Novel Diamino and Diimino Thioethers – Chiral Tridentate Ligands for Asymmetric Michael Reactions?

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Novel C_2-symmetric enantiopure β,β′-diamino thioethers **1** and β,β′-diimino thioethers **2** have been prepared from chiral α-amino acids. Nine of these compounds have been screened as ligands, in combination with 13 metal salts, with a view to achieving the enantioselective catalysis of a Michael reaction of a β-oxo ester with methyl vinyl ketone resulting in an optimal *ee* of 17%.

Introduction

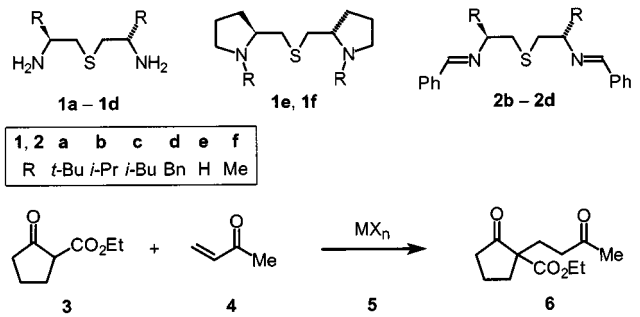
The Michael reaction of β-dicarbonyl compounds and α,β-unsaturated ketones can be catalyzed by a number of transition metal compounds.[1] Due to their neutral reaction conditions the chemoselectivity is significantly improved in these cases compared to the classic base-catalyzed method, since a number of side (and subsequent) reactions are avoided, namely ester solvolyses, aldol cyclizations and retro Claisen decomposition reactions.

Recently, Shibasaki et al.[2] have introduced an excellent heterobimetallic catalyst for the Michael reaction, however these systems are basic and require inert and anhydrous conditions. In the past years only a few chiral catalysts have been reported which do not require strongly basic conditions.[3]

The work described here has been carried out with a view to an interest in the development of new chiral tridentate ligands, which bear O-, S- and N-donor atoms, thus avoiding phosphanes which are often air-sensitive. In a continuation of previous work[4] the synthesis of new C_2-symmetric tridentate diamino thioethers **1** and diimino thioethers **2**, whose stereoinformation is derived from the chiral pool, namely α-amino acids, is reported. Moreover, the catalytic activity of these compounds with respect to enantioselective Michael reactions with a number of transition metal salts **5**, which are known to be non-basic catalysts for the reaction of β-oxo ester **3** with methyl vinyl ketone (**4**) to form the product **6** (without the addition of chiral ligands), has been screened (see Scheme 1).

Ligand Synthesis

Following the sequence reported previously,[4a] the *N*-Boc-protected amino alcohols derived from L-*tert*-leucine (**7a**)[5] and *L*-valine (**7b**)[6] were *O*-activated as tosylates (**8a**, **8b**[7]), which were then further converted with Na_2S to give the thioethers **9** without significant thiol byproduct formation. Subsequent protonolysis of the carbamate protective groups gave the title compounds **1** in satisfying overall yields (see Scheme 2) (**1a**: 35% from **7a**; **1b**: 42% from **8b**). For the synthesis of compounds **1c–e** see ref.[4a]



Scheme 1. Chiral tridentate ligands **1** and **2**; metal-catalyzed Michael reaction of **3** and **4**

The bis(tertiary) diamine **1f** was accessed either by reduction of the bis(*N*-Boc) precursor **9e**[4a] with $LiAlH_4$, or by methylation of the bis(secondary) diamine **1e**[4a] with NaH/MeI. Both protocols gave **1f** in moderate yields.

The diimino derivatives of **2b–d** were prepared according to a standard procedure:[8] Diamines **1** were stirred in toluene suspension at room temp. for about 1 d with a small excess of benzaldehyde and a catalytic amount of protonated cation exchanger resin, as well as anhydrous Na_2SO_4 to bind liberated water. After filtration, and the removal of solvent and the excess of aldehyde in high vacuum at elevated temp., the compounds **2b–d** were obtained as practically pure materials and single stereoisomers (by NMR). The diimines were unstable towards moisture as well as to SiO_2, thus, no further attempts at purification were undertaken. Spectral data of all new compounds are compiled in the Experimental Section.

