**anti isomer 11b:**  $\delta_{\text{H}}$  0.91 (d, 6.7 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 0.99 (d, 6.7 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.91 (oct, 6.7 Hz, 1H,  $(\text{CH}_3)_2\text{CH}$ ), 2.46-2.68 (m, 2H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ), 3.2-3.4 and 3.46-3.55 (m, 2H,  $\text{CHC}=\text{S}$  and  $\text{CHOH}$ ), 3.37 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 4.05 (d, 8.2 Hz, 1H, OH), 4.98 (dd, 10.4 Hz and 1.5

Hz, 1H, CH=CH<sub>cis</sub>H), 5.13 (dd, 16.8 Hz and 1.5 Hz, 1H, CH=CH<sub>trans</sub>H), 5.66-5.82 (m, 1H, CH=CH<sub>2</sub>);  $\delta_C$  17.9 and 20.1 (CH<sub>3</sub>CH), 31.1 (CH<sub>3</sub>CH), 38.1 (CH<sub>2</sub>CH=CH<sub>2</sub>), 42.2 and 44.5 (NCH<sub>3</sub>), 50.1 (CHC=S), 79.0 (CHOH), 117.5 (CH=CH<sub>2</sub>), 135.3 (CH=CH<sub>2</sub>), 206 (C=S).

IR (NaCl) (cm<sup>-1</sup>): 3418 (ν O-H), 3076 (ν C-H ethylen.), 2960, 2872 (ν C-H), 1640 (ν C=C), 1148 (ν C-O), 1394 (δ O-H); M/e %: 215 (2), M<sup>+</sup>; 200 (34), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 172 (10), CH<sub>2</sub>=CHCH<sub>2</sub>CH[CH(OH)]-C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 143 (100), CH<sub>2</sub>=CHCH<sub>2</sub>CH<sub>2</sub>-C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 142 (77), CH<sub>2</sub>=CHCH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 128 (71), CH<sub>3</sub>CH=C-C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 88 (93), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 70 (83), CH=CHC=S<sup>+</sup>; 44 (35), N(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 43, CH<sub>3</sub>CHCH<sub>3</sub><sup>+</sup>; 41 (23), CH<sub>2</sub>=CCH<sub>3</sub><sup>+</sup>.

Anal.: calcd. for C<sub>11</sub>H<sub>21</sub>NOS: C, 61.35; H, 9.83; N, 6.50; S, 14.89. Found: C, 59.67; H, 9.87; N, 6.46; S, 14.68.

#### N,N-dimethyl-2-(1-hydroxy-2,2-dimethylpropyl)-4-pentenethioamide 12

From the reaction between aldol 5 and allyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 30% yield. Syn / Anti ratio > 98 / 2.

**syn isomer 12a:**  $\delta_H$  1.00 (s, 3H, (CH<sub>3</sub>)<sub>3</sub>C), 2.53-2.62 and 2.77-2.9 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.34 (s, 3H, NCH<sub>3</sub>), 3.4-3.47 (m, 2H, CHC=S and CHOH), 3.51 (s, 3H, NCH<sub>3</sub>), 4.31 (d, 1.8 Hz, 1H, OH), 4.96 (dd, 10.1 Hz and 1.3 Hz, 1H, CH=CH<sub>cis</sub>H), 5.08 (dd, 16.8 Hz and 1.3 Hz, 1H, CH=CH<sub>trans</sub>H), 5.58-5.75 (m, 1H, CH=CH<sub>2</sub>);  $\delta_C$  27.2 ((CH<sub>3</sub>)<sub>3</sub>C), 35.8 ((CH<sub>3</sub>)<sub>3</sub>C), 36.1 (CH<sub>2</sub>CH=CH<sub>2</sub>), 42.3 and 44.8 (NCH<sub>3</sub>), 48.3 (CHC=S), 80.4 (CHOH), 117 (CH=CH<sub>2</sub>), 136.2 (CH=CH<sub>2</sub>), 209.6 (C=S).

**anti isomer 12b:** not detected

IR (NaCl) (cm<sup>-1</sup>): 3380 (ν O-H), 3074 (ν C-H ethylen.), 2954, 2868 (ν C-H), 1638 (ν C=C), 1098 (ν C-O), 1396 (δ O-H); M/e %: 229 (7), M<sup>+</sup>; 214 (36), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 142 (54), CH<sub>2</sub>=CHCH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 88 (84), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 70 (100), CH=CHC=S<sup>+</sup>; 44 (41), N(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 43 (79), CH=CHOH<sup>+</sup>; 41 (45), CH<sub>2</sub>=CHCH<sub>2</sub><sup>+</sup>. Anal.: calcd. for C<sub>12</sub>H<sub>23</sub>NOS: C, 62.84; H, 10.11; N, 6.11; S, 13.98. Found: C, 62.38; H, 10.09; N, 5.85; S, 13.80.

#### N,N-dimethyl-2-(1-hydroxy-1-phenylmethyl)-4-pentenethioamide 13

From the reaction between aldol 6 and allyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a yellow oil in 40% yield. Syn / Anti ratio 80 / 20.

