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Enantioselective Synthesis of α-Sulfenylated Ketones and Aldehydes via α-Thiolation of Metalated SAMP/RAMP Hydrazones

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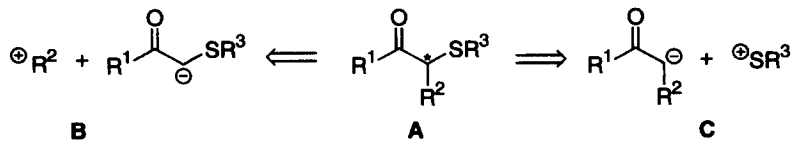
Abstract: Asymmetric α-sulfenylation of lithiated SAMP/RAMP hydrazones (*S*)-**2** with disulfides afforded α-thiolated hydrazones (*S,R*)-**3** in good yields (48-87%) and high diastereomeric excesses (91-96%). Subsequent oxidative cleavage or acidic hydrolysis of the hydrazones furnished α-thiolated ketones (*R*)-**4a-d** with high enantiomeric excesses (87->96%). α-Sulfenylated aldehydes (*R*)-**8a-d** were prepared by a similar reaction sequence with 45-93% *ee*.

INTRODUCTION

α-Sulfenylated carbonyl compounds (**A**) are important key building blocks in organic chemistry.[1,2] They have been used as precursors for a large number of target molecules as for instance vicinal thioether alcohols.[3] Synthetic methods for the preparation of *a*-thiolated optically active carboxylic acids derivatives have been established.[4] However, despite the significance of the corresponding ketone and aldehyde compounds only a few methods for the preparation of enanantiomerically enriched α-sulfenylated ketones and/or aldehydes have been reported.[5,6] A variety of these synthetic approaches are based on a stereoselective bond formation in α-position to the carbonyl functionality. We have recently reported on an enantioselective synthesis of α-thiolated aldehydes via alkylation of sulfenylated acetaldehyde SAMP hydrazones (**B**), opening an efficient and convenient access to α-sulfenylated aldehydes of high enantiomeric purity.[7,8] The recent publication of Warren et al.[9] on the synthesis of optically active 2-phenylthio aldehydes by sulfenylation of phenylalanine-derived oxazolidinone imides prompted us to disclose the results of our group on the asymmetric α-thiolation of SAMP/RAMP hydrazones by thiolation of metalated SAMP/RAMP hydrazones with disulfides (**C**) as an efficient and flexible alternative.[10]



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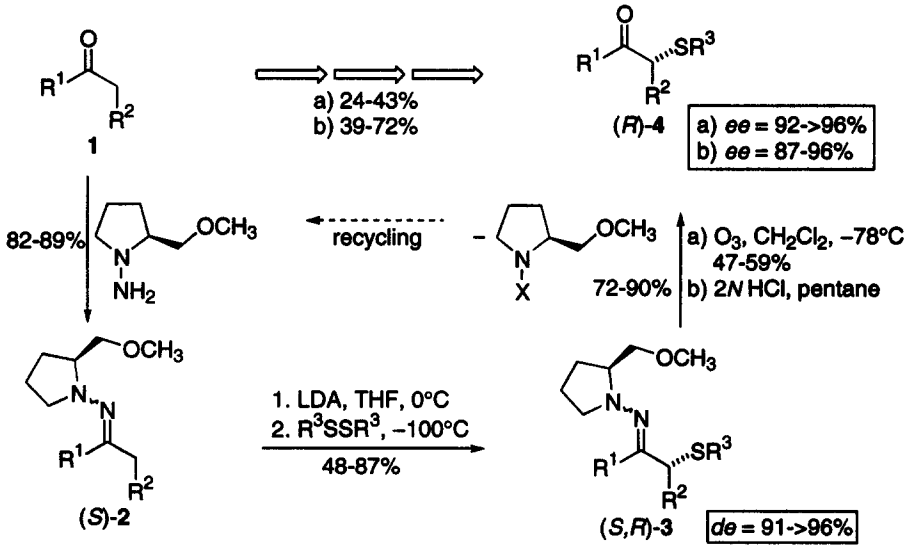
RESULTS AND DISCUSSION

As is shown in Scheme 1, a variety of commercially available ketones **1** were transformed to the corresponding SAMP/RAMP hydrazones (*S*)/(*R*)-**2** in good yields (82-89%), following standard literature procedures.[11,12] Then, the hydrazones **2** were metalated with lithium diisopropylamide in tetrahydrofuran at 0°C. After complete formation of the aza enolates, the sulfenylation reactions were carried out by addition of the corresponding disulfides to the tetrahydrofuran solutions of the enolates at –100°C, and the reaction mixtures were allowed to warm to room temperature overnight. Standard aqueous work-up and purification by column chromatography furnished the α-thiolated hydrazones **3** as yellow oils in good yields and very high diastereomeric excesses (Table 1).



Scheme 1. Enantioselective Synthesis of α-Thiolated Ketones

Spectra and chromatograms showed a mixture of *E*/*Z* isomers. The pure *E*-isomer of **3c** was obtained by „Kugelrohr" distillation of the hydrazone. However, the determination of the diastereomeric excess turned out to be difficult. In the case of **3c** and (*S*,*R*)-**3d**, we were able to determine the diastereomeric excesses by ^{13}C NMR spectroscopic analysis. The de-values of the further examples were finally deduced from the enantiomeric excess of the corresponding α-thiolated carbonyl compounds **4**. Hydrazone **3c** was originally formed in 70% diastereomeric excess, however, we were able to enrich the main isomer by crystallization.

As is evident from the data in Table 1, slightly higher diastereoselectivities were observed when employing the sterically more demanding diisopropyldisulfide (*de* = >96%) instead of dimethyldisulfide (*de* = 91->96%) in the sulfenylation reactions. On the basis of many previous results of electrophilic substitutions via SAMP/RAMP hydrazones, we assumed that the reaction had taken place following the established mechanism of electrophilic substitutions via SAMP hydrazones, forming the new stereogenic center with (*R*) configuration. Fortunately, we obtained crystals of compound **3c** for a X-ray structure analysis, and we unambiguously deter-

mined the configuration to (*S,R*) in complete agreement with the model for the diastereofacial approach of electrophiles to lithiated SAMP hydrazones. The structural details of this X-ray analysis have already been reported in a separate publication.[13]

Table 1. Diastereoselective Synthesis of α-Sulfenylated Hydrazones **3**

3	R^1	R^2	R^3	yield[a] [%]	α_D^{25} neat or (*c*, C_6H_6)	*de*[a] [%]	Config.
a	Et	Me	Me	87	+162.2	91	*S,R*
b	Et	Me	*i*Pr	86	+159.9	>96	*S,R*
c	Ph	Me	Me	84 (52)	+737.9 (0.8)	70 (>96)[b]	*S,R*
c[c]	Ph	Me	Me	87 (48)	–733.1 (0.26)	70 (92)[b]	*R,S*
d	Ph	Me	*i*Pr	82	+724.0	>96	*S,R*
d[c]	Ph	Me	*i*Pr	87	–718.5	>96	*R,S*

[a] Yields are based on **1**. - Values in brackets refer to yields and *de*'s after crystallization. - [b] Confirmed by ^{13}C NMR spectroscopy. - [c] RAMP was used instead of SAMP as auxiliary.