Michael Reactions

All nine ligands **1a–f** and **2b–d** were separately screened together with each of the thirteen metal salts **5a–m**, listed

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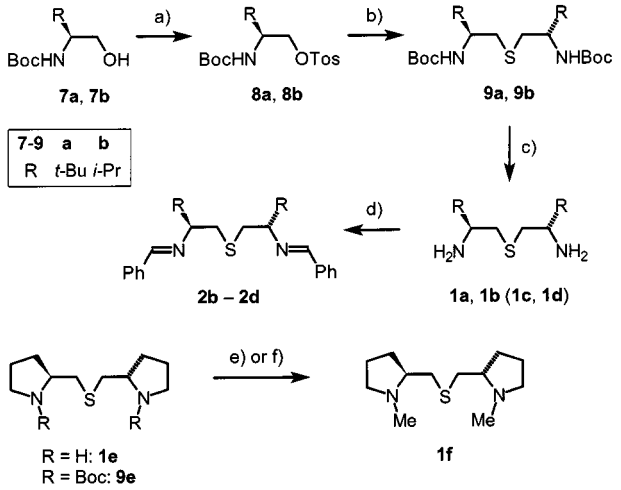

Scheme 2. Synthesis of diamino thioethers **1a**, **1b** and **1f**, and diimino thioethers **2b–d**; reagents, conditions, and yields: a) NEt_3, TosCl, CH_2Cl_2, room temp., **8a**: 77%; b) Na_2S, MeOH (**9a**) or MeOH–THF (**9b**), room temp., **9a**: 51%, **9b**: 43%; c) TFA/CH_2Cl_2, room temp., **1a**: 90%, **1b**: 97%; d) PhCHO, cat. H^+, Na_2SO_4, toluene, room temp., **2b**, **2c**, **2d**: quantitative yields; e) from **1e**, NaH, MeI, THF, room temp., **1f**: 32%; f) from **9e**, $LiAlH_4$, THF, room temp., **1f**: 27%; Boc = *t*BuOCO, Tos = *p*$MeC_6H_4SO_2$

in Table 1, forming the catalytically active complexes in situ. In practice 1.0 equiv. of donor **3** was treated with 0.05 equiv. of **5** and 0.075 equiv. of the chiral ligands, in CH_2Cl_2 as solvent at room temp. After equilibration (1–2 h), a small excess of the acceptor **4** (1.1–1.5 equiv.) was added, and after stirring the mixture for about 12 h at room temp., all metal-containing materials were removed by filtration through SiO_2. Analysis of the conversion and of the enantiomeric excess of **6**[9][10] were performed by chiral GC. Conversions were usually > 10% with all compounds **5**, and with Fe^{III}, Ni^{II} and Co^{II} (and some other single metal/ligand combinations) > 95%. Moreover, it was checked that the ligand itself, without any metal, did not catalyze the reaction of **3** with **4**.

Table 1. List of metal salts **5a** to **5m**

Compound	MX_n
5a	$CrCl_3 \cdot 6\,H_2O$
5b	$Mn(OAc)_2 \cdot 4\,H_2O$
5c	$FeCl_3 \cdot 6\,H_2O$
5d	$Ni(OAc)_2 \cdot 4\,H_2O$
5e	$NiCl_2 \cdot 6\,H_2O$
5f	$Co(OAc)_2 \cdot 4\,H_2O$
5g	$CoCl_2 \cdot 6\,H_2O$
5h	$RhCl_3 \cdot 3\,H_2O$
5i	$Cu(OAc)_2 \cdot H_2O$
5j	AgOAc
5k	$ZnCl_2$
5l	$SnCl_2$
5m	$Pb(OAc)_2 \cdot 3\,H_2O$

With respect to enantioselectivity, significant results were only obtained with ligands **1a** and **1c** (see Table 2). The optimal value ($NiCl_2 \cdot 6\,H_2O$/**1c**: 17% *ee*) was taken as the basis for the further optimization of the parameters solvent, metal/ligand ratio and temp. With respect to the solvent, it turned out that the use of CH_2Cl_2 was already optimal (together with toluene); all other (coordinating) solvents investigated (i.e. dioxane, THF, Et_2O and MeCN) caused lower enantioselectivities. Moreover, the initial ligand/metal ratio (3:2) also turned out to be the one of choice. Even more surprising was the temp. dependence, which showed a maximum *ee* at 25°C (17%). At lower or higher temp. the resulting *ee* values were lower: 50°C: 0%, 35°C: 13%, 10°C: 12%, −20°C: 6%.

Table 2. Selected screening results

Metal salt	Ligand	*ee* (%)	Conversion (%)
5e	**1c**	17	76
5f	**1a**	11	23
5c	**1a**	10	100
5k	**1a**	10	65
5d	**1c**	9	68
5h	**1c**	9	84
5e	**1a**	8	78
5i	**1a**	7	88

Both results, temp. dependence and ligand/metal ratio dependence, obviously indicate that equilibria, and more than one catalytically active species, are present in the reaction mixture. This combinatorial type of approach by testing of a large number of ligand/metal combinations in situ showed that ligands of the type **1** might give suitable new asymmetric catalysts for the Michael reaction of β-oxo esters with enones.

