

Synthesis of Chiral Thiazoline Ligands Tethered to a Sulfur Function and First Immobilization of a Thiazoline-Ligand

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ABSTRACT: A new family of thiazoline ligands tethered to a sulfanyl or a sulfinyl group has been prepared using short and efficient reaction sequences. Among the different structures, one sulfanyl-thiazoline homopolymer was synthesized as a first example of an immobilized thiazoline ligand. The catalytic properties of these new ligands were evaluated in the Pd-catalyzed allylic substitution. © 2010 Wiley Periodicals, Inc. *Heteroatom Chem* 21:242–249, 2010; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20603

INTRODUCTION

Compared with the widely used nitrogen and phosphorus-containing chiral ligands in asymmetric metal-catalyzed reactions, the sulfur counterparts have been less studied for this purpose. However, in recent years, the number of studies dealing with the chiral sulfur-containing ligands has increased con-

siderably leading to the publication of some reviews [1].

Among the large variety of chiral ligands, the thiazolines, which are sulfur-analogues of oxazolines, represent a young family of ligands [2]. They have proved to be useful sulfur-containing ligands in various metal-catalyzed reactions and to behave sometimes differently from oxazolines. Among the various structures of thiazoline-ligands including bis(thiazolines) [3a–f], phosphine-thiazolines [3d,e], pyridyl-thiazolines [3d–f], oxazoline-thiazolines [3g,l], ferrocenyl-bis(thiazolines) [3h], hydroxyalkyl-thiazolines [3j], and tris(thiazolines) [3k], only one example of sulfanyl-thiazoline ligand has been described [3i]. These ligands are of interest because they contain one S-coordinating and one S-noncoordinating atom [1a].

This paper describes the preparation of a series of sulfanyl- and sulfinyl-thiazolines, and the first example of the immobilization of a thiazoline ligand. The catalytic properties of these new ligands have been evaluated in the well-known reaction test, the Pd-catalyzed allylic substitution, and the results are reported herein.

RESULTS AND DISCUSSION

Four types of structures have been selected for this study (Fig. 1). Some of them can be considered as the sulfur analogues of sulfanyl-oxazoline *N*, *S*-ligands described by Williams [4]. Ligands of type **I** and **II** are thiazolines bearing, respectively, a sulfanyl or a

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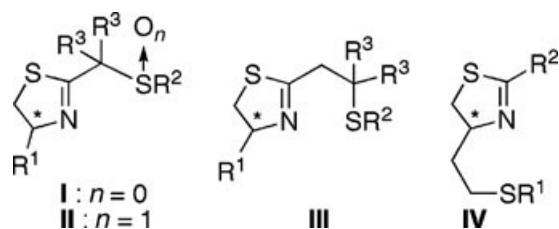
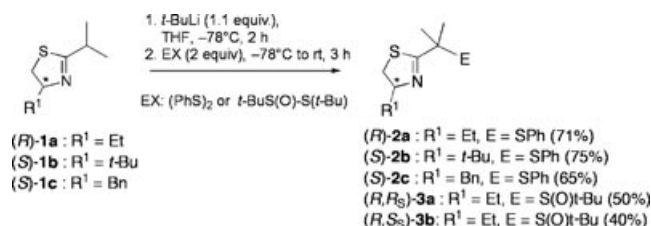


FIGURE 1 Selected structures of thiazoline ligands.

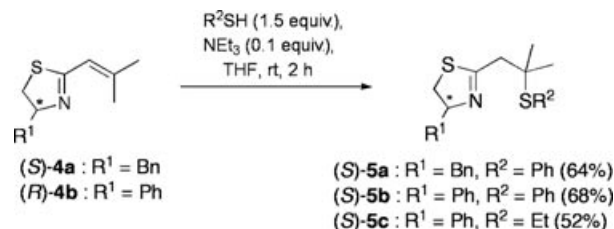
sulfinyl group in α -position. Ligands **III** possess a sulfanyl group in β -position. In the case of ligands **IV**, the sulfanyl group belongs to the substituent placed in the 4-position of the thiazoline. Depending on the position of the sulfur function on the thiazoline, the proposed bidentate thiazoline-ligands may form five- or six-membered ring metal complexes (five for **I** and **II**; six for **III** and **IV**).

We first prepared α -sulfanyl-thiazolines **2a–c**, which are, respectively, substituted in the 4-position with an ethyl, a tert-butyl, and a benzyl group. They were prepared from the corresponding enantiopure 2-isopropyl-thiazolines **1a–c** [3b] by deprotonation in α -position with tert-butyllithium and addition of diphenyl disulfide (Scheme 1). The expected products were obtained in satisfactory yields (65–75%). In a similar way, diastereomeric α -sulfanyl-thiazolines (*R*, *Rs*)-**3a** and (*R*, *Ss*)-**3b** were synthesized from thiazoline (*R*)-**1a** and the (*R*) or (*S*) tert-butyl thiosulfinate [5] respectively.