Cleavage of the hydrazones **3** was readily achieved by ozonolysis at –78°C in dichloromethane, leading to *a*-sulfenylated ketones **4** in 47-59% yield and 91-96% *ee*. Enantiomeric excesses of the slightly yellow oils were determined by ^1H NMR shift experiments employing Eu(hfc)$_3$ (Table 2).

Table 2. Ketones **4** Obtained by Oxidative Cleavage or Acidic Hydrolysis

4	R^1	R^2	R^3	yield[a] [%]	yield[a,b] [%]	α_D^{25}[a] neat or (*c*, C_6H_6)		*ee*[a,c] [%]	Config.
a	Et	Me	Me	52 {90}	42 {72}	+249.0	{+227.3}	>91 {83}	*R*
b	Et	Me	*i*Pr	47 {85}	37 {67}	+148.4	{+123.7 (0.79)}	96 {88}	*R*
c	Ph	Me	Me	58 {89}	26 {39}	+3.7 (0.9)	{+3.8 (1.05)}	>96 {96}	*R*
c[d]	Ph	Me	Me	56	24	–3.4 (0.5)		92	*S*
d	Ph	Me	*i*Pr	59 {72}	41 {53}	+119.6	{+85.3 (1.05)}	96 {87}	*R*
d[d]	Ph	Me	*i*Pr	56	43	–117.7		95	*S*

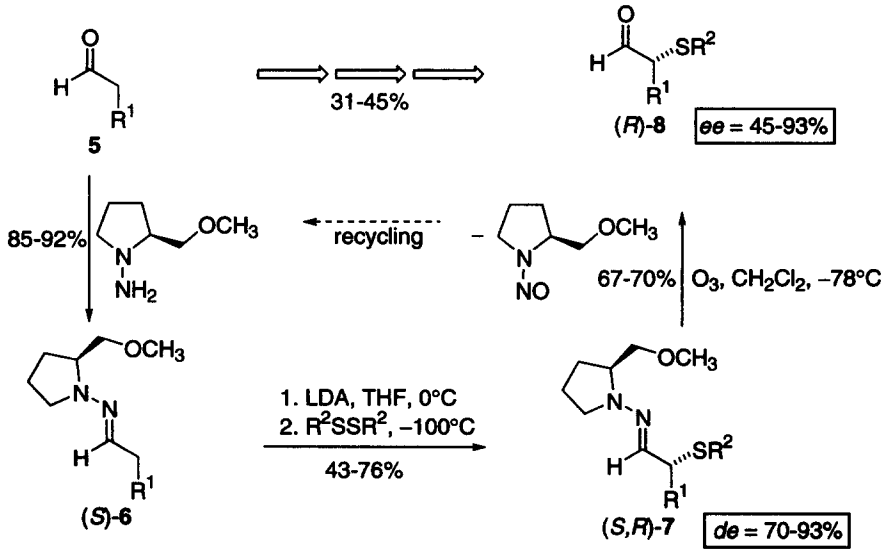
[a] Yields, optical rotations and *ee*'s in brackets { } refer to ketones obtained by acidic hydrolysis. - Yields refer to hydrazones **2**. - [b] Yields refer to carbonyl compounds **1**. - [c] Determined by LIS NMR experiments. - [d] RAMP was used instead of SAMP as auxiliary.

The chemoselective oxidative cleavage of the hydrazone proceeded without racemisation. However, due to the competing oxidation of the thioether moiety to the corresponding sulfoxides only moderate yields were obtained, therefore, another cleavage method was applied. Hence, the hydrazones were vigorously stirred with

2*N* HCl/pentane in a two phase system, giving the *a*-thiolated ketones **4** in 72-90% yield with 87-96% *ee*, again determined by LIS shift experiments. Obviously, a partial racemisation occurred under these relatively harsh reaction conditions applied. However, despite this minor disadvantages, a convenient preparation of thiolated ketones has been worked out. Needless to mention that the auxiliary can efficiently be recovered.[11,12]

Then, we focused on the enantioselective synthesis of α-thiolated aldehydes (Scheme 2). In our recent publication we had presented an efficient method for the preparation of 2-sulfenylated aldehydes of high enantiomeric purity, starting from sulfenylated acetaldehyde derivatives.[7]

This time, the commercially available aldehydes **5** were converted to the corresponding SAMP hydrazones (*S*)-**6**, metalated with lithium diisopropylamide in THF at 0°C and sulfenylated by addition of the dialkyldisulfides at –100°C. The reaction mixtures were allowed to warm to room temperature overnight and after standard work-up and purification by column chromatography, the thiolated aldehyde hydrazones (*S,R*)-**7** were isolated in 43-76% yield and diastereomeric excesses of 70-93% (Table 3). The yellow oils slowly decomposed in air at room temperature, however, they proofed to be stable at –20°C under an inert atmosphere.



Scheme 2. Enantioselective Synthesis of α-Thiolated Aldehydes

Diastereomeric excesses were determined by ^{13}C NMR spectroscopy or gaschromatography. Higher diastereoselectivities were observed in this reaction series when dimethyldisulfide was utilized as sulfenylation agent. The NMR spectra also revealed that the hydrazones were isolated in the thermodynamically favored (*E*) configuration. The configurations of the newly generated stereogenic centre were deduced from the corresponding carbonyl compounds and were in agreement with the expected mechanism for electrophilic substitutions of SAMP hydrazones.[12] It is important to mention that the formation of the (*S,R*) diastereomer constitutes a stereochemical alternative of our previously published method where the (*S,S*) isomer is dominantly formed.[7] By combination of both methods it is possible to prepare both diastereomers, utilizing the same auxiliary.

Table 3. α-Thiolated Aldehyde SAMP Hydrazones

7	R^1	R^2	yield [%]	α_D^{25} neat or (*c*, C_6H_6)	*de* [%]	Config.[a]
a	Et	Me	69	–56.1	85	*S,R*
b	*n*Pr	Me	70	–67.8	93	*S,R*
c	*n*Pr	*i*Pr	43	–9.5	82	*S,R*
d	*i*Pr	Me	65	–60.0	91	*S,R*
e	Bn	Me	76	–99.2 (0.9)	84	*S,R*
f	Bn	*i*Pr	52	–59.3 (0.7)	70	*S,R*

[a] Configurations were deduced from corresponding aldehydes.

The cleavage of the hydrazones was firstly carried out in the two phase system, employing 2*N* HCl and pentane. Low yields and virtual complete racemisation was observed in these experiments. Therefore, our standard cleavage protocol using ozone as oxidizing agent was applied, furnishing the 2-sulfenylated aldehydes **8** in 67-70% yield and 45-93% *ee* as yellow, smelly oils that decomposed at room temperature in the presence of air. Thus, the oxidative cleavage of the hydrazone moiety proceeded without racemisation, as is shown in Table 4, only the benzyl substituted aldehyde **8d** did undergo partial racemisation.

