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Highly Diastereoselective Lithiation and Substitution of an (*S*)-Prolinyl Thiocarbamate via Sterically Homogeneous Lithio(thiocarbamate): Synthesis of Enantiomerically Pure Prolinethiols

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Dedicated to Professor Hans J. Schäfer on the occasion of his 70th birthday

Abstract: Highly diastereoselective lithiation–substitution reactions of an (*S*)-proline derived S-alkyl thiocarbamate was accomplished. The configuration of the predominant alkyllithium species and the stereochemical course of the electrophilic substitution reactions are deduced by a combination of X-ray crystal structure analysis, NMR spectroscopic studies, deuteration/dedeuteration experiments, and quantum chemical calculations. The lithium intermediate (*S*,*S*)-**9** was found to be kinetically and thermodynamically favoured, whereas (*S*,*R*)-**9** rapidly epimerizes.

Keywords: carbamates · chiral auxiliaries · configuration analysis · lithium

Introduction

Asymmetric induction on prochiral methylene groups through deprotonation followed by electrophilic substitution is one of the basic asymmetric C–C bond forming reactions.[1] In this process, the chiral induction can occur either in the deprotonation or in the post deprotonation step.[2] Synthetic utility of these processes have been limited to the α-heteroatom substituted organolithium compounds wherein excellent enantio- and diastereoselectivities have been achieved. Especially, α-oxy[1a,b,d] and α-amino[1c] organolithium compounds have proven highly valuable in synthetic organic chemistry. The generation of these α-heteroatom substituted organolithium compounds can often be controlled in a manner that the chiral induction is achieved via an asymmetric deprotonation pathway. The most important prerequisite for the successful employment of asymmetric deprotonation is the necessity of configurational stability of intermediate lithium species under the reaction conditions. Although many of the α-oxy and α-amino organolithium compounds exhibit necessary levels of configurational stability, their sulfur counterparts are known for their high configurational instability and rapid epimerization even at low temperatures.[3,4] In this situation, one has to rely on the post deprotonation enantioenrichment (either thermodynamic resolution or dynamic kinetic resolution) to obtain good selectivity.[5] Evidences for a very different mechanism of racemization for α-thio substituted organolithium compounds were put forth by the work of R. W. Hoffmann et al.[4] and H. J. Reich et al.[6] who suggest that the bulky substituents and branching at the carbanionic center renders some stability to the organolithium species.

Indeed, tertiary thiobenzylic[7] and tertiary thioallylic[8] lithiated carbanions investigated by our group showed remarkably high configurational stability. However, there is no report until date of an unbranched, configurationally stable, highly enantioenriched alkylthio lithium compound[9] (Scheme 1).

It is important to clarify the reaction pathways of unbranched α-sulfenyl carbanions and develop highly enantio- and diastereoselective reactions owing to the increasing importance of α-chiral sulfides as chiral templates[10] or asymmetric catalysts.[11] With this objective we synthesized and investigated the deprotonation reactions of thiocarbamate **8**

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[+] Quantum chemical calculations

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[$] NMR experiments

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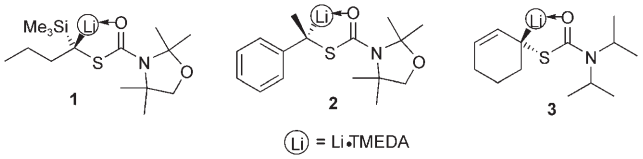
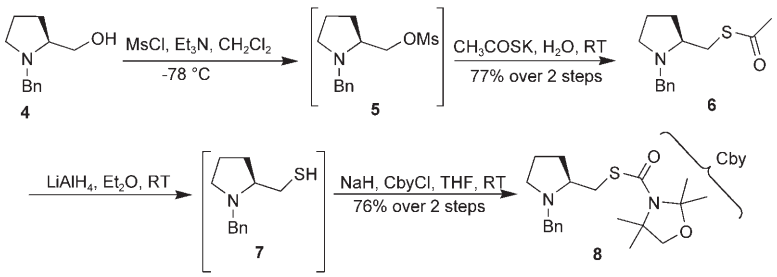


Scheme 1. Configurationally stable α-thio-organolithium compounds.

derived from (*S*)-proline (Scheme 2).[12] Herein, we present the detailed results of this investigation.

Results and Discussion

The synthesis of the starting material is depicted in Scheme 2. *N*-Benzyl-(*S*)-prolinol (**4**)[13] was mesylated at −78 °C followed by thioesterification with potassium thioacetate to obtain **6** in 77 % yield[14] (Scheme 2). Reductive cleavage of the thioester with lithium aluminium hydride followed by carbamoylation with 2,2,4,4-tetramethyl-1,3-oxazolidinyl-3-carbonyl chloride (CbyCl) afforded the desired thiocarbamate **8** in 76 % yield.

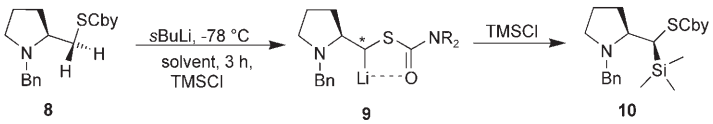


Scheme 2. Preparation of starting material **8**.