**syn isomer 13a:**  $\delta_H$  2.38-2.48 and 2.77-2.89 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 3.23 (s, 3H, NCH<sub>3</sub>), 3.3-3.39 (m, 1H, CHC=S), 3.45 (s, 3H, NCH<sub>3</sub>), 4.73 (d, 0.9 Hz, 1H, OH), 4.87-5.02 (m, 3H, CHOH and CH=CH<sub>cis</sub>H and CH=CH<sub>trans</sub>H), 5.46-5.62 (m, 1H, CH=CH<sub>2</sub>), 7.22-7.41 (m, 5H, H arom.);  $\delta_C$  33.7 (CH<sub>2</sub>CH=CH<sub>2</sub>), 42.2 and 44.7 (NCH<sub>3</sub>), 54.9 (CHC=S), 75.0 (CHOH), 117.4 (CH=CH<sub>2</sub>), 126.3, 127.6 and 128.4 (o., m., p. aromat. C), 135.6 (CH=CH<sub>2</sub>), 142.2 (quatern. aromat. C), 206 (C=S).

**anti isomer 13b:**  $\delta_H$  2.41-2.51 and 2.68-2.89 (m, 2H, CH<sub>2</sub>CH=CH<sub>2</sub>), 2.96 and 3.37 (s, 6H, NCH<sub>3</sub>), 3.42-3.49 (m, 1H, CHC=S), 4.75 (d, 7.3 Hz, 1H, CHOH), 4.95-5.12 (m, 3H, OH and CH=CH<sub>cis</sub>H and CH=CH<sub>trans</sub>H), 5.6-5.77 (m, 1H, CH=CH<sub>2</sub>), 7.25-7.35 (m, 5H, H arom.);  $\delta_C$  38.3 (CH<sub>2</sub>CH=CH<sub>2</sub>), 41.9 and 44, 6 (NCH<sub>3</sub>), 54.6 (CHC=S), 76.4 (CHOH), 117.6 (CH=CH<sub>2</sub>), 126.4, 127.8 and 128.4 (o., m., p. aromat. C), 135.1 (CH=CH<sub>2</sub>), 142.9 (quatern. aromat. C), 203.6 (C=S).

IR (NaCl) (cm<sup>-1</sup>): 3286 (ν O-H), 3062, 3028 (ν C-H ethylen. and aromat.), 2974 and 2934 (ν C-H), 1640 (ν C=C), 1602 and 1520 (ν C=C aromat.), 1096 (ν C-O), 1396 (δ O-H); M/e %: 249 (10), M<sup>+</sup>; 234 (7), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 207 (12), C<sub>6</sub>H<sub>5</sub>C=OCH<sub>2</sub>-C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 142 (33), CH<sub>2</sub>=CHCH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 88 (16), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 84 (84), CH<sub>2</sub>=CHCH<sub>2</sub>CHCHOH<sup>+</sup>; 77 (100), C<sub>6</sub>H<sub>5</sub><sup>+</sup>.

Anal.: calcd. for C<sub>14</sub>H<sub>19</sub>NOS: C, 67.43; H, 7.68; N, 5.62; S, 12.86. Found: C, 68.66; H, 8.00; N, 5.65; S, 13.08.

#### N,N-dimethyl-2-(1-hydroxy-2-phenylethyl)-4-pentenethioamide 14

From the reaction between aldol 7 and allyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 70 / 30) gives a yellow oil in 60% yield. Syn / Anti ratio 90 / 10.

**syn isomer 14a:**  $\delta_H$  2.48-3.16 (m, 5H, CH<sub>2</sub>CH=CH<sub>2</sub>, CHC=S and Ph-CH<sub>2</sub>), 2.89 (s, 3H, NCH<sub>3</sub>), 3.43 (s, 3H, NCH<sub>3</sub>), 3.94-3.97 (m, 1H, CHOH), 4.38 (d, 0.6 Hz, 1H, OH), 4.98 (dd, 9.9 Hz and 1.5 Hz, 1H, CH=CH<sub>cis</sub>H), 5.12 (dd, 17 Hz and 1.5 Hz, 1H, CH=CH<sub>trans</sub>H), 5.6-5.8 (m, 1H, CH=CH<sub>2</sub>), 7.14-7.34 (m, 5H, H arom.);  $\delta_C$  34.0 (CH<sub>2</sub>CH=CH<sub>2</sub>), 40.8 (Ph-CH<sub>2</sub>), 41.7 and 44, 6 (NCH<sub>3</sub>), 49.6 (CHC=S), 74.8 (CHOH), 117.3 (CH=CH<sub>2</sub>), 126.7, 128.7 and 129.5 (o., m., p. aromat. C), 135.8 (CH=CH<sub>2</sub>), 138.3 (quatern. aromat. C), 206.8 (C=S).