β -Sulfanyl-thiazolines **5** were prepared by 1,4-addition of a thiol to α,β -unsaturated thiazolines **4**. The synthesis of thiazolines of type **4** was previously described by some of us and consists in a Horner–Wadsworth–Emmons (HWE) reaction of the corresponding thiazoline-phosphonates with acetone [6]. The two-methyl groups on the double bond were placed to avoid the formation of a new stereogenic center after the 1,4-addition. Thus, two α,β -unsaturated thiazolines **4a** and **4b**, substituted in the 4-position with a benzyl and with a phenyl group, respectively, were reacted with thiophenol or ethanethiol, in the presence of a catalytic amount of



SCHEME 1



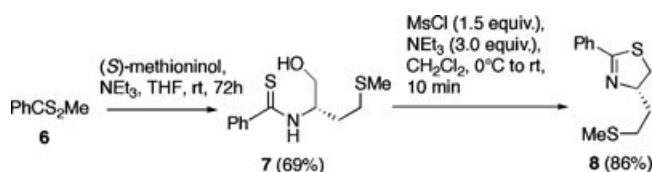
SCHEME 2

triethylamine, to afford β -sulfanyl-thiazolines **5a–c** in moderate yields (52–68% yield; Scheme 2).

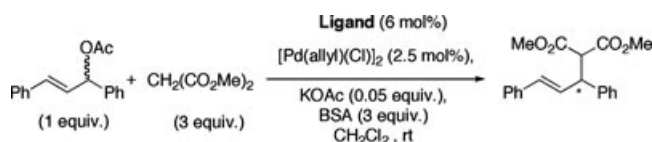
Compound **8** was chosen as an example of sulfanyl-thiazoline ligand, in which the chain bearing the sulfanyl group is placed in the 4-position of the thiazoline. The synthesis was performed in two steps (thioacylation and intramolecular cyclization) starting from phenyldithioic methyl ester [7] and commercially available (*S*)-methioninol [8]. The nonoptimized overall yield was 59% (Scheme 3).

All prepared ligands were tested in the Pd-catalyzed allylic substitution using 1,3-diphenylpropenyl acetate and dimethylmalonate, in the presence of bis(trimethylsilyl)acetamide, potassium acetate (KOAc), and $[\text{Pd}(\text{C}_6\text{H}_5)_2\text{Cl}]_2$ (Scheme 4). The results are given in Table 1.

α -Sulfanyl-thiazolines **2a–c** (Table 1, entries 1–3) gave almost complete conversion after 24 h and quite similar enantiomeric excess (37%, 43%, and 40% ee, respectively). Ligand (*R*)-**2a** favored the formation of product (*R*), and ligands (*S*)-**2b,c** favored the (*S*) product. These results show that in this series the steric hindrance of the substituent in the 4-position of the thiazoline does not influence the asymmetric induction, which is probably under electronic control (the trans effect of the sulfur atom). α -Sulfanyl-thiazolines **3a** and **3b**, which



SCHEME 3



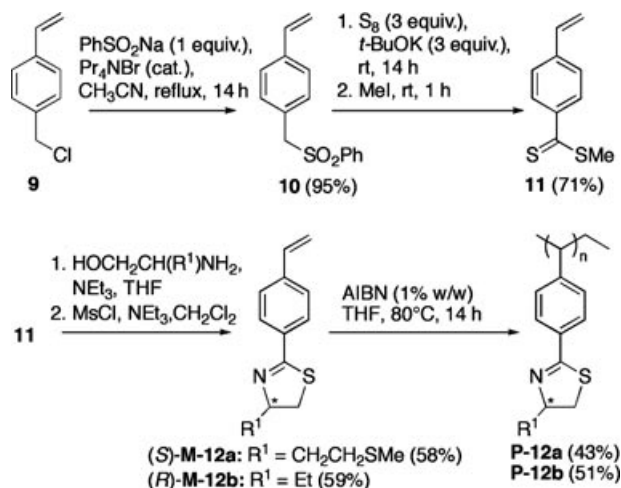
SCHEME 4

TABLE 1 Pd-Catalyzed Asymmetric Allylic Substitution Using Ligands **2a–c**, **3a–b**, **5a–c**, and **8**

Entry	Ligand	Conversion % (time)	Enantiometric Excess (ee) (%)	Product Configuration
1	(<i>R</i>)- 2a	>95 (24 h)	37	(<i>R</i>)
2	(<i>S</i>)- 2b	>95 (24 h)	43	(<i>S</i>)
3	(<i>S</i>)- 2c	>95 (48 h)	40	(<i>S</i>)
4	(<i>R,R_S</i>)- 3a	30 (168 h)	47	(<i>R</i>)
5	(<i>R,S_S</i>)- 3b	30 (168 h)	47	(<i>R</i>)
6	(<i>S</i>)- 5a	50 (120 h)	49	(<i>S</i>)
7	(<i>S</i>)- 5b	60 (120 h)	73	(<i>S</i>)
8	(<i>S</i>)- 5c	80 (120 h)	42	(<i>S</i>)
9	(<i>S</i>)- 8	>95 (24 h)	66	(<i>R</i>)

are diastereomers having the same thiazoline and opposite configurations on the sulfur stereocenter, gave a low conversion of 30% after 168 h (entries 4 and 5), probably due to the weaker coordination of the metal by the sulfinyl ligand (compared to a sulfanyl group). Both of them afforded an enantiomeric excess of 47% in favor of the (*R*) product, indicating that the sense of the asymmetric induction is determined by the configuration of the carbon stereocenter of the thiazoline (in this case *R*) and not by that of the sulfinyl group. This result differs from the results obtained with some sulfinyl-oxazolines ligands, for which the configuration at the sulfur center was found to be important for the enantioselectivity [9]. With β -sulfanyl-thiazoline ligands **5a–c**, conversions were still incomplete after 120 h (entries 6–8). The three ligands of (*R*) configuration afforded the (*R*) stereoisomer as the main product. Phenylsulfanyl-thiazoline **5b** (with R^1 , R^2 = Ph) gave the best enantiomeric excess (73% ee). Upon replacing the phenyl by benzyl in ligand **5a** (R^1 = Bn, R^2 = Ph), or the phenylsulfanyl by an ethylsulfanyl in ligand **5c**, the enantioselectivity decreased (from 73% to 49% and 42%, respectively). For this type of ligand, both steric and electronic effects seem to be involved in the asymmetric induction. Sulfanyl-thiazoline **8** derived from (*S*)-methioninol afforded a total conversion after 24 h and an enantiomeric excess of 66% in favor of the (*R*) product.