Further experiments on the optimization of the results presented here, including isolation and investigation of unique (diamino thioether)nickel(II) complexes, are currently taking place.

Experimental Section

General: CC: Merck silica gel (type 60, 0.063–0.200 mm) using *tert*-butyl methyl ether (MTB) and petroleum ether (PE, boiling range 40–60°C). – ^1H NMR: Bruker AM 400 (400 MHz). – ^{13}C NMR: Bruker AC 200 (50 MHz), assignments were made using DEPT experiments. – MS: Varian MAT 711 and MAT 955Q (high resolution). – IR: Nicolet Magna IR 750. – Elemental analysis: Analytik Jena Vario EL. – Optical rotations: Perkin–Elmer Polarimeter 341. – Chiral GC analysis: HP 5890 II with FI detection and a Shimadzu C-R6A integrator, Macherey–Nagel column FS-LIPODEX E (25 m, 0.25 mm), nitrogen carrier gas. – All reagents used were commercially available. – The following compounds were prepared according to literature procedures: **1c**, **1d**, **1e**, **9e**;[4b] **7a**;[5] **7b**;[6] **8b**.[7]

***tert*-Butyl (*S*)-*N*-[1-(*tert*-Butyl)-2-(*p*-tolylsulfonyloxy)ethyl]carbamate (8a):** TosCl (1.56 g, 8.17 mmol) was added in one portion to a solution of *N*-Boc-*tert*-leucinol (**7a**) (1.78 g, 8.17 mmol) and NEt_3 (1.65 g, 16.4 mmol) in CH_2Cl_2 (5 mL). The resulting suspension was stirred overnight at room temp., water (10 mL) was added, and after separation of the layers the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with citric acid (10 mL of a 20% aqueous solution), dried with Na_2SO_4, and after filtration and evaporation of the solvent the residue was chromatographed on SiO_2 (PE/MTB, 1:1, R_f = 0.44) to yield the title compound as a colorless oil (2.33 g, 6.27 mmol, 77%).

− $[\alpha]_D^{20}$ = −10 (*c* = 0.32, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3394 cm^{-1} (m), 2967 (s), 2873 (m), 1715 (vs), 1599 (m), 1506 (s), 1478 (m), 1365 (vs), 1243 (s), 1189 (s), 1176 (vs), 1098 (s), 1058 (s), 1009 (m), 969 (s), 927 (m), 834 (m), 815 (m), 770 (m), 665 (s). − ^{1}H NMR ($CDCl_3$): δ = 0.90 (s, 9 H; *t*Bu), 1.41 (s, 9 H; *t*Bu), 2.45 (s, 3 H; CH_3), 3.57−3.62 (m, 1 H; 2-CH), 4.04−4.14 (m, 2 H; 1-CH_2), 4.61 (d br., *J* = 10.1 Hz, 1 H; NH), 7.34−7.36 (m, 2 H; ArH), 7.77−7.79 (m, 2 H; ArH). − ^{13}C NMR ($CDCl_3$): δ = 21.60 (CH_3), 26.75 (CH_3), 28.27 (CH_3), 34.09 (C), 56.89 (CH), 69.53 (CH_2), 79.43 (C), 127.89 (CH), 129.84 (CH), 132.73 (C), 144.84 (C), 155.61 (C=O). − MS (EI, 70 eV); *m*/*z* (%): 372 (1) [M + H^+], 314 (13) [M^+ − *t*Bu], 298 (8) [M^+ − *t*BuO], 214 (100) [M + H^+ − 2 *t*Bu − CO_2], 155 (18) [$C_7H_7SO_2^+$], 57 (19) [tBu^+]. − $C_{18}H_{29}NO_5S$ (371.50): calcd. C 58.20, H 7.87, N 3.77; found C 58.02, H 7.90, N 3.80. − Mol. mass: calcd. 314.1062 ($C_{14}H_{20}NO_5S$); found 314.1062 [M^+ − *t*Bu] (HRMS).