Table 4. Aldehydes **8** Obtained by Oxidative Cleavage with Ozone

8	R^1	R^2	yield [%]	$[\alpha]_D^{22}$ (*c*, C_6H_6)	*ee* [%]	Config.
a	*n*Pr	Me	67	+64.1 (0.36)	93	*R*
b	*i*Pr	Me	68	–142.7 (1.0)	91	*R*
c	Bzl	Me	70	+116.5 (0.54)	79	*R*
d	Bzl	*i*Pr	70	+13.1 (1.1)	45	*R*

All new aldehydes were fully characterized. The spectroscopic data of the known aldehydes matched those reported in the literature.[7] Configurations were determined to be (*R*) by comparison with the data known for thiolated aldehydes prepared by alkylation of sulfenylated acetaldehyde SAMP hydrazones.[7]

CONCLUSION

The enantioselective α-sulfenylation of ketones and aldehydes presented in this paper opens a practical entry to these important classes of carbonyl compounds by carbon sulfur bond formation employing simple ketones, aldehydes and disulfides as starting materials. In addition, in the case of α-sulfenylated aldehydes it

constitutes an efficient and flexible alternative to our previously reported method via α-alkylation of thiolated acetaldehyde SAMP hydrazones. Needless to mention that both enantiomers are available by these methods, respectively.

EXPERIMENTAL SECTION

General. All reactions were carried out using standard Schlenk techniques. Solvents were dried and purified by conventional methods prior to use. Tetrahydrofuran was freshly distilled from sodium under argon. Reagents were purchased from common commercial suppliers and were used from freshly opened containers unless otherwise stated. SAMP/RAMP hydrazones **2** and **6** were prepared following standard literature procedures.[11,12]

Apparatus. Optical rotations: Perkin-Elmer P 241 polarimeter; solvents of Merck UVASOL quality. - IR spectra: Beckman Acculab 4, Perkin-Elmer FT 1750. - ^{1}H NMR spectra (90 or 300 MHz) and ^{13}C NMR spectra (20 or 75 MHz): Varian EM 390 or Varian VXR 300 (δ in ppm, solvent: $CDCl_3$, TMS as internal standard). - Mass spectra: Finnigan MAT 212 (EI 70 eV). - Microanalyses: Heraeus Mikro U/D or Heraeus CHN-O-RAPID. - Ozonolyses: Fischer ozone generator type 502. - HPLC: Du Pont HPLC 830, UV detection; Waters 590, UV detection.

General procedure 1 for the thiolation of SAMP/RAMP hydrazones **2** *and* **6***:*

A solution of *n*BuLi (1.1 equiv., 1.6 M in *n*-hexane) was added dropwise to a solution of diisopropylamine (1.1 equiv.) in THF (30 ml/10 mmol) at 0°C under an atmosphere of argon. After 15 min. the LDA (1.1 equiv.) solution had been generated and the SAMP hydrazone (*S*)-**2** (1.0 equiv.), dissolved in THF (20 ml/10 mmol), was added dropwise, and the reaction mixture was stirred at 0°C.[11] After 5-8 h the reaction mixture was cooled to –100°C and the dialkyldisulfide (1.0 equiv.) was added at once. The reaction mixture was stirred for 30 min. at –100°C and was allowed to slowly warm to room temperature overnight. Diethylether (100 ml) was added and the organic layer was washed with pH-7 buffer (2x10 ml) and H_2O (10 ml). The organic layer was separated, dried ($NaSO_4$) and concentrated under reduced pressure, yielding the crude thiolated hydrazone, which was purified by column chromatography (silica gel; pentane/diethylether 1:1 to 3:2) or Kugelrohr distillation.

General procedure 2 for the oxidative cleavage of the thiolated hydrazones **3** *and* **7***:*

The hydrazone (10 mmol) was dissolved in CH_2Cl_2 (50 ml), and the solution was cooled to –78°C. A gentle stream of ozone (60 lh^{-1}) was flushed through the solution for 3 min. Then, the addition of ozone was slowly continued until the completion of the reaction was indicated by TLC. To avoid an oxidation of the sulfide to the corresponding sulfoxide, the amount of ozone had to be carefully chosen. The solvent was removed in vacuum and the thiolated ketone was purified by column chromatography (silica gel; pentane/diethylether 3.5:1.5 to 3:7, diethyl ether for nitrosamine isolation).

General procedure 3 for the acidic hydrolysis of the sulfenylated hydrazones **3**:

The ketone hydrazone was dissolved in pentane (100 ml/mmol) at 0°C and 2*N* HCl (10 ml/mmol) was added with vigorous stirring. After stirring for 30 min., TLC control indicated the completion of the reaction. The organic layer was separated, washed with H_2O (3x30 ml), dried ($MgSO_4$) and concentrated under reduced pressure, yielding the crude thiolated ketone which was purified by column chromatography (silica gel; pentane/diethylether 3.5:1.5 to 3:7).

(2S,2'R)-(+)-1-(1'-Ethyl-2'-(methylsulfanyl)-1'-propylidenamino)-2-methoxymethylpyrrolidine [(*S,R*)-**3a**]: 1.39 g (7 mmol) 3-Pentanone SAMP hydrazone and dimethyldisulfide were reacted according to general procedure 1, yielding 1.48 g of (*S,R*)-**3a** (87%) as a pale yellow oil after Kugelrohr distillation. - b.p. = 90°C (0.03 mbar). - α_D^{22} = +162.2° (neat). - *de* = 91%. - IR (film): $\tilde{\nu}$ = 3000-2800 cm^{-1}, 1615, 1450, 1375, 1280, 1200, 1130, 1035, 970. - ^1H NMR (90 MHz) δ = 1.15 (t, 3H, *J* = 7.5 Hz, $\boldsymbol{H}_3CCH_2$), 1.22 (d, 3H, *J* = 7.5 Hz, $CHC\boldsymbol{H}_3$), 1.50-2.20 (m, 4H, CH_2CH_2), 1.95 (s, 3H, SCH_3), 2.20-2.70 (m, 3H, $CH\boldsymbol{H}N$, $H_3CC\boldsymbol{H}_2$), 2.90-3.60 (m, 4H, $C\boldsymbol{H}HN$, CHN, $C\boldsymbol{H}_2OCH_3$), 3.30 (s, 3H, OCH_3), 4.65 (q, 1H, *J* = 7.5 Hz, CHS). - MS (70eV); *m/z* (%) = 244 (21) [M^+], 200 (11), 199 (87) [$M^+ - SCH_3$], 197 (20), 130 (11), 114 (12), 75 (100), 70 (23), 56 (42), 45 (20), 41 (33). - $C_{12}H_{24}N_2OS$ (244.4): calcd. C 58.97, H 9.89, N 11.46; found C 58.76, H 9.94, N 11.47.