Immobilized chiral ligands for asymmetric metal-catalyzed reactions have been widely studied and reviewed because of their major advantages: easy recoverability and possibility of the catalyst recycling [10]. If immobilized oxazolines have been well studied [11], to the best of our knowledge, no example with thiazolines has ever been reported. Therefore, we decided to immobilize a thiazoline-ligand by polymerization of a chiral thiazoline monomer [12], to examine the effect of the

**SCHEME 5**

polymer on the activity and selectivity of the catalyst and then to attempt its recycling.

From a structural point of view, the chosen ligand was the polymeric analogue of the sulfanyl-thiazoline **8** described above, which gave a satisfactory ee of 66% and seemed to be easy to tether to a polymer through the 2-position of the thiazoline. Thus, monomer **M-12a** was synthesized from the commercially available 1-(chloromethyl)-4-vinylbenzene **9**, in four steps, according to Scheme 5. First, we prepared the styrene-dithioester **11** using a general method described previously to access aromatic dithioesters [13]. The overall yield via sulfone **10** was 68%. Starting from dithioester **11**, sulfanyl-thiazoline **M-12a** was prepared in 58% yield by a two-steps sequence (thioacylation with methioninol and cyclization). Finally, the radical polymerization of **M-12a** was performed using AIBN as initiator, in THF at 80°C. The polymer **P-12a** was obtained in a moderate yield of 43%. Unfunctionalized thiazoline **M-12b** was prepared similarly, as the precursor of the homopolymer monodentate ligand **P-12b**, to compare it to the former polymeric bidentate thiazoline ligand **P-12a**. The synthesis of **P-12b** was similar, just replacing the (*S*)-methioninol with (*R*)-2-amino-1-butanol. The overall yield for **M-12b** starting from **11** was 59%, and the polymer **P-12b** was obtained in a 51% yield.

Tested in the selected Pd-catalyzed allylic substitution, the polymeric ligand **P-12a** showed the same catalytic activity as the corresponding monomeric ligand **8** (full conversion after 24 h) and also favored the (*R*) product, albeit with a lower enantiomeric excess (36% ee). Both monomeric and polymeric monodentate ligands **M-12b** and **P-12b** were found to be totally inactive in the test reaction. This result seems to indicate that two nearby thiazolines in the

polymer do not behave as a bidentate ligand and that the sulfanyl-thiazoline moiety in **P-12a** clearly acts as a bidentate ligand. We then attempted to reuse the catalyst with **P-12a** as ligand. After the first run, the catalyst was recovered by precipitation in diethyl ether and filtration and used in a second catalytic cycle. After 48 h, the conversion poorly reached 15% (probably due to metal leaching during the precipitation. Black precipitate of Pd(0) could be observed in the reaction mixture.) and the enantiomeric excess decreased from 36% to 8%. Although this result is rather disappointing, supplementary experiments should be done to improve the treatment at the end of the catalytic cycle (change of the solvent), but also by changing the polymer structure by copolymerization of **M-12a** with styrene or divinylstyrene.

CONCLUSION

In conclusion, a new family of thiazoline ligands, which are tethered to a sulfanyl or a sulfinyl group through their 2- or 4-position, was synthesized. A first example of an immobilized thiazoline ligand prepared in five steps starting from 1-(chloromethyl)-4-vinylbenzene is also described. The methods used for the syntheses should allow easy modulation of the ligand structure by modifying the substituents on the thiazoline or on the sulfur atom, or the spacer between the thiazoline and the sulfanyl function. In the case of the immobilized sulfanyl-thiazoline, the structure of the polymeric support could also be changed. All the newly synthesized ligands were examined for their ability to introduce asymmetric induction in the Pd-catalyzed allylic substitution, but none of them gave a high-enantiomeric excess in this reaction. Thiazoline-polymer **P-12a** gave total conversion after 24 h (the same as its monomeric analogous **8**), but lower ee (36% vs 66% ee). The polymer structure did not allow the recycling of the catalyst. Further studies concerning the described sulfanyl- and sulfinyl-thiazolines in other metal-catalyzed reactions will be undertaken to expand the application of these new thiazoline ligands in asymmetric catalysis.

EXPERIMENTAL

General

NMR spectra were recorded on a Bruker DRX 400 or a DPX 250 spectrometer. Chemical shifts (δ) are reported in ppm (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad) and are indicated in ppm using TMS as internal standard. Coupling constants (J) are given in hertz. Mass spectra were obtained on a GC/MS Saturn 2000 spectrometer and

HRMS on a Waters QTOF micro spectrometer. IR spectra were recorded with a Perkin Elmer 16 PC FT-IR instrument. Analytical data were obtained using a THERMOQUEST NA 2500 instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. THF was purified with a PURE-SOLV apparatus developed by Innovative Technology Inc. Reaction progress was monitored by thin-layer chromatography (TLC) using Merck silica gel 60 aluminum sheets (F254). The plates were visualized by either UV light (254 nm), or by a solution of potassium permanganate. Column chromatography was performed using Merck silica gel Si 60 (40–63 μ m).