(*S*,*S*)-Bis[2-(*tert*-butyloxycarbonylamino)-3,3-dimethylbutyl] Sulfide (9a): A suspension of tosylate **8a** (2.33 g, 6.27 mmol) and $Na_2S \cdot x\,H_2O$ (65%, 722 mg, 6.01 mmol) in MeOH (10 mL) was stirred at room temp. overnight. The solvent was removed by rotary evaporation, KOH (10 mL of a 10% aqueous solution) added, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), and after evaporation of the solvent, the residue was chromatographed on SiO_2 (PE/MTB 2:1, R_f = 0.39) to yield the title compound as a colorless oil (690 mg, 1.59 mmol, 51%). − $[\alpha]_D^{20}$ = −13 (*c* = 0.22, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3373 cm^{-1} (m), 2966 (s), 2934 (m), 1691 (vs), 1517 (s), 1391 (m), 1366 (m), 1343 (m), 1249 (s), 1172 (s), 1051 (m), 999 (m). − ^{1}H NMR ($CDCl_3$): δ = 0.90 (s, 9 H; *t*Bu), 1.43 (s, 9 H; *t*Bu), 2.32 (dd, *J* = 13.6 Hz, *J* = 11.0 Hz, 1 H; 1-CH*H*), 2.81 (dd, *J* = 13.6 Hz, *J* = 3.0 Hz, 1 H; 1-C*H*H), 3.50 (td, *J* = 10.5 Hz, *J* = 2.9 Hz, 1 H; 2-CH), 4.41 (d br., *J* = 10.1 Hz, 1 H; NH). − ^{13}C NMR ($CDCl_3$): δ = 26.44 (CH_3), 28.39 (CH_3), 33.13 (CH_2), 34.96 (C), 57.24 (CH), 78.85 (C), 156.29 (C=O). − MS (EI, 70 eV); *m*/*z* (%): 433 (2) [M + H^+], 377 (11) [M + H^+ − C_4H_8], 333 (13) [M + H^+ − C_4H_8 − CO_2], 321 (9) [M + H^+ − 2 C_4H_8], 277 (63) [M + H^+ − 2 C_4H_8 − CO_2], 219 (11) [M^+ − 2 C_4H_8 − C_4H_9 − CO_2], 186 (29) [*t*BuCHNHCO_2*t*Bu^+], 130 (59) [$CH_2NHCO_2tBu^+$], 86 (28) [*t*BuCHNH_2^+], 57 (100) [tBu^+]. − Mol. mass: calcd. 433.3100 ($C_{22}H_{44}N_2O_4S$), found 433.3102 [M + H^+] (HRMS).

(*S*,*S*)-Bis[2-(*tert*-butyloxycarbonylamino)-3-methylbutyl] Sulfide (9b): According to the procedure described for **9a** *O*-Tos-*N*-Boc-valinol (**8b**) (6.14 g, 17.2 mmol) was converted with $Na_2S \cdot x\,H_2O$ (65%, 1.55, 19.8 mmol) in THF/MeOH (3:1, 16 mL) to yield the title compound (1.47 g, 7.38 mmol, 43%) as a colorless solid (m.p. 113 °C) after chromatography on SiO_2 (PE/MTB, 5:1, R_f = 0.31). − $[\alpha]_D^{20}$ = +19 (*c* = 0.47, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3333 cm^{-1} (m), 2968 (m), 2959 (m), 1681 (vs), 1521 (s), 1390 (m), 1365 (m), 1294 (m), 1246 (m), 1167 (s), 1043 (m), 1017 (m). − ^{1}H NMR ($CDCl_3$): δ = 0.89 (d, *J* = 6.8 Hz, 3 H; 4-CH_3), 0.93 (d, *J* = 6.8 Hz, 3 H; 4′-CH_3), 1.45 (s, 9 H; *t*Bu), 1.78−1.89 (m, 1 H; 3-CH), 2.66 (d, *J* = 5.9 Hz, 2 H; 1-CH_2), 3.52−3.62 (m, 1 H; 2-CH), 4.60 (d br., *J* = 8.6 Hz, 1 H; NH). − ^{13}C NMR ($CDCl_3$): δ = 17.81 (CH_3), 19.37 (CH_3), 28.34 (CH_3), 31.09 (CH), 35.81 (CH_2), 54.88 (CH), 79.01 (C), 155.78 (C=O). − MS (EI, 70 eV); *m*/*z* (%): 405 (1) [M + H^+], 350 (9) [M + H^+ − C_4H_8], 306 (20) [M + H^+ − *i*Pr − C_4H_8], 249 (100) [M + H^+ − 2 C_4H_8 − CO_2], 164 (8) [$SCH_2CH(iPr)NH_2CO_2^+$], 132 (6) [$CH_2SCH_2CH(iPr)NH_2^+$], 116 (17) [*t*BuOCONH^+], 72 (7) [*i*PrCHNH_2^+], 69 (12) [*i*PrCN^+], 57 (42) [tBu^+]. − $C_{20}H_{40}N_2O_4S$ (404.61): calcd. C 59.37, H 9.96, N 6.92; found C 59.03, H 9.96, N 6.79. − Mol. mass: calcd. 405.2787 ($C_{20}H_{41}N_2O_4S$), found 405.2784 [M + H^+] (HRMS).