**anti isomer 14b:**  $\delta_{\text{H}}$  2.48-3.16 (m, 5H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ,  $\text{CHC}=\text{S}$  and  $\text{Ph-CH}_2$ ), 2.93 (s, 3H,  $\text{NCH}_3$ ), 3.49 (s, 3H,  $\text{NCH}_3$ ), 4.0-4.1 (m, 1H,  $\text{CHOH}$ ), 4.83 (d, 9Hz, 1H,  $\text{CHOH}$ ), 4.96-5.15 (m, 2H,  $\text{CH}=\text{CH}_{\text{cisH}}$  and  $\text{CH}=\text{CH}_{\text{transH}}$ ), 5.6-5.8 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 7.14-7.34 (m, 5H,  $\text{H}_{\text{aromat.}}$ );  $\delta_{\text{C}}$  37.9 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 42.1 ( $\text{Ph-CH}_2$ ), 41.7 and 44.3 ( $\text{NCH}_3$ ), 50.4 ( $\text{CHC}=\text{S}$ ), 74.3 ( $\text{CHOH}$ ), 117.8 ( $\text{CH}=\text{CH}_2$ ), 126.5, 128.6 and 129.2 (o., m., p.  $\text{aromat. C}$ ), 135.0 ( $\text{CH}=\text{CH}_2$ ), 138.6 (quatern.  $\text{aromat. C}$ ), 205.0 ( $\text{C}=\text{S}$ ).

IR (NaCl) ( $\text{cm}^{-1}$ ): 3370 ( $\nu$  O-H), 3074, 3026 ( $\nu$  C=C-H ethylen. and  $\text{aromat.}$ ), 2934 ( $\nu$  C-H), 1640 ( $\nu$  C=C), 1600 and 1518 ( $\nu$  C=C  $\text{aromat.}$ ), 1100 ( $\nu$  C-O), 1416 ( $\delta$  O-H); M/e %: 263 (17),  $\text{M}^+$ ; 248 (100), ( $\text{M}^+ - \text{CH}_3$ ) $^+$ ; 222 (15),  $\text{C}_6\text{H}_5\text{CH}_2\text{-CH(OH)CHC}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 204 (29),  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}=\text{CHC}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 173 (44),  $\text{C}_6\text{H}_5\text{CH}_2\text{C}=\text{OCHCH}_2\text{CH}=\text{CH}_2$  $^+$ ; 91 (16),  $\text{C}_6\text{H}_5\text{CH}_2$  $^+$ ; 88 (16),  $\text{C}=\text{SN}(\text{CH}_3)_2$  $^+$ .

Anal.: calcd. for  $\text{C}_{15}\text{H}_{21}\text{NOS}$ : C, 68.40; H, 8.04; N, 5.32; S, 12.17. Found: C, 66.47; H, 8.34; N, 5.22; S, 12.35.

#### N,N-dimethyl-2-(1-hydroxy-2-phenylpropyl)-4-pentenethioamide 15

From the reaction between aldol syn **8a** and allyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a yellow oil in 30% yield. Syn / Anti ratio >95 / 5.

**syn syn isomer 15a:**  $\delta_{\text{H}}$  1.41 (d, 7 Hz, 3H,  $\text{Ph-CHCH}_3$ ), 2.47-3.25 (m, 4H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ,  $\text{CHC}=\text{S}$  and  $\text{Ph-CHCH}_3$ ), 2.62 (s, 3H,  $\text{NCH}_3$ ), 3.39 (s, 3H,  $\text{NCH}_3$ ), 3.67 (m, 1H,  $\text{CHOH}$ ), 4.88-5.1 (m, 3H,  $\text{OH}$  and  $\text{CH}=\text{CH}_2$ ), 5.46-5.68 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 7.2-7.36 (m, 5H,  $\text{H}_{\text{aromat.}}$ );  $\delta_{\text{C}}$  18.9 ( $\text{CH}_3$ ), 33.5 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 41.4 and 44.6 ( $\text{NCH}_3$ ), 43.8 ( $\text{Ph-CH}$ ), 48.4 ( $\text{CHC}=\text{S}$ ), 77.8 ( $\text{CHOH}$ ), 117.1 ( $\text{CH}=\text{CH}_2$ ), 126.9, 127.9 and 128.9 (o., m., p.  $\text{aromat. C}$ ), 135.8 ( $\text{CH}=\text{CH}_2$ ), 144.6 (quatern.  $\text{aromat. C}$ ), 207.4 ( $\text{C}=\text{S}$ ).

**syn anti isomer 15b:** not detected

From the reaction between aldol anti **8b** and allyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 60 / 40) gives a yellow oil in 30% yield. Syn / Anti ratio >95 / 5.

**anti syn isomer 15c:**  $\delta_{\text{H}}$  1.33 (d, 7.3 Hz, 3H,  $\text{Ph-CHCH}_3$ ), 2.4-3.2 (m, 4H,  $\text{CH}_2\text{CH}=\text{CH}_2$ ,  $\text{CHC}=\text{S}$  and  $\text{Ph-CHCH}_3$ ), 2.9 (s, 3H,  $\text{NCH}_3$ ), 3.47 (s, 3H,  $\text{NCH}_3$ ), 4.01-4.05 (m, 1H,  $\text{CHOH}$ ), 4.88-5.1 (m, 3H,  $\text{OH}$  and  $\text{CH}=\text{CH}_2$ ), 5.55-5.78 (m, 1H,  $\text{CH}=\text{CH}_2$ ), 7.2-7.36 (m, 5H,  $\text{H}_{\text{aromat.}}$ );  $\delta_{\text{C}}$  19.2 ( $\text{CH}_3$ ), 36.4 ( $\text{CH}_2\text{CH}=\text{CH}_2$ ), 41.7 and 44.5 ( $\text{NCH}_3$ ), 42.5 ( $\text{Ph-CH}$ ), 50.7 ( $\text{CHC}=\text{S}$ ), 78.7 ( $\text{CHOH}$ ), 117.3 ( $\text{CH}=\text{CH}_2$ ), 126.5, 128.4 and 128.5 (o., m., p.  $\text{aromat. C}$ ), 135.7 ( $\text{CH}=\text{CH}_2$ ), 144.1 ( $\text{aromat. quatern. C}$ ), 206.0 ( $\text{C}=\text{S}$ ).