Synthesis of α -Sulfanyl Thiazolines (**2**) and of α -Sulfinyl Thiazolines (**3**)

General Procedure. *t*-BuLi (1.1 equiv) was added dropwise to a solution of thiazoline **1** (1 equiv) in dry THF ($c = 0.4$ M) at -78°C . The yellow solution was stirred for 2 h at this temperature before the corresponding sulfur electrophile (2 equiv dissolved in dry THF) was added. The mixture was allowed to reach room temperature within 1 h and was stirred overnight. Water was added, and the product was extracted with Et_2O . The organic layers were dried over MgSO_4 , filtered, and solvents were removed in vacuum to yield the crude product, which was purified by column chromatography.

(R)-4-Ethyl-2-(1-phenylsulfanyl-1-methylethyl)-thiazoline (2a): Prepared by the general procedure from **1a** and diphenyl disulfide, purified by chromatography on silica gel (eluent: pentane/ Et_2O 85:15), yellow oil, 71% yield, $[\alpha]_D^{20} +52$ (c 0.95, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): $\delta = 0.89$ (t, $^3J_{\text{HH}} = 7.4$ Hz, 3H, CH_2CH_3), 1.43–1.73 (m, 2H, CH_2CH_3), 1.55 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.57 (s, 3H, $\text{C}(\text{CH}_3)_2$), 2.95 (dd, $^2J_{\text{HH}} = 10.8$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, 1H, SCHH), 3.35 (dd, $^2J_{\text{HH}} = 10.8$ Hz, $^3J_{\text{HH}} = 8.3$ Hz, 1H, SCHH), 4.25–4.32 (m, 1H, CHET), 7.26–7.35, and 7.51–7.55 (m, 5H, C_6H_5). ^{13}C NMR (CDCl_3 , 101 MHz): $\delta = 10.9$ (CH_2CH_3), 27.7 (CH_2CH_3), 28.4, and 28.5 ($\text{C}(\text{CH}_3)_2$), 38.0 (SCH $_2$), 51.9 ($\text{C}(\text{CH}_3)_2$), 78.7 (CHET), 128.6 (C_6H_5), 129.1 (C_6H_5), 131.9 (C_{ipso}), 136.2 (C_6H_5), 175.3 (SCN). IR (cm^{-1}): 2964, 2827, 1610, 1438, 1128, 1026, 879, 749, 692.

(S)-4-Tert-Butyl-2-(1-phenylsulfanyl-1-methylethyl)thiazoline (2b): Prepared by the general procedure from **1b** and diphenyl disulfide, purified by chromatography on silica gel (eluent: pentane/ Et_2O 85:15), yellow oil, 75% yield, $[\alpha]_D^{20} -48$ (c 1.05, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): $\delta = 0.88$ (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.566 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.568 (s, 3H, $\text{C}(\text{CH}_3)_2$), 3.05 (“t”, 1H, SCHH), 3.20

(dd, $^2J_{\text{HH}} = 10.9$ Hz, $^3J_{\text{HH}} = 8.7$ Hz, 1H, SCHH), 4.03 (dd, $^3J_{\text{HH}} = 10.7$ Hz, $^3J_{\text{HH}} = 8.7$ Hz, 1H, CHtBu), 7.25–7.34 and 7.51–7.55 (m, 5H, C₆H₅). ¹³C NMR (CDCl₃, 101 MHz): $\delta = 26.8$ (C(CH₃)₃), 28.2 and 28.8 (C(CH₃)₂), 34.6 (SCH₂), 35.0 (C(CH₃)₃), 52.3 (C(CH₃)₂), 87.3 (CHtBu), 128.6 (C₆H₅), 128.9 (C₆H₅), 132.1 (C_{ipso}), 136.2 (C₆H₅), 174.4 (SCN).

(S)-4-Benzyl-2-(1-phenylsulfanyl-1-methylethyl)thiazoline (**2c**): Prepared by the general procedure from **1c** and diphenyl disulfide, purified by chromatography on silica gel (eluent: pentane/Et₂O 95:5); yellow oil, 65% yield. ¹H NMR (CDCl₃, 250 MHz) $\delta = 1.57$ and 1.59 (2s, 6H, C(CH₃)₂), 2.53 (dd, $^2J_{\text{HH}} = 13.6$, $^3J_{\text{HH}} = 9.3$, 1H, CHHPh), 3.00 (dd, $^2J_{\text{HH}} = 13.6$, $^3J_{\text{HH}} = 4.9$, 1H, CHHPh), 3.01 (dd, $^2J_{\text{HH}} = 11.1$, $^3J_{\text{HH}} = 6.2$, 1H, CHHS), 3.18 (dd, $^2J_{\text{HH}} = 11.1$, $^3J_{\text{HH}} = 8.5$, 1H, CHHS), 4.59 (m, 1H, CHN), 7.11–7.35 and 7.54–7.58 (m, 10H, Har). ¹³C NMR (CDCl₃, 63 MHz) $\delta = 28.2$ and 28.3 (C(CH₃)₂), 37.4 (CH₂Ph), 39.8 (CH₂S), 51.8 (C(CH₃)₂), 78.3 (CHN), 126.4, 128.4, 128.6, 129.3, 129.4, 131.7, 136.3, 138.5, 176.3 (S–C=N). IR (cm⁻¹): 3010, 2960, 2920, 2850, 1640, 1490, 1450, 1030.