(*S*,*S*)-Bis(2-amino-3,3-dimethylbutyl) Sulfide (1a): Bis-*N*-Boc compound **9a** (600 mg, 1.39 mmol) was dissolved in CH_2Cl_2 (3 mL), TFA (2 mL) added, and the mixture stirred overnight at room temp. All volatile materials were removed in high vacuum, KOH (10 mL of a 10% aqueous solution) was added and the resulting mixture extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by Kugelrohr distillation (0.1 Torr, oven temp. 100 °C) to yield the title compound (290 mg, 1.25 mmol, 90%) as a colorless oil. − $[\alpha]_D^{20}$ = +23 (*c* = 0.42, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3376 cm^{-1} (w), 3310 (w), 2956 (vs), 2908 (sh), 2868 (s), 1668 (m), 1600 (m), 1479 (s), 1393 (m), 1363 (s), 1232 (m), 1200 (m), 850 (m), 827 (m), 800 (m). − ^{1}H NMR ($CDCl_3$): δ = 0.91 (s, 9 H; *t*Bu), 1.50 (s, 2H; NH_2), 2.15 (dd, *J* = 13.1 Hz, *J* = 11.1 Hz, 1 H; 1-C*H*H), 2.54 (dd, *J* = 11.1 Hz, *J* = 2.0 Hz, 1 H; 1-CH*H*), 2.81 (dd, *J* = 13.2 Hz, *J* = 2.0 Hz, 1 H; 2-CH). − ^{13}C NMR ($CDCl_3$): δ = 26.11 (CH_3), 34.15 (C), 35.10 (CH_2), 58.57 (CH). − MS (EI, 70 eV); *m*/*z* (%): 233 (2) [M + H^+], 200 (4) [M^+ − 2 NH_2], 175 (28) [M^+ − *t*Bu], 158 (13) [M^+ − *t*Bu − NH_3], 130 (25) [*t*BuCH(NH)CHS^+], 86 (100) [*t*BuCHNH_2^+], 74 (36) [SCH_2CHNH^+], 57 (10) [tBu^+]. − Mol. mass: calcd. 233.2051 ($C_{12}H_{29}N_2S$), found 233.2054 [M + H^+] (HRMS).

(*S*,*S*)-Bis(2-amino-3-methylbutyl) Sulfide (1b): According to the procedure given for **1a** bis(*N*-Boc) compound **9b** (1.35 g, 3.34 mmol) was deprotected with TFA (3 mL) in a CH_2Cl_2 solution (4 mL) to give the diamine **1b** (665 mg, 3.25 mol, 97%) as a colorless liquid, which was purified by Kugelrohr distillation (0.1 Torr, oven temp. 90 °C). − $[\alpha]_D^{20}$ = +160 (*c* = 0.53, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3362 cm^{-1} (w), 3293 (w), 2957 (vs), 2930 (s), 2912 (s), 2872 (s), 1665 (m), 1590 (m), 1467 (m), 1385 (m), 1366 (m), 1233 (m), 922 (m), 876 (m), 825 (m). − ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, *J* = 6.2 Hz, 3 H; 4-CH_3), 0.93 (d, *J* = 6.6 Hz, 3 H, 4′-CH_3), 1.46 (s br., 2 H; NH_2), 1.60−1.75 (m, 1 H; 3-CH), 2.34 (dd, *J* = 12.7 Hz, *J* = 9.6 Hz, 1 H; 1-C*H*H), 2.61−2.68 (m, 1 H; 2-CH), 2.72 (dd, *J* = 12.7 Hz, *J* = 3.4 Hz, 1 H; 1-CH*H*). − ^{13}C NMR ($CDCl_3$): δ = 17.48 (CH_3), 18.91 (CH_3), 32.72 (CH), 37.79 (CH_2), 55.24 (CH). − MS (EI, 70 eV); *m*/*z* (%): 205 (29) [M + H^+], 188 (4) [M^+ − NH_2], 118 (100) [$NH_2CH(iPr)CH_2S^+$], 115 (14) [$CH_2SCHCH iPr^+$], 101 (46) [$SCHCH iPr^+$], 86 (16) [*i*PrCH(NH_2)CH_2^+], 72 (53) [*i*PrCHNH_2^+], 69 (29) [*i*PrCHCH^+]. − $C_{10}H_{24}N_2S$ (204.38): calcd. C 58.77, H 11.84, N 13.71; found C 57.82, H 11.65, N 13.21. − Mol. mass: calcd. 205.1738 ($C_{10}H_{25}N_2S$), found 205.1737 [M + H^+] (HRMS).