**anti anti isomer 15d:** not detected

IR (NaCl) ( $\text{cm}^{-1}$ ): 3336 ( $\nu$  O-H), 3080, 3026 ( $\nu$  C=C-H ethylen. and  $\text{aromat.}$ ), 2970, 2932, 2872 ( $\nu$  C-H), 1638 ( $\nu$  C=C), 1602 and 1494 ( $\nu$  C=C  $\text{aromat.}$ ), 1120 ( $\nu$  C-O), 1436 ( $\delta$  O-H); M/e %: 277 (17),  $\text{M}^+$ ; 269 (100), ( $\text{M}^+ - \text{CH}_3$ ) $^+$ ; 236 (19),  $\text{C}_6\text{H}_5\text{CH}-(\text{CH}_3)\text{CH(OH)CHC}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 214 (50), 200 (21),  $\text{CH}(\text{CH}_3)\text{CH(OH)-CH(C}=\text{SN}-(\text{CH}_3)_2\text{)CH}_2\text{CH}=\text{CH}_2$  $^+$ ; 186 (27); 143 (38),  $\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{-C}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 88 (18),  $\text{C}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 77 (3),  $\text{C}_6\text{H}_5$  $^+$ .

Anal.: calcd. for  $\text{C}_{16}\text{H}_{23}\text{NOS}$ : C, 69.27; H, 8.36; N, 5.05; S, 11.56. Found: C, 69.0; H, 8.45; N, 5.0; S, 11.43.

#### N,N-dimethyl-2-(1-hydroxyethyl)-4-methyl-4-pentenethioamide 16

From the reaction between aldol **2** and methylallyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 40 / 60) gives a yellow oil in 63% yield. Syn / Anti ratio 80 / 20.

**syn isomer 16a:**  $\delta_{\text{H}}$  1.24 (d, 6.4 Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.75 (s, 3H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ ), 2.47-2.78 (m, 2H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ ), 3.13-3.2 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.33 (s, 3H,  $\text{NCH}_3$ ), 3.5 (s, 3H,  $\text{NCH}_3$ ), 3.94-4.02 (m, 1H,  $\text{CHOH}$ ), 4.34 (s, 1H,  $\text{OH}$ ), 4.72-4.74 (m, 2H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ );  $\delta_{\text{C}}$  21.3 ( $\text{CH}_3\text{CHOH}$ ), 23.4 ( $\text{CH}_3\text{C}=\text{CH}$ ), 37.7 ( $\text{CH}_2\text{C}=\text{CH}_2$ ), 42.1 and 44.7 ( $\text{NCH}_3$ ), 52.2 ( $\text{CHC}=\text{S}$ ), 69.4 ( $\text{CHOH}$ ), 112.5 ( $\text{CH}=\text{CH}_2$ ), 143.6 ( $\text{CH}=\text{CH}_2$ ), 207.7 ( $\text{C}=\text{S}$ ).

**anti isomer 16b:**  $\delta_{\text{H}}$  1.25 (d, 6.2 Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.73 (s, 3H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ ), 2.4-2.78 (m, 2H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ ), 3.13-3.22 (m, 1H,  $\text{CHC}=\text{S}$ ), 3.36 (s, 3H,  $\text{NCH}_3$ ), 3.51 (s, 3H,  $\text{NCH}_3$ ), 4.0-4.11 (m, 1H,  $\text{CHOH}$ ), 4.34 (s, 1H,  $\text{OH}$ ), 4.74-4.76 (m, 2H,  $\text{CH}_2\text{C}(\text{CH}_3)=\text{CH}_2$ );  $\delta_{\text{C}}$  21.4 ( $\text{CH}_3\text{CHOH}$ ), 23.4 ( $\text{CH}_3\text{C}=\text{CH}$ ), 37.7 ( $\text{CH}_2\text{C}=\text{CH}_2$ ), 42.2 and 44.7 ( $\text{NCH}_3$ ), 53.1 ( $\text{CHC}=\text{S}$ ), 70.1 ( $\text{CHOH}$ ), 112.9 ( $\text{CH}=\text{CH}_2$ ), 142.7 ( $\text{CH}=\text{CH}_2$ ), 205.4 ( $\text{C}=\text{S}$ ).