(R,Rs)-4-Ethyl-2-(1-tert-butylsulfinyl-1-methylethyl)thiazoline (**3a**): Prepared by the general procedure from **1a** and (R)-tert-butyl-tert-butanethiosulfinate, purified by chromatography on silica gel (eluent: pentane/AcOEt 50:50), $[\alpha]_{\text{D}}^{20} +128$ (c 0.9, acetone). ¹H NMR (CDCl₃, 400 MHz): $\delta = 1.01$ (t, $^3J_{\text{HH}} = 7.4$ Hz, 3H, CH₂CH₃), 1.31 (s, 9H, C(CH₃)₃), 1.53–1.89 (m, 2H, CH₂CH₃), 1.57 (s, 3H, C(CH₃)₂), 1.59 (s, 3H, C(CH₃)₂), 2.95 (dd, $^2J_{\text{HH}} = 11.0$ Hz, $^3J_{\text{HH}} = 8.0$ Hz, 1H, SCHH), 3.32 (dd, $^2J_{\text{HH}} = 11.0$ Hz, $^3J_{\text{HH}} = 8.6$ Hz, 1H, SCHH), 4.28–4.36 (m, 1H, CHEt). ES-MS *m/z* (%): 262 (M + H, 21), 157 (100), 156 (32).

(R,Ss)-4-Ethyl-2-(1-tert-butylsulfinyl-1-methylethyl)thiazoline (**3a**): Prepared by the general procedure from **1a** and (S)-tert-butyl-tert-butanethiosulfinate, purified by chromatography on silica gel (eluent: pentane/AcOEt 50:50), $[\alpha]_{\text{D}}^{20} -117$ (c 1.1, acetone). ¹H NMR (CDCl₃, 400 MHz): $\delta = 1.00$ (t, $^3J_{\text{HH}} = 7.4$ Hz, 3H, CH₂CH₃), 1.29 (s, 9H, C(CH₃)₃), 1.54–1.88 (m, 2H, CH₂CH₃), 1.55 (s, 3H, C(CH₃)₂), 1.59 (s, 3H, C(CH₃)₂), 2.89 (dd, $^2J_{\text{HH}} = 11.0$ Hz, $^3J_{\text{HH}} = 8.9$ Hz, 1H, SCHH), 3.33 (dd, $^2J_{\text{HH}} = 11.0$ Hz, $^3J_{\text{HH}} = 8.6$ Hz, 1H, SCHH), 4.26–4.34 (m, 1H, CHEt). ES-MS *m/z* (%): 262 (M + H, 22), 157 (100), 156 (25).

Synthesis of β -Sulfanyl Thiazolines **5**

General Procedure. Thiophenol (1.2 mmol) and then NEt₃ (0.1 mmol) were added to the α,β -unsaturated thiazoline **4** (1 mmol), dissolved in dry THF (20 mL), at room temperature. The result-

ing mixture was stirred until completion (about 1 h, monitored by TLC). The solvent was evaporated, and the product was purified by column chromatography.

(S)-4-Benzyl-2-[2-phenylsulfanyl-2-methylpropyl]thiazoline (**5a**): Prepared by the general procedure from **4a** and thiophenol, purified by chromatography on silica gel (eluent: pentane/Et₂O 95:5); yellow oil, 64% yield, $[\alpha]_{\text{D}}^{20} -79$ (c 1, acetone). ¹H NMR (CDCl₃, 250 MHz) $\delta = 1.46$ and 1.48 (2s, 6H, (CH₃)₂C), 2.51 (dd, $^2J_{\text{HH}} = 13.6$, $^3J_{\text{HH}} = 9.2$, 1H, CHHPh), 2.64 (s, 2H, CH₂C=N), 3.07 (dd, $^2J_{\text{HH}} = 13.6$, $^3J_{\text{HH}} = 4.9$, 1H, CHHPh), 3.35 (dd, $^3J = 9.4$, $^2J_{\text{HH}} = 10.9$, 1H, CHHS), 3.51 (dd, $^3J_{\text{HH}} = 8.8$, $^2J_{\text{HH}} = 10.9$, 1H, CHHS), 4.62 (m, 1H, CHN), 7.26–7.63 (m, 10Har). ¹³C NMR (CDCl₃, 63 MHz) $\delta = 27.6$ and 28.1 (CH₃), 37.6 (CH₂Ph), 42.8 (CH₂S), 44.1 (CH₂C=N), 47.6 (C(CH₃)₂), 80.3 (CHPh), 125.6, 126.5, 127.7, 142.2, 170.8 (S–C=N).

(R)-4-Phenyl-2-[2-phenylsulfanyl-2-methylpropyl]thiazoline (**5b**): Prepared by the general procedure from **4b** and thiophenol, purified by chromatography on silica gel (eluent: pentane/Et₂O 95:5); yellow oil, 68% yield. ¹H NMR (CDCl₃, 250 MHz) δ (ppm): 1.45 and 1.50 (2s, 6H, (CH₃)₂C), 2.64 (s, CH₂C=N), 3.35 (t, $^3J_{\text{HH}} = 7.50$, 1H, CHHS), 3.42 (dd, $^3J_{\text{HH}} = 7.5$, $^2J_{\text{HH}} = 10.0$, 1H, CHHS), 5.46 (t, $^3J_{\text{HH}} = 10.0$, 1H, CHN), 7.26–7.63 (m, 10Har). ¹³C NMR (CDCl₃, 63 MHz) δ (ppm): 27.9 (CH₃), 28.8 (CH₃), 42.8 (CH₂S), 44.2 (CH₂C=N), 47.8 (C(CH₃)₂), 80.3 (CHPh), 125.6, 126.5, 127.7, 142.2, 171.5 (S–C=N). IR (cm⁻¹): 2900, 1600, 1440, 1020. Anal. calcd for: C₁₉H₂₁NS₂: C, 69.68%; H, 6.46%; N, 4.28%; S 19.58%. Found: C, 69.62%; H, 6.46%; N, 4.38%; S 19.32%.