(*S*,*S*)-Bis[(2-methyl-2-azacyclopentyl)methyl] Sulfide (1f). − Preparation from 1e: Under an inert atmosphere and anhydrous conditions a solution of **1e** (80 mg, 0.40 mmol) in THF (1.5 mL) was treated with NaH (1.6 mmol, 48 mg of a 80% suspension in mineral oil). At −10 °C MeI (100 μL, 1.6 mmol) was added within 10 min. The mixture was warmed up to room temp. and stirred for 24 h. Subsequently, the mixture was diluted with toluene (3 mL), and after filtration all volatile materials were evaporated in vacuum to yield the title compound as a colorless oil (36 mg, 0.16 mmol, 32%), which was shown to be pure by NMR and could be used without further purification. − **Preparation from 9e:** A solution of **9e** (2.31 g, 7.44 mmol) in anhydrous THF (15 mL) was added within 15 min to a suspension of $LiAlH_4$ (1.50 g, 39.5 mmol) in THF (40 mL). The resulting mixture was heated for 18 h to reflux, then at 0 °C ethyl acetate (4.5 mL), water (3.2 g) and NaOH (1.5 mL of a 15% aqueous solution) were added. The mixture was heated to the b.p. and filtered hot by suction. The residue was washed with MTB, and the combined solutions were concentrated in a rotary evaporator. The residue was redissolved in MTB (10 mL) and dried (Na_2SO_4). Subsequent evaporation of the solvent and Kugelrohr

distillation of the crude material (0.1 Torr, oven temp. 130°C) yielded the title compound as a colorless oil (458 mg, 2.01 mmol, 27%). − $[\alpha]_D^{20} = -17$ ($c = 0.58$, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 2964 cm^{-1} (s), 2943 (s), 2910 (s), 2873 (m), 2837 (m), 2775 (vs), 1454 (m), 1418 (w), 1353 (m), 1346 (m), 1210 (m), 1161 (m), 1142 (m), 1114 (m), 1042 (m), 905 (m). − ^{1}H NMR ($CDCl_3$): δ = 1.55−1.82 (m, 3 H), 1.96−2.06 (m, 1 H), 2.14−2.23 (m, 1 H), 2.24−2.25 (m, 1 H), 2.31 (s, 3 H; CH_3), 2.45 (dd, J = 12.2 Hz, J = 8.8 Hz, 1 H; SC*H*H), 2.76 (dd, J = 12.3 Hz, J = 3.4 Hz, 1 H; SCH*H*), 3.01−3.08 (m, 1 H; NCH). − ^{13}C NMR ($CDCl_3$): δ = 22.14 (CH_2), 30.84 (CH_2), 37.22 (CH_2), 40.68 (CH_3), 57.40 (CH_2), 65.52 (CH). − MS (EI, 70 eV); *m*/*z* (%): 229 (1) [M + H^+], 130 (2) [*cyclo*-($CH_2CH_2CH_2CHNCH_3$)CH_2S^+], 98 (14) [*cyclo*-($CH_2CH_2CH_2$-$CHNCH_3$)CH_2^+], 84 (100) [*cyclo*-($CH_2CH_2CH_2CHNCH_3$)$^+$]. − Mol. mass: calcd. 229.1738 (for $C_{12}H_{25}N_2S$); found 229.1736 [M + H^+] (HRMS).