(2S,2'R)-(+)-1-(1'-Ethyl-2'-(isopropylsulfanyl)-1'-propylidenamino)-2-methoxymethylpyrrolidine [(*S,R*)-**3b**]: 0.99 g (5 mmol) 3-Pentanone SAMP hydrazone and diisopropyldisulfide were reacted according to general procedure 1, yielding 1.17 g of (*S,R*)-**3b** (86%) as a pale yellow oil after column chromatography. - α_D^{22} = +159.9° (neat). - *de* = >96%. - IR (film): $\tilde{\nu}$ = 3000-2800 cm^{-1}, 2730, 1620, 1450, 1370, 1350, 1245, 1200, 1125, 1050, 975, 950. - ^1H NMR (90 MHz) δ = 1.20 (m, 12H, 4 CH_3), 1.80 (m, 4H, CH_2CH_2), 2.20-2.90 (m, 4H, $C\boldsymbol{H}(CH_3)_2$, $CH\boldsymbol{H}N$, $H_3CC\boldsymbol{H}_2$), 2.90-3.50 (m, 4H, $C\boldsymbol{H}HN$, CHN, $C\boldsymbol{H}_2OCH_3$), 3.28 (s, 3H, OCH_3), 4.60 (q, 1H, *J* = 7.5 Hz, CHS). - MS (70eV); *m/z* (%) = 272 (33) [M^+], 229 (40), 228 (12), 227 (82), 198 (28), 197 (28) [$M^+ - SCH(CH_3)_2$], 158 (12), 153 (20), 116 (17), 114 (57), 103 (100), 84 (21), 82 (18), 71 (13), 70 (40), 61 (71), 59 (15), 56 (74), 55 (15), 54 (11), 45 (40), 43 (32), 42 (14), 41 (55). - $C_{14}H_{28}N_2OS$ (272.5): calcd. C 61.76, H 10.31, N 10.31; found C 61.87, H 10.16, N 10.47.

(2S,2'R)-(+)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-1'-phenyl-1'-propylidenamino)pyrrolidine [(*S,R*)-**3c**]: 1.85 g (6.5 mmol) Propiophenon SAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 1.60 g of (*S,R*)-**3c** (84%) as a pale yellow oil after column chromatography. - *de* = 70%. - The yellow oil was crystallised from *n*-hexane at –78°C, yielding 0.98 g (52%) of yellow crystalls. - m.p. = 61-62°C. - $[\alpha]_D^{21}$ = +737.9 (*c* = 0.8, C_6H_6). - *de* = >96%.[14] - IR (film): $\tilde{\nu}$ = 3080 cm^{-1}, 3030, 3020, 3000-2800, 2730, 1575, 1570, 1480, 1450, 1370, 1350, 1275, 1200, 1170-1050, 1025, 970, 810, 780, 725, 705, 680, 640, 605, 525. - ^1H NMR (*E* isomer) (90 MHz) δ = 1.29 (d, 3H, *J* = 7.5 Hz, $CHC\boldsymbol{H}_3$), 1.35-2.90 (m, 6H, CH_2CH_2, CH_2N), 2.05 (s, 3H, SCH_3), 3.20-3.80 (m, 4H, CHN, $C\boldsymbol{H}_2OCH_3$, CHS), 3.30 (s, 3H, OCH_3), 7.32

(m, 5H, C_6H_5). - ^{13}C NMR (20 MHz) δ = 13.2 ($CHCH_3$), 18.8 (SCH_3), 23.2, 26.8 (CH_2CH_2), 47.8 (SCH), 55.3 (NCH_2), 59.2 (OCH_3), 66.6 (NCH), 75.5 (CH_2OCH_3), 127.7, 127.9, 128.3 ($CH_{arom.}$), 137.6 ($C_{arom.}$), 150.5 (C=N). - MS (70eV); *m/z* (%) = 292 (12) [M^+], 247 (47) [M^+ –SCH_3], 245 (37), 199 (53), 178 (10), 132 (65), 130 (48), 115 (13), 114 (16), 104 (41), 77 (64), 75 (100), 70 (23), 51 (12), 47 (16), 45 (20), 41 (21). - $C_{16}H_{24}N_2OS$ (292.4): calcd. C 65.71, H 8.27, N 9.58; found C 65.73, H 8.20, N 9.57.

(2R,2'S)-(–)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-1'-phenyl-1'-propylidenamino)pyrrolidine [(*R,S*)-**3c**]: 1.23 g (5 mmol) Propiophenon RAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 1.28 g of (*R,S*)-**3c** (87%) as a pale yellow oil after column chromatography. - $[\alpha]_D^{25}$ = –634.1 (*c* = 1.1, C_6H_6). - *de* = >70%. - The yellow oil was crystallised from *n*-hexane at –78°C, yielding 0.51 g (48%) of yellow crystalls. - $[\alpha]_D^{21}$ = –733.1 (*c* = 0.26, C_6H_6). - *de* = 92%.[14] - IR (film): $\tilde{\nu}$ = 3090 cm^{-1}, 3060, 3000-2800, 2720, 1550, 1500-1400, 1380, 1350, 1320-1250, 1200-1000, 980-900, 790, 770, 700, 650, 605. - ^1H NMR (*Z* isomer) (300 MHz) δ = 1.47 (d, 3H, *J* = 7.4 Hz, $CHCH_3$), 1.60-2.10 (m, 4H, CH_2CH_2), 2.07 (s, 3H, SCH_3), 2.62 (m, 1H, CHHN) 3.20-3.60 (m, 4H, CHHN, CHN, CH_2OCH_3), 3.35 (s, 3H, OCH_3), 4.9 (q, 1H, *J* = 7.4 Hz, CHS), 7.35 (m, 3H, C_6H_5), 7.75 (m, 2H, C_6H_5). - ^{13}C NMR (75 MHz) δ = 15.0 ($CHCH_3$), 18.2 (SCH_3), 22.3, 26.8 (CH_2CH_2), 39.2 (SCH), 56.6 (NCH_2), 59.0 (OCH_3), 66.8 (NCH), 75.4 (CH_2OCH_3), 127.8, 128.3, 128.7 ($CH_{arom.}$), 136.7 ($C_{arom.}$), 165.0 (C=N). - MS (70eV); *m/z* (%) = 292 (14) [M^+], 247 (40) [M^+ –SCH_3], 245 (31), 132 (38), 104 (16), 77 (24), 75 (100), 45 (20), 41 (24). - $C_{16}H_{24}N_2OS$ (292.4): calcd. C 65.71, H 8.27, N 9.58; found C 65.75, H 8.24, N 9.64.

(2S,2'R)-(+)-1-(2'-(Isopropylsulfanyl)-1'-phenyl-1'-propylidenamino)-2-methoxymethylpyrrolidine [(*S,R*)-**3d**]: 1.97 g (8 mmol) Propiophenon SAMP hydrazone and diisopropyldisulfide were reacted according to general procedure 1, yielding 2.10 g of (*S,R*)-**3d** (82%) as a yellow oil after column chromatography. - α_D^{20} = +724.0° (neat). - *de* = >96%.[14] - IR (film): $\tilde{\nu}$ = 3070 cm^{-1}, 3030, 3000-2800, 2740, 1600, 1570, 1500, 1450, 1390, 1370, 1300, 1250, 980, 950, 875, 705. - ^1H NMR (90 MHz) δ = 1.20 (d, 3H, *J* = 7.5 Hz, $CHCH_3$), 1.35 (d, 3H, *J* = 6.0 Hz, $CH(CH_3)_2$), 1.52 (d, 3H, *J* = 7.5 Hz, $CH(CH_3)_2$), 1.90 (m, 4H, CH_2CH_2), 2.50-3.10 (m, 2H, $CH(CH_3)_2$, CHHN), 3.22-3.70 (m, 4H, CHHN, CHN, CH_2OCH_3), 3.35 (s, 3H, OCH_3), 4.90 (q, 1H, *J* = 7.5 Hz, CHS), 7.30 (m, 3H, C_6H_5), 7.80 (m, 2H, C_6H_5). - ^{13}C NMR (20 MHz) δ = 19.4 ($CHCH_3$), 22.8, 27.2 (CH_2CH_2), 23.3 ($CH(CH_3)_2$), 35.6 ($CH(CH_3)_2$), 36.7 (SCH), 56.7 (NCH_2), 59.0 (OCH_3), 66.8 (NCH), 75.5 (CH_2OCH_3), 127.8, 128.1, 128.5 ($CH_{arom.}$), 136.9 ($C_{arom.}$), 165.5 (C=N). - MS (70eV); *m/z* (%) = 320 (20) [M^+], 277 (18), 275 (54), 246 (20), 245 (74) [M^+ –$SCH(CH_3)_2$], 206 (11), 132 (83), 130 (16), 115 (147), 114 (41), 105 (13), 104 (38), 103 (100), 82 (11), 77 (31), 70 (30), 61 (60), 45 (36), 43 (26), 41 (26). - $C_{18}H_{28}N_2OS$ (320.5): calcd. C 67.45, H 8.81, N 8.78; found C 67.35, H 8.66, N 8.79.