(R)-4-Phenyl-2-[2-ethylsulfanyl-2-methylpropyl]thiazoline (**5c**): Prepared by the general procedure from **4b** and ethanethiol, purified by chromatography on silica gel (eluent: pentane/Et₂O 95:5); yellow oil, 52% yield. ¹H NMR (CDCl₃, 250 MHz) δ (ppm): 1.25 (t, $^3J_{\text{HH}} = 7.4$, 3H, CH₃CH₂), 1.46 and 1.47 (2s, 6H, (CH₃)₂C), 2.62 (q, $^3J_{\text{HH}} = 7.4$, 2H, CH₂CH₃), 2.98 (s, 2H, CH₂C=N), 3.20 (dd, $^2J_{\text{HH}} = 10.9$, $^3J_{\text{HH}} = 9.9$, 1H, CHHS), 3.68 (dd, $^2J_{\text{HH}} = 10.9$, $^3J_{\text{HH}} = 8.9$, 1H, CHHS), 5.46 (t, $^3J_{\text{HH}} = 9.0$, 1H, CHN), 7.26–7.36 (m, 5Har). ¹³C NMR (CDCl₃, 63 MHz) δ (ppm): 13.3 (CH₃CH₂), 21.3 (CH₂CH₃), 27.8 and 28.1 (2CH₃), 40.8 (CH₂S), 43.0 (CH₂C=N), 45.8 ((CH₃)₂C), 79.1 (CHN), 125.6, 126.5, 127.6, 141.1, 167.1 (S–C=N).

Synthesis of (S)-4-Methylsulfanylethyl-2-phenyl-2-thiazoline **8**

Step 1: Thioacylation. Thioamide **7** was prepared from dithiobenzoic acid methyl ester (420 mg,

2.5 mmol) and (S)-methioninol (338 mg, 2.5 mmol) according to the procedure described in [8]. Purification by column chromatography (EtOAc/pentane: 60/40, $R_f = 0.61$ in UV) yielded 365 mg (1.43 mmol, 57%) of the title compound as a viscous yellow oil. $[\alpha]_D^{20} +12$ (c 0.9, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): $\delta = 2.05\text{--}2.23$ (m, 2+1H, SCH_2CH_2 and OH), 2.14 (s, 3H, SCH_3), 2.59–2.70 (m, 2H, SCH_2CH_2), 3.85–3.94 (m, 2H, CH_2OH), 4.93–5.00 (OCH_2CH), 7.37–7.48 (m, 3H, C_6H_5), 7.75–7.77 (m, 2H, C_6H_5), 8.04 (br, 1H, NH). ^{13}C NMR (CDCl_3 , 63 MHz): $\delta = 15.8$ (SCH_3), 29.7 (SCH_2CH_2), 30.7 (SCH_2CH_2), 56.7 (OCH_2CH), 63.2 (CH_2OH), 126.9 (C_6H_5), 128.6 (C_6H_5), 131.4 (C_6H_5), 141.9 (C_{ipso}), 199.4 (NCS). IR (cm^{-1}): 3243, 2914, 1516, 1447, 1373, 1231, 1029, 966, 692. TOF MS $\text{ES}^+ [\text{M} + \text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{18}\text{NOS}_2$: 256.0830; found: 256.0830. ES-MS m/z (%): 256 (M + H, 27), 238 (11), 208 (100), 121 (5).

Step 2: Cyclization. Thioamide **7** (693 mg, 2.7 mmol) was transformed into thiazoline **8** according to the procedure described in [8]. Purification by column chromatography (Et_2O /pentane: 10/90, $R_f = 0.18$ in UV) yielded 560 mg (2.34 mmol, 86%) of the title compound as a colorless oil. $[\alpha]_D^{20} -97$ (c 0.95, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): $\delta = 1.93\text{--}2.20$ (m, 2H, SCH_2CH_2), 2.16 (s, 3H, SCH_3), 2.70–2.81 (m, 2H, SCH_2CH_2), 3.10 (dd, $^2J_{\text{HH}} = 10.9$ Hz, $^3J_{\text{HH}} = 8.1$ Hz, 1H, SCHH), 3.53 (dd, $^2J_{\text{HH}} = 10.9$ Hz, $^3J_{\text{HH}} = 8.4$ Hz, 1H, SCHH), 4.74–4.82 (m, 1H, NCH), 7.38–7.84 (m, 5H, C_6H_5). ^{13}C NMR (CDCl_3 , 101 MHz): $\delta = 15.8$ (SCH_3), 31.7 (SCH_2CH_2), 34.9 (SCH_2CH_2), 38.2 (SCH_2), 76.7 (NCH), 128.5 (C_6H_5), 128.6 (C_6H_5), 131.3 (C_6H_5), 133.5 (C_{ipso}), 167.0 (SCN). IR (cm^{-1}): 2914, 2850, 1597, 1446, 1466, 1245, 936, 764, 689, 610. TOF MS $\text{ES}^+ [\text{M} + \text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{16}\text{NS}_2$: 238.0724; found: 238.0728. ES-MS m/z (%): 238 (M + H, 41), 135 (100), 87 (59).