IR (NaCl) ( $\text{cm}^{-1}$ ): 3404 ( $\nu$  O-H), 3074 ( $\nu$  C=C-H ethylen.), 2968, 2932 ( $\nu$  C-H), 1648 ( $\nu$  C=C), 1126 ( $\nu$  C-O), 1374 ( $\delta$  O-H); M/e %: 201 (31),  $\text{M}^+$ ; 186 (100), ( $\text{M}^+ - \text{CH}_3$ ) $^+$ ; 156 (10),  $\text{CH}_2=\text{CH}(\text{CH}_3)\text{CH}_2\text{-CHC}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 88 (10),  $\text{C}=\text{SN}(\text{CH}_3)_2$  $^+$ ; 45 (7),  $\text{N}(\text{CH}_3)_2$  $^+$ .

Anal.: calcd. for  $C_{10}H_{19}NOS$ : C, 59.66; H, 9.51; N, 6.96; S, 15.92. Found: C, 59.72; H, 9.41; N, 6.83; S, 15.88.

**N,N-dimethyl-2-(1-hydroxypropyl)-4-methyl-4-pentenethioamide 17**

From the reaction between aldol 3 and methallyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 60% yield. Syn / Anti ratio 85 / 15.

**syn isomer 17a:**  $\delta_H$  1.00 (t, 7.3 Hz, 3H,  $CH_3CH_2$ ), 1.39-1.74 (m, 2H,  $CH_3CH_2$ ), 1.74 (s, 3H,  $CH_3C=CH$ ), 2.43-2.49 and 2.73-2.83 (m, 2H,  $CH_2C=CH_2$ ), 3.23-3.29 (m, 1H,  $CHC=S$ ), 3.33 (s, 3H,  $NCH_3$ ), 3.5 (s, 3H,  $NCH_3$ ), 3.61-3.68 (m, 1H,  $CHOH$ ), 4.4 (s, 1H, OH), 4.71-4.73 (m, 2H,  $C=CH_2$ );  $\delta_C$  10.7 ( $CH_3CH_2$ ), 23.4 ( $CH_3C=CH$ ), 27.9 ( $CH_3CH_2$ ), 37.7 ( $CH_2C=CH_2$ ), 42.0 and 44.8 ( $NCH_3$ ), 50.4 ( $CHC=S$ ), 74.9 ( $CHOH$ ), 112.4 ( $CH=CH_2$ ), 143.6 ( $CH=CH_2$ ), 207.9 ( $C=S$ ).

**anti isomer 17b:**  $\delta_H$  1.00 (t, 7.3 Hz, 3H,  $CH_3CH_2$ ), 1.39-1.74 (m, 2H,  $CH_3CH_2$ ), 1.75 (s, 3H,  $CH_3C=CH$ ), 2.45-2.65 (m, 2H,  $CH_2C=CH_2$ ), 3.23-3.29 (m, 1H,  $CHC=S$ ), 3.35 (s, 3H,  $NCH_3$ ), 3.5 (s, 3H,  $NCH_3$ ), 3.61-3.68 (m, 1H,  $CHOH$ ), 4.2 (s, 1H, OH), 4.78 (s, 2H,  $C=CH_2$ );  $\delta_C$  10.7 ( $CH_3CH_2$ ), 23.3 ( $CH_3C=CH$ ), 28.4 ( $CH_3CH_2$ ), 37.7 ( $CH_2C=CH_2$ ), 41.7 and 44.6 ( $NCH_3$ ), 51.2 ( $CHC=S$ ), 75.4 ( $CHOH$ ), 113.0 ( $CH=CH_2$ ), 143.6 ( $CH=CH_2$ ), 206.2 ( $C=S$ ).

IR (NaCl) ( $cm^{-1}$ ): 3398 ( $\nu$  O-H), 3074 ( $\nu$  C=C-H ethylen.), 2964, 2934, 2876 ( $\nu$  C-H), 1646 ( $\nu$  C=C), 1108 ( $\nu$  C-O), 1374 ( $\delta$  O-H); M/e %: 215 (11),  $M^+$ ; 200 (100), ( $M^+ - CH_3$ ) $^+$ ; 186 (9),  $CH(OH)CH(C=SN(CH_3)_2)CH_2CH(CH_3)=CH_2^+$ ; 156 (8),  $CH_2=CH-(CH_3)CH_2CHC=SN(CH_3)_2^+$ ; 88 (9),  $C=SN(CH_3)_2^+$ ; 41 (6),  $CH=CHCH_3^+$ .

Anal.: calcd. for  $C_{11}H_{21}NOS$ : C, 61.35; H, 9.83; N, 6.50; S, 14.89. Found: C, 61.08; H, 9.96; N, 6.49; S, 14.75.

**N,N-dimethyl-2-(1-hydroxy-2-methylpropyl)-4-methyl-4-pentenethioamide 18**

From the reaction between aldol 4 and methallyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 75 % yield. Syn / Anti ratio 85 / 15.