(2R,2'S)-(–)-1-(2'-(Isopropylsulfanyl)-1'-phenyl-1'-propylidenamino)-2-methoxymethylpyrrolidine [(*R,S*)-**3d**]: 1.23 g (5 mmol) Propiophenon RAMP hydrazone and diisopropyldisulfide were combined according to general procedure 1, yielding 1.39 g of (*R,S*)-**3d** (87%) as a yellow oil after column chromatography. - α_D^{24} = –

718.5° (neat). - *de* = >96%. - IR (film): $\tilde{\nu}$ = 3070 cm^{-1}, 3000-2800, 1600, 1560, 1490, 1450, 1380, 1365, 1310-1280, 1250, 1200, 1120, 1050, 945, 770. - ^1H NMR (90 MHz) δ = 1.17 (d, 3H, *J* = 7.5 Hz, $CHCH_3$), 1.30 (d, 3H, *J* = 6.0 Hz, $CH(CH_3)_2$), 1.38 (d, 3H, *J* = 7.5 Hz, $CH(CH_3)_2$), 1.85 (m, 4H, CH_2CH_2), 2.45-3.10 (m, 2H, $CH(CH_3)_2$, CHHN), 3.10-3.70 (m, 4H, CHHN, CHN, CH_2OCH_3), 3.30 (s, 3H, OCH_3), 4.85 (q, 1H, *J* = 7.5 Hz, CHS), 7.30 (m, 3H, C_6H_5), 7.75 (m, 2H, C_6H_5). - MS (70eV); *m/z* (%) = 320 (9) [M^+], 275 (24), 246 (12), 245 (34) [M^+ –$SCH(CH_3)_2$], 201 (25), 199 (43), 133 (11), 132 (100), 130 (43), 115 (16), 114 (26), 105 (12), 104 (54), 103 (65), 82 (11), 77 (74), 76 (15), 70 (30), 61 (39), 51 (19), 45 (30), 43 (26), 42 (12), 41 (33). - $C_{18}H_{28}N_2OS$ (320.5): calcd. C 67.45, H 8.81, N 8.78; found C 66.95, H 8.96, N 8.82.

(R)-(+)-2-(Methylsulfanyl)-3-pentanone [(*R*)-**4a**]: 1.33 g (5.4 mmol) (*S,R*)-**3a** were reacted according to general procedure 2, yielding 0.40 g of (*R*)-**4a** (52%) as a bright yellow oil after column chromatography. - α_D^{22} = +249.0° (neat). - *ee* = >91%.[15] - 0.62 g (2.5 mmol) (*S,R*)-**3a** were reacted according to general procedure 3, yielding 0.30 g of (*R*)-**4a** (90%) as a bright yellow oil after column chromatography. - α_D^{25} = +227.3° (neat). - *ee* = 83%.[16] - IR (film): $\tilde{\nu}$ = 3020-2800 cm^{-1}, 1710, 1460-1410, 1380, 1355, 1210, 1180, 1130, 1100, 1065, 1020, 960, 810. - ^1H NMR (90 MHz) δ = 1.03 (t, 3H, *J* = 7.5 Hz, H_3CCH_2), 1.35 (d, 3H, *J* = 7.5 Hz, $CHCH_3$), 1.90 (s, 3H, SCH_3), 2.63 (m, 2H, H_3CCH_2), 3.35 (q, 1H, *J* = 7.5 Hz, CHS). - MS (70eV); *m/z* (%) = 132 (4) [M^+], 75 (100), 57 (15), 47 (21), 41 (30). - $C_6H_{12}OS$ (132.2): calcd. C 54.50, H 9.15; found C 54.38, H 9.07.

(R)-(+)-2-(Isopropylsulfanyl)-3-pentanone [(*R*)-**4b**]: 1.54 g (5.7 mmol) (*S,R*)-**3b** were reacted according to general procedure 2, yielding 0.43 g of (*R*)-**4b** (47%) as a colorless oil after column chromatography. - α_D^{21} = +148.4° (neat). - *ee* = 96%.[15] - 0.30 g (1.1 mmol) (*S,R*)-**3b** were reacted according to general procedure 3, yielding 0.15 g of (*R*)-**4b** (85%) as a colorless oil after column chromatography. - $[\alpha]_D^{22}$ = +123.7 (*c* = 0.79, C_6H_6). - *ee* = 88%.[15] - IR (film): $\tilde{\nu}$ = 3000-2860 cm^{-1}, 1710, 1460, 1415, 1375, 1350, 1250, 1175, 1160, 1135, 1050, 1015. - ^1H NMR (90 MHz) δ = 1.25 (m, 12H, 4 CH_3), 2.68 (q, 2H, *J* = 7.5 Hz, H_3CCH_2), 2.89 (sep, *J* = 6.0 Hz, $CH(CH_3)_2$), 3.45 (q, 1H, *J* = 7.5 Hz, CHS). - MS (70eV); *m/z* (%) = 160 (16) [M^+], 103 (60), 86 (18), 61 (100), 57 (18), 43 (20), 41 (10). - $C_8H_{16}OS$ (160.3): calcd. C 60.00, H 10.00; found C 59.76, H 9.86.

(R)-(+)-2-(Methylsulfanyl)-1-phenyl-1-propanone [(*R*)-**4c**]: 1.25 g (4.3 mmol) (*S,R*)-**3c** were reacted according to general procedure 2, yielding 0.45 g of (*R*)-**4c** (58%) as a yellow oil after column chromatography. - $[\alpha]_D^{27}$ = +3.7 (*c* = 0.92, C_6H_6). - *ee* = >96%.[15] - 0.15 g (0.55 mmol) (*S,R*)-**3c** were reacted according to general procedure 3, yielding 0.084 g of (*R*)-**4c** (95%) as a yellow oil after column chromatography. - $[\alpha]_D^{22}$ = +3.8 (*c* = 1.05, C_6H_6). - *ee* = >96%.[15] - IR (film): $\tilde{\nu}$ = 3070 cm^{-1}, 2980, 2930, 2870, 1675, 1600, 1585, 1450, 1380, 1340, 1250, 1185, 1110, 1085, 1070, 1020, 950, 850, 805, 750-680, 660. - ^1H NMR (90 MHz) δ = 1.50 (d, 3H, *J* = 7.5 Hz, $CHCH_3$), 1.95 (s, 3H, SCH_3), 4.30 (q, 1H, *J* = 7.5 Hz, CHS), 7.45 (m, 3H, C_6H_5), 7.95 (m, 2H, C_6H_5). - MS (70eV); *m/z* (%) = 180 (16) [M^+], 134 (44), 105 (100), 77 (52), 75 (75), 51 (20), 47 (12), 41 (15). - $C_{10}H_{12}OS$ (180.3): calcd. C 66.62, H 6.71; found C 66.58, H 6.85.