Synthesis of Styrene-Dithioester **11**

Step 1: Synthesis of 4-benzene Sulfonyl Methyl Styrene 10. 4-Vinylbenzyl chloride **9** (5.33 g, 31.4 mmol) was added to a mixture of sodium benzenesulfinate (10.31 g, 62.8 mmol) and tetrapropylammonium bromide (0.52 g, 2.3 mmol) in acetonitrile. After heating the mixture for 14 h at 80°C, solvent was evaporated and the residue was quenched by addition of water (100 mL). The sulfone **11** was extracted with dichloromethane (3 × 80 mL); the combined extracts were washed with water (3 × 100 mL), dried over MgSO_4 , filtered, and solvent was evaporated in vacuo to yield 7.71 g (29.8 mmol, 95%) of the title compound as a white solid. ^1H NMR (CDCl_3 , 400 MHz): $\delta = 4.30$ (s, 2H, SCH_2), 5.28 (dd,

$^2J_{\text{HH}} = 0.8$ Hz, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 5.74 (dd, $^2J_{\text{HH}} = 0.8$ Hz, $^3J_{\text{HH}} = 17.6$ Hz, CHCHH), 6.67 (dd, $^3J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 7.02–7.04 (m, 2H, C_6H_5), 7.28–7.30 (m, 2H, C_6H_5), 7.43–7.48 (m, 2H, C_6H_5), 7.58–7.66 (m, 3H, C_6H_5). ^{13}C NMR (CDCl_3 , 101 MHz) $\delta = 62.8$ (SCH_2), 115.0 (CHCH_2), 126.5 (C_6H_5), 127.5 (C_6H_5), 128.8 (C_6H_5), 129.0 (C_6H_5), 131.1 (C_6H_5), 133.9 (C_6H_5), 136.2 (CHCH_2), 138.0 (C_6H_5), 138.2 (C_6H_5). IR (cm^{-1}): 1291, 1145, 1084, 907, 854, 744, 686, 600.

Step 2. Synthesis of 4-Vinyl-dithiobenzoic Acid Methyl Ester 11. Potassium tert-butoxide (5.72 g, 51.0 mmol) was added to a mixture of sulfone **10** (4.39 g, 17.0 mmol) and sulfur (13.1 g, 51.0 mmol) in THF (110 mL). The red solution was allowed to react 14 h before iodomethane (2.12 mL, 34.0 mmol) was carefully added. After another hour, solvent was evaporated under vacuum, the residue suspended in Et_2O /pentane (1:1), filtered, and the filtrate concentrated. The crude product was purified by column chromatography (first pentane, then EtOAc/pentane: 2/98, $R_f = 0.40$, UV or KMnO_4) to afford 2.35 g (12.1 mmol, 71%) of the title compound as a red liquid. ^1H NMR (CDCl_3 , 400 MHz): $\delta = 2.78$ (s, 3H, SCH_3), 5.39 (d, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 5.87 (d, $^3J_{\text{HH}} = 17.6$ Hz, CHCHH), 6.74 (dd, $^3J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 7.41–7.43 (m, 2H, C_6H_5), 8.00–8.02 (m, 2H, C_6H_5). ^{13}C NMR (CDCl_3 , 101 MHz) $\delta = 20.7$ (SCH_3), 116.4 (CHCH_2), 126.2 (C_6H_5), 127.3 (C_6H_5), 136.1 (CHCH_2), 141.6 (C_6H_5), 144.2 (C_6H_5), 288.2 (SCS). IR (cm^{-1}): 2911, 1597, 1402, 1238, 1178, 1050, 884, 841, 773.

Synthesis of Monomeric Thiazolines **M-12**

(S)-4-Methylsulfanylethyl-2-(4-vinyl)phenyl-2-thiazoline M-12a. The product was prepared from dithioester **11** (304 mg, 1.56 mmol) and (S)-methioninol (211 mg, 1.56 mmol) according to the procedure described in [8], without isolation of the thioamide. Purification by column chromatography (Et_2O /pentane: 10/90, $R_f = 0.31$ in UV or iodine) yielded 240 mg (0.91 mmol, 58%) of the title compound as a colorless oil. $[\alpha]_D^{20} -90$ (c 1.0, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): $\delta = 1.92\text{--}2.20$ (m, 2H, SCH_2CH_2), 2.15 (s, 3H, SCH_3), 2.73–2.77 (m, 2H, SCH_2CH_2), 3.09 (dd, $^2J_{\text{HH}} = 10.8$ Hz, $^3J_{\text{HH}} = 8.1$ Hz, 1H, SCHH), 3.52 (dd, $^2J_{\text{HH}} = 10.8$ Hz, $^3J_{\text{HH}} = 8.4$ Hz, 1H, SCHH), 4.73–4.81 (m, 1H, NCH), 5.33 (d, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 5.83 (d, $^3J_{\text{HH}} = 17.6$ Hz, CHCHH), 6.73 (dd, $^3J_{\text{HH}} = 17.6$ Hz, $^3J_{\text{HH}} = 10.9$ Hz, CHCHH), 7.43 (d, $^3J_{\text{HH}} = 7.4$ Hz, 2H, C_6H_5), 7.78 (d, $^3J_{\text{HH}} = 8.4$ Hz, 2H, C_6H_5). ^{13}C NMR (CDCl_3 , 101 MHz): $\delta = 15.8$ (SCH_3), 31.6 (SCH_2CH_2), 34.9 (SCH_2CH_2), 38.2

(SCH₂), 76.7 (NCH), 115.7 (CHCH₂), 126.3 (C₆H₅), 128.8 (C₆H₅), 132.7 (C₆H₅), 136.2 (CHCH₂), 140.4 (C₆H₅), 166.6 (SCN).