**syn isomer 18a:**  $\delta_H$  0.95 (d, 6.4 Hz, 3H,  $(CH_3)_2CH$ ), 1.04 (d, 6.4 Hz, 3H,  $(CH_3)_2CH$ ), 1.73 (s, 3H,  $CH_3C=CH$ ), 1.73-1.92 (m, 1H,  $(CH_3)_2CH$ ), 2.23-2.42 and 2.8-3.05 (m, 2H,  $CH_2C=CH_2$ ), 3.26-3.31 (m, 1H,  $CHOH$ ), 3.34 (s, 3H,  $NCH_3$ ), 3.51 (s, 3H,  $NCH_3$ ), 3.45-3.52 (m, 1H,  $CHC=S$ ), 4.53 (s, 1H, OH), 4.69 and 4.72 (s, 2H,  $C=CH_2$ );  $\delta_C$  19.4 and 19.5 ( $(CH_3)_2CH$ ), 23.6 ( $CH_3C=CH$ ), 31.2 ( $(CH_3)_2CH$ ), 37.5 ( $CH_2C=CH_2$ ), 41.8 and 44.9 ( $NCH_3$ ), 47.9 ( $CHC=S$ ), 78.5 ( $CHOH$ ), 112.2 ( $CH=CH_2$ ), 143.7 ( $CH=CH_2$ ), 208.0 ( $C=S$ ).

**anti isomer 18b:**  $\delta_H$  0.92 (d, 6.7 Hz, 3H,  $(CH_3)_2CH$ ), 1.0 (d, 6.4 Hz, 3H,  $(CH_3)_2CH$ ), 1.75 (s, 3H,  $CH_3C=CH$ ), 1.85-2.0 (m, 1H,  $(CH_3)_2CH$ ), 2.45-2.62 (m, 2H,  $CH_2C=CH_2$ ), 3.36-3.52 (m, 2H,  $CHC=S$  and  $CHOH$ ), 3.37 (s, 3H,  $NCH_3$ ), 3.49 (s, 3H,  $NCH_3$ ), 4.17 (s, 1H, OH), 4.8 (s, 2H,  $C=CH_2$ );  $\delta_C$  18.1 and 20.2 ( $(CH_3)_2CH$ ), 23.3 ( $CH_3C=CH$ ), 31.2 ( $(CH_3)_2CH$ ), 41.5 ( $CH_2C=CH_2$ ), 42.0 and 44.6 ( $NCH_3$ ), 48.5 ( $CHC=S$ ), 79.0 ( $CHOH$ ), 113.2 ( $CH=CH_2$ ), 142.4 ( $CH=CH_2$ ), 206.60 ( $C=S$ ).

IR (NaCl) ( $cm^{-1}$ ): 3356 ( $\nu$  O-H), 3074 ( $\nu$  C=C-H ethylen.), 2960, 2932, 2872 ( $\nu$  C-H), 1646 ( $\nu$  C=C), 1112 ( $\nu$  C-O), 1394 ( $\delta$  O-H); M/e %: 229 (6),  $M^+$ ; 214 (100), ( $M^+ - CH_3$ ) $^+$ ; 186 (43),  $CH(OH)CH(C=SN(CH_3)_2)CH_2CH(CH_3)=CH_2^+$ ; 156 (15),  $CH_2=CH(CH_3)CH_2CHC=SN(CH_3)_2^+$ ; 88 (6),  $C=SN(CH_3)_2^+$ ; 41 (11),  $CH=CH-CH_3^+$ .

Anal.: calcd for  $C_{12}H_{23}NOS$ : C, 62.84; H, 10.11; N, 6.11; S, 13.98. Found: C, 62.58; H, 10.14; N, 6.12; S, 13.90.

**N,N-dimethyl-2-(1-hydroxy-2,2-dimethylpropyl)-4-methyl-4-pentenethioamide 19**

From the reaction between aldol 5 and methallyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 55% yield. Syn / Anti ratio > 98 / 2.

**syn isomer 19a:**  $\delta_H$  1.02 (s,  $(CH_3)_3C$ ), 1.74 (s, 3H,  $CH_3C=CH$ ), 2.49-2.59 and 2.8-2.91 (m, 2H,  $CH_2C=CH_2$ ), 3.36-3.39, (m, 1H,  $CHOH$ ), 3.32 (s, 3H,  $NCH_3$ ), 3.49 (s, 3H,  $NCH_3$ ), 3.5-3.56 (m, 1H,  $CHC=S$ ), 4.25-4.33 (m, 1H, OH), 4.66-4.72 (m, 2H,  $C=CH_2$ );  $\delta_C$  23.5 ( $CH_3C=CH$ ), 27.2 ( $(CH_3)_3C$ ), 35.9 ( $(CH_3)_3C$ ), 39.4 ( $CH_2C=CH_2$ ), 42.1 and 44.8 ( $NCH_3$ ), 47.1 ( $CHC=S$ ), 80.7 ( $CHOH$ ), 112.4 ( $CH=CH_2$ ), 143.7 ( $CH=CH_2$ ), 210.3 ( $C=S$ ).

**anti isomer 19b:** not detected

IR (NaCl) ( $cm^{-1}$ ): 3382 ( $\nu$  O-H), 3074 ( $\nu$  C=C-H ethylen.), 2968, 2954 ( $\nu$  C-H), 1646 ( $\nu$  C=C), 1118 ( $\nu$  C-O), 1394 ( $\delta$  O-H).