(S)-(–)-2-(Methylsulfanyl)-1-phenyl-1-propanone [(*S*)-**4c**]: 0.27 g (0.9 mmol) (*R,S*)-**3c** were reacted according to general procedure 2, yielding 0.092 g of (*S*)-**4c** (56%) as a yellow oil after column chromatography. - $[\alpha]_D^{25} = -3.4$ ($c = 0.5$, C_6H_6). - *ee* = 92%.[15] -The spectroscopic data matched those reported for (*R*)-**4c**.

(R)-(+)-2-(Isopropylsulfanyl)-1-phenyl-1-propanone [(*R*)-**4d**]: 0.845 g (2.6 mmol) (*S,R*)-**3d** were reacted according to general procedure 2, yielding 0.323 g of (*R*)-**4d** (59%) as a yellow oil after column chromatography. - $\alpha_D^{20} = +119.6°$ (neat). - *ee* = 96%.[15] - 0.45 g (1.4 mmol) (*S,R*)-**3d** were reacted according to general procedure 3, yielding 0.21 g of (*R*)-**4d** (72%) as a bright yellow oil after column chromatography. - $[\alpha]_D^{22} = +85.3$ ($c = 1.05$, C_6H_6). - *ee* = 87%.[16] - IR (film): $\tilde{\nu}$ = 3080 cm^{-1}, 2980, 2940, 2880, 1680, 1605, 1590, 1455, 1380, 1315, 1240, 1185, 1160, 1055, 1005, 955, 805. - ^1H NMR (90 MHz) δ = 1.25 (d, 6H, J = 6.0 Hz, $CH(CH_3)_2$), 1.63 (d, 3H, J = 7.5 Hz, $CHCH_3$), 3.03 (sep, 1H, J = 6.0 Hz, $SCH(CH_3)_2$), 4.40 (q, 1H, J = 7.0 Hz, CHS), 7.50 (m, 3H, C_6H_5), 8.05 (m, 2H, C_6H_5). - MS (70eV); *m/z* (%) = 208 (11) [M^+], 134 (70), 105 (69), 103 (100), 77 (39), 61 (100), 51 (13), 43 (19), 41 (10). - $C_{12}H_{16}OS$ (208.2): calcd. C 69.23, H 7.60; found C 69.29, H 7.77.

(S)-(–)-2-(Methylsulfanyl)-1-phenyl-1-propanone [(*S*)-**4d**]: 0.66 g (3.0 mmol) (*R,S*)-**3d** were reacted according to general procedure 2, yielding 0.242 g of (*S*)-**4d** (56%) as a pale yellow oil after column chromatography. - $\alpha_D^{26} = -117.7°$ (neat). - *ee* = 95%.[16] -The spectroscopic data matched those reported for (*R*)-**4d**.

(2S,2'R)-(–)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-1'-butylidenamino)pyrrolidine [(*S,R*)-**7a**]: 0.74 g (4 mmol) Butanal SAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 0.64 g of (*S,R*)-**7a** (69%) as a colorless oil after Kugelrohr distillation. - b.p. = 85°C (0.03 mbar). - $\alpha_D^{21} = -56.1°$ (neat). - *de* = 85%.[14] - IR (film): $\tilde{\nu}$ = 3000-2800 cm^{-1}, 1600, 1465, 1385, 1350, 1310, 1290, 1200, 1125, 975, 915. - ^1H NMR (300 MHz) δ = 1.00 (t, 3H, J = 7.4 Hz, H_3CCH_2), 1.67 (m, 2H, H_3CCH_2), 1.75-1.98 (m, 4H, CH_2CH_2), 2.00 (s, 3H, SCH_3), 2.80 (m, 1H, CHHN), 3.18 (m, 1H, CHS), 3.23-3.50 (m, 3H, CHHN, CH_2OCH_3), 3.38 (s, 3H, OCH_3), 3.55 (m, 1H, CHN), 6.38 (d, 1H, J = 7.6 Hz, CH=N). - ^{13}C NMR (75 MHz) δ = 11.9 (H_3CCH_2), 13.5 (SCH_3), 22.2, 26.2, 26.6 (CH_2CH_2, CH_3CH_2), 50.2 (CH_2N), 50.6 (SCH), 59.2 (OCH_3), 63.6 (CHN), 74.6 (CH_2OCH_3), 137.7 (CH=N). - MS (70eV); *m/z* (%) = 230 (10) [M^+], 185 (41), 184 (11), 183 (100) [$M^+ - SCH_3$], 137 (15), 116 (17), 114 (13), 112 (10), 82 (12), 74 (13), 71 (16), 70 (25), 68 (10), 55 (10), 45 (15), 41 (22). - $C_{11}H_{22}N_2OS$ (230.1): calcd. C 57.35, H 9.63, N 12.16; found C 57.58, H 9.59, N 12.25.

(2S,2'R)-(–)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-1'-pentylidenamino)pyrrolidine [(*S,R*)-**7b**]: 0.99 g (5 mmol) Pentanal SAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 0.85 g of (*S,R*)-**7b** (70%) as a yellow oil after Kugelrohr distillation. - b.p. = 90-92°C (0.05 mbar). - $\alpha_D^{20} = -67.8°$ (neat). - *de* = 92%.[17] - IR (film): $\tilde{\nu}$ = 3000-2800 cm^{-1}, 1600, 1460, 1380, 1345, 1305, 1200, 1150-1070, 975, 910-880, 760. - ^1H NMR (90 MHz) δ = 0.90 (t, 3H, J = 7.5 Hz, H_3CCH_2), 1.20 (m, 2H, H_3CCH_2), 1.40-1.90 (m, 6H, CH_2CH_2, CH_2CHS), 2.00 (s, 3H, SCH_3), 2.80 (q, 1H, J = 7.5 Hz, CHS), 3.10-

3.80 (m, 5H, C*H*HN, CH_2OCH_3, CHN), 3.35 (s, 3H, OCH_3), 6.35 (d, 1H, *J* = 7.6 Hz, CH=N). - ^{13}C NMR (20 MHz) δ = 13.6 (H$_3$*C*CH$_2$), 13.9 (SCH$_3$), 20.5 (CH$_3$*C*H$_2$), 22.2, 26.6 (*C*H$_2$*C*H$_2$), 35.0 (*C*H$_2$CHS), 48.7 (CHS), 50.3 (CH$_2$N), 59.2 (OCH$_3$), 63.7 (CHN), 74.7 (*C*H$_2$OCH$_3$), 137.9 (CH=N). - MS (70eV); *m/z* (%) = 244 (4) [M$^+$], 199 (36), 198 (12), 197 (100) [M$^+$ –SCH$_3$], 151 (21), 130 (22), 114 (25), 112 (20), 87 (11), 84 (13), 82 (32), 80 (12), 74 (13), 71 (27), 70 (38), 68 (13), 67 (10), 61 (26), 55 (23), 45 (33), 43 (13), 42 (14), 41 (43). - $C_{12}H_{24}N_2OS$ (244.4): calcd. C 58.97, H 9.89, N 11.46; found C 58.85, H 9.84, N 11.20.