(S)-4-Ethyl-2-(4-vinyl)phenyl-2-thiazoline M-12b. The product was prepared from dithioester **11** (420 mg, 2.5 mmol) and (*R*)-2-amino-1-butanol (148 mg, 1.66 mmol) according to the procedure described in [8], without isolation of the thioamide. Purification by column chromatography (Et₂O/pentane: 10/90, *R_f* = 0.28 in UV or iodine) yielded 213 mg (0.98 mmol, 59%) of the title compound as a colorless oil. ¹H NMR (CDCl₃, 250 MHz): δ = 1.10 (t, ³*J*_{HH} = 7.5 Hz, 3H, CH₂CH₃), 1.60–2.00 (m, 2H, CH₂CH₃), 3.01–3.52 (m, 2H, SCH₂), 4.45–4.54 (m, 1H, NCH), 5.33 (d, ³*J*_{HH} = 10.9 Hz, CHCHH), 5.83 (d, ³*J*_{HH} = 17.6 Hz, CHCHH), 6.77 (dd, ³*J*_{HH} = 17.6 Hz, ³*J*_{HH} = 10.9 Hz, CHCHH), 7.42 (d, ³*J*_{HH} = 7.4 Hz, 2H, C₆H₅), 7.79 (d, ³*J*_{HH} = 7.4 Hz, 2H, C₆H₅).

Synthesis of Polymeric Thiazolines P-12

General Procedure. Degassed THF (0.9 M in monomer concentration) was added to the corresponding thiazoline monomer (1 equiv) and AIBN (0.12 equiv) in a Schlenk tube under nitrogen. The mixture was heated for 14 h at 80°C, before the polymer was precipitated into pentane (10 times the volume of the reaction mixture). The polymer was washed with ether, dried first under slight vacuum, then under oil pump vacuum.

Thiazoline P-12a. The product was prepared by the general procedure from monomer **M-12a**. Yield: 43%. ¹H NMR (CDCl₃, 250 MHz): δ = 1.26 (br, 2H, PhCHCH₂), 1.58 (br, 1H, PhCHCH₂), 1.95 (br, 2H, SCH₂CH₂), 2.14 (br, 3H, SCH₃), 2.74 (br, 2H, SCH₂CH₂), 3.05 (br, 1H, SCHH), 3.49 (br, 1H, SCHH), 4.71 (br, 1H, NCH), 6.48 (br, 2H, C₆H₅), 7.52 (br, 2H, C₆H₅). ¹³C NMR (CDCl₃, 101 MHz): δ = 14.1 (PhCHCH₂), 15.8 (SCH₃), 22.6 (PhCHCH₂), 31.6 (SCH₂CH₂), 34.9 (SCH₂CH₂), 38.2 (SCH₂), 76.7 (NCH), 127.5 (C₆H₅), 128.4 (C₆H₅), 132.7 (C₆H₅), 140.4 (C₆H₅), 166.6 (SCN). Molecular weight (GPC): *M_w* = 15,700 g/mol; *M_w*/*M_n* = 1.73.

Thiazoline P-12b. The product was prepared by the general procedure from monomer **M-12b**. Yield: 51%. ¹H NMR (CDCl₃, 250 MHz): δ = 0.90 (br, 3H, CH₂CH₃), 1.25 (br, 2H, PhCHCH₂), 1.72–2.05 (br, CH₂CH₃), 2.87 (br, 1H, PhCHCH₂), 3.06 (br, 1H, SCHH), 3.44 (br, 1H, SCHH), 4.55 (br, 1H, NCH), 6.51 (br, 2H, C₆H₅), 7.56 (br, 2H, C₆H₅). Molecular weight (GPC): *M_w* = 18,200 g/mol; *M_w*/*M_n* = 1.81.

Typical Procedure for the Pd-Catalyzed Allylic Substitution

(*E*)-1,3-Diphenyl-2-propenyl acetate (156 mg, 0.62 mmol), ligand (6 mol%, 0.04 mmol), allylpalladium chloride dimer (6 mg, 2.5 mol%, 0.02 mmol), and potassium acetate (3 mg, 5 mol%, 0.03 mmol) were introduced into a Schlenk flask and 2 mL of dichloromethane was added. The mixture was stirred for 20 min before the successive addition of dimethyl malonate (0.21 mL, 1.86 mmol) and *N, O*-bis(trimethylsilyl)acetamide (0.49 mL, 1.86 mmol). The mixture was stirred at room temperature and monitored by TLC (SiO₂, EtOAc/pentane: 10/90). After completion, solvents were evaporated, the residue dissolved in ether and filtered (syringe filter). After evaporation of ether, the residue was analyzed by HPLC using a Daicel Chiralpak AD analytical column (*n*-heptane/2-propanol: 90/10, flow rate: 1 mL/min, 251.0 nm). Enantiomeric excess of (*E*)-dimethyl-(1,3-diphenylallyl)malonate was measured by HPLC: (*R*)-enantiomer, *t*₁ = 12.4 min; (*S*)-enantiomer, *t*₂ = 17.4 min.

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