(*S*,*S*)-Bis(2-benzylideneamino-3-methylbutyl) Sulfide (2b): Under anhydrous conditions freshly distilled benzaldehyde (62 mg, 0.59 mmol), Na_2SO_4 (500 mg) and the ion exchange resin DOWEX 50 W X 4 (strongly acidic; 0.5 mg) were added to a solution of diamine **1b** (50 mg, 0.25 mmol) in toluene (1 mL). The resulting suspension was stirred for 24 h at room temp. and, after filtration and washing of the residue with CH_2Cl_2, the combined solutions were concentrated in a rotary evaporator. From the residual oil the excess of benzaldehyde was removed by Kugelrohr distillation at 0.1 Torr and 85°C oven temp. for 2 h. The title compound was obtained as a highly viscous, colorless oil in quantitative yield (95 mg) and it was pure by ^{1}H and ^{13}C NMR. − $[\alpha]_D^{20} = +130$ ($c = 0.31$, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3082 cm^{-1} (w), 3061 (w), 3026 (w), 2958 (s), 2928 (m), 2870 (m), 2843 (m), 1644 (vs), 1580 (m), 1493 (s), 1469 (m), 1451 (m), 1387 (m), 1380 (m), 1380 (m), 754 (s), 693 (vs). − ^{1}H NMR ($CDCl_3$): δ = 0.86 (d, J = 6.9 Hz, 6 H; 4-CH_3), 1.82−1.96 (m, 1 H; 3-CH), 2.73 (dd, J = 12.6 Hz, J = 9.1 Hz, 1 H; 1-C*H*H), 2.82−2.94 (m, 2 H; 1-CH*H* and 2-CH), 7.34−7.45 (m, 3 H; *m*-CH and *p*-CH), 7.69 (dd, J = 7.2 Hz, J = 1.7 Hz, 2 H; *o*-CH), 8.16 (s, 1 H; N=CH). − ^{13}C NMR ($CDCl_3$): δ = 18.47 (CH_3), 19.65 (CH_3), 32.70 (CH), 36.92 (CH_2), 77.27 (CH), 128.20 (CH), 128.38 (CH), 130.28 (CH), 136.21 (C), 160.37 (N=CH). − MS (EI, 70 eV); *m*/*z* (%): 380 (1) [M^+], 337 (1) [M^+ − *i*Pr], 275 (19) [M^+ − PhCHNH], 232 (24) [M^+ − PhCHNH − *i*Pr], 174 (18) [PhCHNHCH(*i*Pr)CH_2^+], 160 (100) [*i*PrCHNCHPh$^+$], 106 (12) [PhCHNH_2^+], 104 (13) [PhCHN$^+$], 91 (20) [$C_7H_7^+$]. − $C_{24}H_{32}N_2S$ (380.60): calcd. C 75.74, H 8.48, N 7.36; found C 75.18, H 8.34, N 7.34. − Mol. mass calcd. 380.2286, found 380.2288 (HRMS).

(*S*,*S*)-Bis(2-benzylideneamino-4-methylpentyl) Sulfide (2c): According to the previous procedure diamine **1c** (100 mg, 0.43 mmol) was converted with benzaldehyde (110 mg, 1.03 mmol) in toluene (1 mL) with Na_2SO_4 (700 mg) and ion exchanger resin (1 mg) to give the title compound in quantitative yield (175 mg) as a highly viscous colorless oil, which was pure by ^{1}H and ^{13}C NMR. − $[\alpha]_D^{20} = +67$ ($c = 0.60$, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3083 cm^{-1} (w), 3062 (w), 3026 (w), 2954 (s), 2923 (m), 2913 (m), 2868 (m), 2846 (m), 1643 (vs), 1581 (m), 1466 (m), 1451 (m), 1384 (m), 1367 (m), 1308 (m), 755 (s), 693 (s). − ^{1}H NMR ($CDCl_3$): δ = 0.79 (d, J = 6.3 Hz, 3 H; 5-CH_3), 0.85 (d, J = 6.5 Hz, 3 H; 5′-CH_3), 1.38 (ddd, J = 12.9 Hz, J = 9.4 Hz, J = 3.5 Hz, 1 H; 3-C*H*H), 1.42−1.54 (m, 1 H; 4-CH), 1.64 (ddd, J = 13.3 Hz, J = 9.9 Hz, J = 4.3 Hz, 1 H; 3-CH*H*), 2.67−2.78 (m, 2 H; 1-CH_2), 3.24−3.33 (m, 1 H; 2-CH), 7.35−7.44 (m, 3 H; *m*-CH and *p*-CH), 7.67−7.73 (m, 2 H; *o*-CH), 8.22 (s br., 1 H; CH=N). − ^{13}C NMR ($CDCl_3$): δ = 21.30 (CH_3), 23.48 (CH_3), 24.51 (CH), 39.58 (CH_2), 44.61 (CH_2), 69.55 (CH), 128.18 (CH), 128.44 (CH), 130.43 (CH), 136.05 (C), 160.35 (CH=N). − MS (EI, 70 eV); *m*/*z* (%): 408 (1) [M^+], 351 (1) [M^+ − *i*Bu], 303 (8) [M^+ − PhCHNH], 260 (20) [M^+ − PhCHNH − *i*Pr], 234 (6) [PhCHNCH(*i*Bu)CH_2S^+], 220 (12) [PhCHNCH(*i*Bu)CH_2S-CH_2^+], 174 (100) [PhCHNCH*i*Bu$^+$], 132 (17) [PhCHNHCH-CH_2^+], 105 (19) [PhCHNH], 91 (17) [$C_7H_7^+$]. − Mol. mass: calcd. 408.2599, found 408.2602 (HRMS).