(2S,2'R)-(–)-2-Methoxymethyl-1-(2'-(isopropylsulfanyl)-1'-pentylidenamino)pyrrolidine [(*S,R*)-**7c**]: 0.79 g (4 mmol) Pentanal SAMP hydrazone and diisopropyldisulfide were combined according to general procedure 1, yielding 0.47 g of (*S,R*)-**7d** (43%) as a yellow oil after column chromatography. - α_D^{20} = –9.5° (neat). - *de* = 92%.[17] - IR (film): $\tilde{\nu}$ = 3000-2800 cm^{-1}, 1595, 1460, 1382, 1345, 1305, 1250, 1200, 1125, 1055, 975, 900. - ^{1}H NMR (300 MHz) δ = 0.90 (t, 3H, *J* = 7.2 Hz, *H*$_3$CCH$_2$), 1.22 (d, 3H, *J* = 6.9 Hz, SCH(C*H*$_3$)$_2$), 1.28 (d, 3H, *J* = 6.6 Hz, SCH(C*H*$_3$)$_2$), 1.45 (m, 2H, H$_3$CC*H*$_2$), 1.60 (m, 2H, C*H*$_2$CHS), 1.75-2.05 (m, 4H, CH$_2$CH$_2$), 2.80 (m, 2H, CH*H*N, SC*H*(CH$_3$)$_2$), 3.30-3.60 (m, 5H, C*H*HN, C*H*$_2$OCH$_3$, CHN, CHS), 3.35 (s, 3H, OCH$_3$), 6.38 (d, 1H, *J* = 7.9 Hz, CH=N). - ^{13}C NMR (20 MHz) δ = 13.8 (H$_3$*C*CH$_2$), 20.4 (CH$_3$*C*H$_2$), 22.1, 26.6 (*C*H$_2$*C*H$_2$), 23.8, 24.0 (CH(*C*H$_3$)$_2$), 33.7 (*C*H(CH$_3$)$_2$), 35.5 (*C*H$_2$CHS), 46.3 (CHS), 50.2 (CH$_2$N), 59.2 (OCH$_3$), 63.6 (CHN), 74.6 (*C*H$_2$OCH$_3$), 138.9 (CH=N). - MS (70eV); *m/z* (%) = 272 (2) [M$^+$], 227 (11), 198 (12), 197 (100) [M$^+$ –SCH$_3$], 114 (12), 82 (11), 71 (12), 70 (16), 55 (12), 45 (15), 43 (11), 41 (18). - $C_{14}H_{28}N_2OS$ (272.5): calcd. C 61.72, H 10.36, N 10.28; found C 61.89, H 10.31, N 10.44.

(2S,2'R)-(–)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-3'-methyl-1'-butylidenamino)pyrrolidine [(*S,R*)-**7d**]: 1.18 g (6 mmol) 2-Methylbutanal SAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 0.95 g of (*S,R*)-**7c** (65%) as a bright yellow oil after column chromatography. - α_D^{20} = –60.0° (neat). - *de* = 91%.[17] - IR (film): $\tilde{\nu}$ = 3040-2800 cm^{-1}, 1600, 1470, 1395, 1380, 1350, 1335, 1315, 1295, 1200, 1185-1080, 980, 910-890. - ^{1}H NMR (90 MHz) δ = 0.95 (d, 3H, *J* = 7.5 Hz, (*H*$_3$C)$_2$CH), 1.05 (d, 3H, *J* = 7.5 Hz, (*H*$_3$C)$_2$CH), 1.60-2.10 (m, 5H, C*H*$_2$C*H*$_2$, (CH$_3$)$_2$C*H*), 1.95 (s, 3H, SCH$_3$), 2.80 (m, 1H, CHS), 3.05 (m, 1H, C*H*HN), 3.20-3.60 (m, 7H, CH*H*N, C*H*$_2$OCH$_3$, CHN, OCH$_3$), 6.40 (d, 1H, *J* = 7.5 Hz, CH=N). - ^{13}C NMR (20 MHz) δ = 14.0 (SCH$_3$), 20.4, 20.6 ((H$_3$*C*)$_2$CH), 22.1, 26.6 (CH$_2$CH$_2$), 31.5 ((H$_3$C)$_2$*C*H), 50.3 (CHS), 56.6 (CH$_2$N), 59.2 (OCH$_3$), 63.7 (CHN), 74.7 (*C*H$_2$OCH$_3$), 137.0 (CH=N). - MS (70eV); *m/z* (%) = 244 (9) [M$^+$], 199 (35), 198 (13), 197 (100) [M$^+$ –SCH$_3$], 151 (12), 114 (20), 103 (10), 82 (13), 74 (20), 71 (11), 70 (40), 55 (22), 45 (19), 41 (26). - $C_{12}H_{24}N_2OS$ (244.4): calcd. C 58.97, H 9.89, N 11.46; found C 58.77, H 10.11, N 11.52.

(2S,2'R)-(–)-2-Methoxymethyl-1-(2'-(methylsulfanyl)-3'-phenyl-1'-propylidenamino)pyrrolidine [(*S,R*)-**7e**]: 1.23 g (5 mmol) Dihydrocinnamyl aldehyde SAMP hydrazone and dimethyldisulfide were combined according to general procedure 1, yielding 1.10 g of (*S,R*)-**7e** (76%) as a yellow oil after Kugelrohr distillation. - b.p. = 140-150°C (0.07 mbar). - $[\alpha]_D^{22}$ = –99.2 (*c* = 0.9, C_6H_6). - *de* = 84%.[14] - IR (film): $\tilde{\nu}$ = 3100-2800 cm^{-}

^{1}, 1600, 1500, 1460, 1350, 1310, 1290, 1250-1070, 1040, 990-960, 930. - ^{1}H NMR (300 MHz) δ = 1.75-1.95 (m, 4H, CH_2CH_2), 2.00 (s, 3H, SCH_3), 2.80 (m, 1H, C*H*HN), 2.92 (q, 1H, *J* = 7.4 Hz, CH*H*CHS), 3.08 (q, 1H, *J* = 7.6 Hz, C*H*HCHS), 3.22-3.50 (m, 4H, CH*H*N, C*H*$_2$OCH$_3$, CHN), 3.32 (s, 3H, OCH_3), 3.56 (m, 1H, CHS), 6.40 (d, 1H, *J* = 7.2 Hz, CH=N), 7.15-7.30 (m, 5H, C_6H_5). - ^{13}C NMR (75 MHz) δ = 13.6 (SCH_3), 22.0, 26.5 (CH_2CH_2), 39.1 (*C*H_2CHS), 49.9 (CH_2N), 50.0 (CHS), 59.2 (OCH_3), 63.4 (CHN), 74.4 (*C*H_2OCH$_3$), 126.3, 128.7, 129.3 ($CH_{arom.}$), 136.1 (CH=N), 138.7 ($C_{arom.}$). - MS (70eV); *m/z* (%) = 292 (9) [M$^+$], 247 (47), 246 (16), 245 (100) [M$^+$ –SCH_3], 201 (36), 199 (21), 151 (11), 132 (13), 130 (11), 114 (15), 112 (11), 109 (16), 103 (10), 91 (18), 74 (17), 71 (13), 70 (28), 55 (73), 45 (21), 41 (16). - $C_{16}H_{24}N_2OS$ (292.4): calcd. C 65.71, H 8.27, N 9.58; found C 65.75, H 8.48, N 9.40.