M/e %: 243 (7), M<sup>+</sup>; 228 (100), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 186 (31), CH(OH)CH(C=SN(CH<sub>3</sub>)<sub>2</sub>)-CH<sub>2</sub>CH(CH<sub>3</sub>)=CH<sub>2</sub><sup>+</sup>; 156 (60), CH<sub>2</sub>=CH(CH<sub>3</sub>)CH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 114 (52), CH<sub>2</sub>=CC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; **88** (100), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 70 (93), CH=CHC=S<sup>+</sup>; 43 (79), CH=CHOH<sup>+</sup>; 41 (36), CH<sub>2</sub>=CCH<sub>3</sub><sup>+</sup>.  
 Anal.: calcd. for C<sub>13</sub>H<sub>25</sub>NOS: C, 64.15; H, 10.35; N, 5.75; S, 13.17. Found: C, 63.95; H, 10.3; N, 5.8; S, 13.05.

#### N,N-dimethyl-2-(1-hydroxy-2-phenylethyl)-4-methyl-4-pentenethioamide **20**

From the reaction between aldol **7** and methallyl bromide. Separation by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow solid in 55% yield. Syn / Anti ratio: 95 / 5.

**syn isomer 20a**: δ<sub>H</sub> 1.71 (s, 3H, CH<sub>3</sub>C=CH), 2.7-3.25 (m, 5H, CH<sub>2</sub>C=CH<sub>2</sub>, Ph-CH<sub>2</sub> and CHC=S), 2.81 (s, 3H, NCH<sub>3</sub>), 3.41 (s, 3H, NCH<sub>3</sub>), 3.9-3.98 (m, 1H, CHOH), 4.47 (d, 1.22 Hz 1H, OH), 4.68-4.71 (m, 2H, C=CH<sub>2</sub>), 7.2-7.37 (m, 5H, H aromat); δ<sub>C</sub> 23.5 (CH<sub>3</sub>C=CH), 37.2 (CH<sub>2</sub>CH=CH<sub>2</sub>), 40.6 (Ph-CH<sub>2</sub>), 41.4 and 44.7 (NCH<sub>3</sub>), 48.0 (CHC=S), 75.0 (CHOH), 112.5 (CH=CH<sub>2</sub>), 126.7, 128.7 and 129.6 (o., m., p. aromat. C), 138.2 (quatern. aromat. C), 143.3 (CH=CH<sub>2</sub>), 207.4 (C=S).

**anti isomer 20b**: δ<sub>H</sub> 1.66 (s, 3H, CH<sub>3</sub>C=CH), 2.4-3.5 (m, 5H, CH<sub>2</sub>C=CH<sub>2</sub>, Ph-CH<sub>2</sub> and CHC=S), 2.90 (s, 3H, NCH<sub>3</sub>), 3.46 (s, 3H, NCH<sub>3</sub>), 4.01-4.2 (m, 1H, CHOH), 4.78 (s, 1H, OH), 4.93-4.97 (m, 2H, C=CH<sub>2</sub>), 7.2-7.37 (m, 5H, H aromat.); δ<sub>C</sub> 23.0 (CH<sub>3</sub>C=CH), 37.2 (CH<sub>2</sub>CH=CH<sub>2</sub>), 41.2 (Ph-CH<sub>2</sub>), 41.8 and 44.3 (NCH<sub>3</sub>), 48.5 (CHC=S), 73.9 (CHOH), 113.4 (CH=CH<sub>2</sub>), 126.4, 128.6 and 129.2 (o., m., p. aromat. C), 138.8 (quatern. aromat. C), 142.1 (CH=CH<sub>2</sub>), 205.6 (C=S).

IR (NaCl) (cm<sup>-1</sup>): 3368 (ν O-H), 3068, 3024 (ν C=C-H ethylen. and aromat.), 2964, 2928 (ν C-H), 1644 (ν C=C ethylen.), 1602, 1494 (ν C=C aromat.), 1114 (ν C-O), 1394 (δ O-H); M/e %: **277** (3), M<sup>+</sup>; 262 (19), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 186 (M<sup>+</sup> - C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>)<sup>+</sup>; 157 (73), CH<sub>2</sub>=CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 156 (60), CH<sub>2</sub>=CH(CH<sub>3</sub>)-CH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 91 (77), C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub><sup>+</sup>; 88 (98), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 77 (25), C<sub>6</sub>H<sub>5</sub><sup>+</sup>; **70** (100), CH=CHC=S<sup>+</sup>.

Anal.: calcd. for C<sub>17</sub>H<sub>25</sub>NOS: C, 69.27; H, 8.36; N, 4.05; S, 11.56. Found: C, 68.61; H, 8.12; N, 4.87; S, 13.00.

#### N,N-dimethyl-2-(1-hydroxy-2-phenylpropyl)-4-methyl-4-pentenethioamide **21**

From the reaction between aldol **8a** and methallyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 45% yield. Syn-Syn / Syn-Anti ratio > 95/5.