(*S*,*S*)-Bis(2-benzylideneamino-3-phenylpropyl) Sulfide (2d): According to the previous procedure diamine **1d** (50 mg, 0.17 mmol) was converted with benzaldehyde (42 mg, 0.40 mmol) in toluene (1 mL) with Na_2SO_4 (500 mg) and ion exchanger resin (0.5 mg) to give the title compound in quantitative yield (81 mg) as a highly viscous colorless oil, which was pure by ^{1}H and ^{13}C NMR. − $[\alpha]_D^{20} = -49$ ($c = 0.5$, $CHCl_3$). − IR (ATR): $\tilde{\nu}$ = 3083 cm^{-1} (w), 3060 (w), 3026 (m), 1642 (s), 1580 (m), 1494 (m), 1451 (m), 1382 (m), 1308 (m), 1081 (m), 1030 (m), 749 (s), 693 (vs). − ^{1}H NMR ($CDCl_3$): δ = 2.78 (d, J = 6.4 Hz, 2 H; 3-CH_2), 2.88 (dd, J = 13.0 Hz, J = 8.2 Hz, 1 H; 1-C*H*H), 3.00 (dd, J = 13.5 Hz, J = 4.9 Hz, 1 H; 1-CH*H*), 3.37−3.46 (m, 1 H; 2-CH), 7.06 (dd, J = 7.5 Hz, J = 1.5 Hz, 2 H; *o*-CH), 7.10−7.23 (m, 3 H; *m*-CH and *p*-CH), 7.33−7.43 (m, 3 H; *m*-CH and *p*-CH), 7.62 (dd, J = 7.5 Hz, J = 1.3 Hz, 2 H; *o*-CH), 7.88 (s br., 1 H; NH). − ^{13}C NMR ($CDCl_3$): δ = 38.69 (CH_2), 42.22 (CH_2), 73.20 (CH), 126.05 (CH), 128.09 (CH), 128.14 (CH), 128.42 (CH), 129.64 (CH), 130.46 (CH), 135.96 (C), 138.61 (C), 160.96 (CH=N). − MS (EI, 70 eV); *m*/*z* (%): 477 (1) [M + H^+], 385 (6) [M^+ − Bn], 371 (15) [M^+ − PhCHNH], 281 (20) [M + H^+ − Bn − PhCHNH], 280 (99) [M^+ − Bn − $PhCHNH_2$], 268 (13) [PhCHNHCH(Bn)$CH_2SCH_2^+$], 254 (24) [PhCHNCH(Bn)CH_2S^+], 222 (13) [PHCHNCH(Bn)CH_2^+], 208 (100) [BnCHNCHPh$^+$], 164 (42) [BnCH$CH_2SCH_2^+$], 162 (39) [PhCHCHCHSCH_2^+], 149 (23) [PhCHCHCH_2S^+], 130 (20) [PhCHNCCH_2^+], 117 (47) [PhCHCHCH_2^+], 106 (43) [PhCH-NH_2^+], 91 (94) [$C_7H_7^+$]. − $C_{32}H_{32}N_2S$ (476.69): calcd. C 80.63, H 6.77, N 5.88; found C 79.53, H 6.78, N 5.74. − Mol. mass: calcd. 477.2364 ($C_{32}H_{32}N_2S$), found 477.2361 [M + H^+] (HRMS).

Ethyl 2-Oxo-1-(3-oxobutyl)cyclopentane-1-carboxylate (6). − General Procedure: The metal salt **5** (0.017 mmol, 5 mol-%), chiral ligand **1** or **2** (0.025 mmol, 7.5 mol-%) and oxo ester **3** (52 mg, 0.33 mmol) were dissolved in CH_2Cl_2 (0.5 mL). After stirring for 1 h at room temp., MVK (**4**) (30 µL, 0.37 mmol) was added and the mixture stirred overnight, again at room temp. Subsequently, the mixture was diluted with MTB (1 mL) and directly transferred on an SiO_2 column (3 cm) and the product eluted with PE/MTB, 1:1 (R_f = 0.25). The product mixture was analyzed by chiral GC, isothermic elution (130°C); enantiomers of **6**: t_R = 30.3 min and 32.4 min.

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