(2S,2'R)-(–)-1-(2'-(Isopropylsulfanyl)-3'-phenyl-1'-butylidenamino)-2-methoxymethylpyrrolidine [(*S,R*)-**7f**]: 1.23 g (5 mmol) Dihydrocinnamyl aldehyde SAMP hydrazone and diisopropyldisulfide were combined according to general procedure 1, yielding 0.84 g of (*S,R*)-**7f** (52%) as a yellow oil after Kugelrohr distillation. - b.p. = 125-130°C (0.04 mbar). - $[\alpha]_D^{22}$ = –59.3 (*c* = 0.7, C_6H_6). - *de* = 70%.[14] - IR (film): $\tilde{\nu}$ = 3080 cm^{-1}, 3040, 3000-2800, 1610-1580, 1500, 1465-1455, 1385, 1370, 1345, 1310, 1285, 1205, 1180-1090, 1035, 975, 755, 705. - ^{1}H NMR (300 MHz) δ = 1.21 (d, 3H, *J* = 6.9 Hz, SCH(C*H*$_3$)$_2$), 1.24 (d, 3H, *J* = 6.6 Hz, SCH(C*H*$_3$)$_2$), 1.75-2.00 (m, 4H, CH_2CH_2), 2.75-3.65 (m, 4H, C*H*$_2$CHS, C*H*(CH$_3$)$_2$, C*H*HN), 3.20-3.55 (m, 4H, CH*H*N, C*H*$_2$OCH$_3$, CHN), 3.30 (s, 3H, OCH_3), 3.77 (m, 1H, CHS), 6.40 (d, 1H, *J* = 7.7 Hz, CH=N), 7.14-7.30 (m, 5H, C_6H_5). - ^{13}C NMR (75 MHz) δ = 22.0, 26.6 (CH_2CH_2), 23.4, 23.8 (CH(*C*H$_3$)$_2$), 34.0 (*C*H(CH$_3$)$_2$), 39.9 (*C*H_2CHS), 47.6 (CHS), 49.9 (CH_2N), 59.2 (OCH_3), 63.3 (CHN), 74.4 (*C*H_2OCH$_3$), 126.3, 128.2, 129.4 ($CH_{arom.}$), 137.2 ($C_{arom.}$), 138.7 (CH=N). - MS (70eV); *m/z* (%) = 320 (6) [M$^+$], 275 (24), 246 (20), 245 (100), 229 (28), 199 (21), 164 (11), 132 (14), 114 (16), 112 (11), 109 (11), 91 (21), 82 (11), 71 (10), 70 (24), 45 (15), 43 (13), 41 (17). - $C_{18}H_{28}N_2OS$ (320.7): calcd. C 67.46, H 8.81, N 8.74; found C 67.61, H 8.66, N 8.70.

(R)-(+)-2-(Methylsulfanyl)pentanal [(*R*)-**8a**]: 0.72 g (2.9 mmol) (*S,R*)-**7b** were reacted according to general procedure 2, yielding 0.28 g of (*R*)-**8a** (67%) as a colorless oil after column chromatography. - $[\alpha]_D^{19}$ = +64.1 (*c* = 0.365, C_6H_6). - *ee* = 93% (Lit.:[7] $[\alpha]_D^{20}$.= –64.5 (*c* = 0.7, C_6H_6); ee = 95%). - The spectroscopic data matched those reported in the literature.[7]

(R)-(–)-3-Methyl-2-(methylsulfanyl)butanal [(*R*)-**8b**]: 0.80 g (3.3 mmol) (*S,R*)-**7c** were reacted according to general procedure 2, yielding 0.29 g of (*R*)-**8b** (68%) as a colorless oil. - $[\alpha]_D^{27}$ = –56.9 (*c* = 1, C_6H_6). - *ee* = 91%.[15] - The spectroscopic data matched those reported in the literature.[7]

(R)-(+)-2-(Methylsulfanyl)-3-phenylpropanal [(*R*)-**8c**]: 0.22 g (0.75 mmol) (*S,R*)-**7e** were reacted according to general procedure 2, yielding 0.10 g of (*R*)-**8d** (70%) as a yellow oil after column chromatography. - $[\alpha]_D^{21}$ = +116.5 (*c* = 0.54, C_6H_6). - *ee* = 79%.[18] - IR (film): $\tilde{\nu}$ = 3080 cm^{-1}, 3040, 3020, 2920, 1730, 1600,

1500, 1450, 1430, 1420, 1060, 1030, 860, 700. - ^{1}H NMR (90 MHz) δ = 1.95 (s, 3H, SCH_3), 3.05 (m, 2H, CH_2CHS), 3.30 (m, 1H, CHS) 7.33 (m, 5H, C_6H_5), 9.35 (d, 1H, J = 3.0 Hz, CHO). - MS (70eV); *m/z* (%) = 181 (2) [M$^+$], 180 (20), 152 (12), 151 (85), 136 (22), 131 (32), 105 (12), 104 (20), 103 (21), 91 (100), 78 (19), 77 (25), 65 (12), 51 (14). - $C_{10}H_{13}OS$ (181.1): calcd. 181.0646; found 181.0645.

(R)-(+)-2-(Isopropylsulfanyl)-3-phenylpropanal [(*R*)-**8d**]: 0.56 g (1.76 mmol) (*S,R*)-**7f** were reacted according to general procedure 2, yielding 0.26 g of (*R*)-**8d** (70%) as a slightly yellow oil after column chromatography. - $[\alpha]_D^{22}$ = +13.1 (*c* = 1.1, C_6H_6). - *ee* = 45%.[19] - IR (film): $\tilde{\nu}$ = 3100 cm^{-1}, 3085, 3040, 3000-2800, 2730, 1750-1690, 1610, 1500, 1460, 1390, 1375, 1320, 1260, 1160, 1060, 1040, 920, 865. - ^{1}H NMR (90 MHz) δ = 1.18 (d, 3H, J = 7.2 Hz, $SCH(CH_3)_2$), 1.22 (d, 3H, J = 7.2 Hz, $SCH(CH_3)_2$), 2.60-3.20 (m, 3H, CH_2CHS, $CH(CH_3)_2$), 3.50 (m, 1H, CHS), 7.20 (m, 5H, C_6H_5). - MS (70eV); *m/z* (%) = 208 (27) [M$^+$], 180 (11), 179 (78), 138 (11), 137 (100), 135 (18), 134 (42), 133 (36), 105 (24), 103 (16), 92 (10), 91 (79), 77 (14), 59 (12), 43 (19). - $C_{12}H_{16}OS$ (208.2): calcd. C 69.19, H 7.74; found C 68.98, H 7.66.

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