**syn syn isomer 21a**: δ<sub>H</sub> 1.41 (d, 6.7 Hz, 3H, PhCH(CH<sub>3</sub>)), 1.58 (s, 3H, CH<sub>3</sub>C=CH), 2.36-2.45 (m, 1H, Ph-CH(CH<sub>3</sub>)), 2.58 (s, 3H, NCH<sub>3</sub>), 2.78-2.97 (m, 2H, CH<sub>2</sub>C=CH<sub>2</sub>), 3.02-3.10 (m, 1H, CHC=S), 3.37 (s, 3H, NCH<sub>3</sub>), 3.64-3.70 (m, 1H, CHOH), 4.57-4.62 (m, 2H, C=CH<sub>2</sub>), 4.93 (d, 0.7 Hz 1H, OH), 7.18-7.38 (m, 5H, H aromat.); δ<sub>C</sub> 19.1 (PhCH(CH<sub>3</sub>)), 23.4 (CH<sub>3</sub>C=CH), 37.0 (CH<sub>2</sub>CH=CH<sub>2</sub>), 44.0 (Ph-CH(CH<sub>3</sub>)), 41.2 and 44.6 (NCH<sub>3</sub>), 47.3 (CHC=S), 78.0 (CHOH), 112.4 (CH=CH<sub>2</sub>), 126.9, 128.0 and 128.9 (o., m., p. aromat. C), 144.6 (quatern. aromat. C), 143.2 (CH=CH<sub>2</sub>), 208.0 (C=S).

**syn anti isomer 21b**: not detected.

From the reaction between aldol **8b** and methallyl bromide. Purification by chromatography (petroleum ether / ethyl acetate: 80 / 20) gives a yellow oil in 45% yield. Syn / Anti ratio > 95/5.

**Anti-syn isomer 21c**: δ<sub>C</sub> 19.1 (PhCH(CH<sub>3</sub>)), 23.4 (CH<sub>3</sub>C=CH), 39.6 (CH<sub>2</sub>CH=CH<sub>2</sub>), 42.8 (Ph-CH(CH<sub>3</sub>)), 41.5 and 44.2 (NCH<sub>3</sub>), 49.3 (CHC=S), 78.5 (CHOH), 112.7 (CH=CH<sub>2</sub>), 126.5, 127.5 and 128.5 (o., m., p. aromat. C), 144.4 (quatern. aromat. C), 143.4 (CH=CH<sub>2</sub>), 206.7 (C=S).

**Anti-anti isomer 21d**: not detected

IR (NaCl) (cm<sup>-1</sup>): 3362 (ν O-H), 3072, 3028 (ν C=C-H ethylen. and aromat.), 2964, 2930 and 2872 (ν C-H), 1644 (ν C=C ethylen.), 1602, 1514 (ν C=C aromat.), 1098 (ν C-O), 1394 (δ O-H); M/e %: **291** (9), M<sup>+</sup>; 276 (43), (M<sup>+</sup> - CH<sub>3</sub>)<sup>+</sup>; 236 (5), C<sub>6</sub>H<sub>5</sub>CH-CH<sub>3</sub>CH(OH)CH<sub>2</sub>C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 218 (25), C<sub>6</sub>H<sub>5</sub>CH(CH<sub>3</sub>)-CH=CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 186 (60), (M<sup>+</sup> - C<sub>6</sub>H<sub>5</sub>CH(CH<sub>3</sub>))<sup>+</sup>; 157 (60), CH<sub>2</sub>=CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>-C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 156 (60), CH<sub>2</sub>=CH(CH<sub>3</sub>)CH<sub>2</sub>CHC=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; **105** (100), C<sub>6</sub>H<sub>5</sub>CH(CH<sub>3</sub>)<sup>+</sup>; 88 (22), C=SN(CH<sub>3</sub>)<sub>2</sub><sup>+</sup>; 77 (26), C<sub>6</sub>H<sub>5</sub><sup>+</sup>; 55 (11), CH<sub>2</sub>=CH(CH<sub>3</sub>)CH<sub>2</sub><sup>+</sup>.

Anal.: calcd. for C<sub>18</sub>H<sub>27</sub>NOS: C, 70.77; H, 8.91; N, 4.59; S, 10.49. Found: C, 70.38; H, 8.64; N, 4.64; S, 10.85.

#### Synthesis of thioamides from dithioesters.

In a solution of dithioester (1 mmol) in THF, N,N-dimethylamine gas in excess was bubbled for 10 minutes at room temperature. The mixture is then washed with brine and extracted with ether and dried over MgSO<sub>4</sub>. After filtration and concentration *in vacuo*, the products were purified by chromatography on silicagel.

**N,N-dimethyl-2-(1-hydroxyethyl)-4-methyl-4-pentenethioamide 16**

From the reaction between methyl-(1-hydroxyethyl)-4-methyl-4-pentenedithioate **8a**, in ratio Syn / Anti 8/2 and dimethyl amine gaz. Purification by chromatography (petroleum ether/ethyl acetate) gives **16a** and **16b** in 80 % yield. Syn / Anti ratio 8/2.

**N,N-dimethyl-2-(1-hydroxy-2-methylpropyl)-4-methyl-4-pentenethio-amide 18**

From the reaction between Methyl-(1-hydroxy-2-methylpropyl)-4-methyl-4-pentenedithioate **8a** (Syn / Anti 100 / 0) and dimethyl amine. Purification by chromatography (petroleum ether / ethyl acetate) gives **18a** in 90 % yield. (Syn / Anti 100 / 0).

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