Thiocarbamate **8** was then subjected to extensive deprotonation reactions using different conditions. Thus, deprotonation of **8** using 1.2 equiv of *s*BuLi and 1.2 equiv of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) at −78 °C for 3 h proceeded smoothly in various solvents (Scheme 3).

Trapping the intermediate lithium species **9** with trimethylsilyl chloride afforded the corresponding silane **10** as a single diastereomer in good to excellent yields (Scheme 3).

Thus, the high induction by the internal stereocenter is evident from the high selectivities obtained for the silylation product. As shown in Scheme 3, toluene is the best solvent.



solvent	THF	cumene	pentane	toluene
yield [%]	74	65	70	83

Scheme 3. Deprotonation experiments of **8**.

The above process was found to be generally applicable for other silyl electrophiles as well as for alkylation, benzylation, allylation, and carbonyl additions (Scheme 4). Thus, deprotonation of **8** under the above described conditions followed by trapping the intermediate lithium species with various electrophiles (Scheme 4) afforded the corresponding substitution products in excellent diastereoselectivity and in good to excellent yields.

Thus, variously substituted benzylic halides and linear chain alkyl halides react smoothly furnishing the benzylation and alkylation products in good yields and with high diastereoselectivity within 1–3 h at −78 °C. When the nature of the electrophile is changed from primary alkyl halides to open chain secondary or cyclic halides, the alkylation did not occur. This can be attributed to the low reactivity of these electrophiles with the lithium species due to steric reasons.

An X-ray crystal structure (Figure 1) of silane **13** established the configuration of the newly generated stereocenter to be *R*. The absolute configuration of all silylated products was assigned as *R* assuming that silylation by each electrophile takes the same stereochemical course as that of TBDMSOTf.

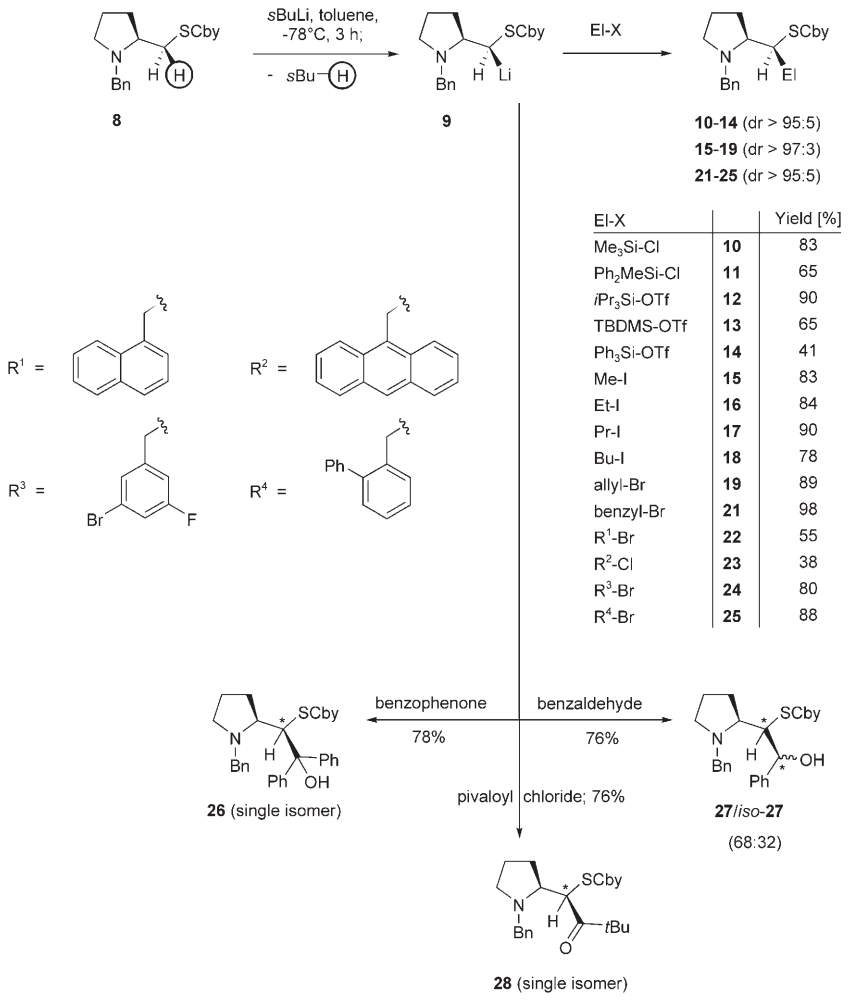
Also, the absolute configurations of alkylation and benzylation products were proven to be *S* from the X-ray crystal structure of (*S*)-**20** and (*S*)-**23** (Figures 2 and 3, respectively).

The absolute configurations for the products obtained from addition of lithiated **8** to benzophenone, *p*-bromobenzaldehyde and pivaloyl chloride were assigned as *R* assuming the similar mode of the S_E process as in the above proven cases.

Thus, assuming a diastereomerically pure alkyllithium intermediate, silylation, alkylation, and benzylation occur under similar stereochemical mode to furnish the substitution products. However, configurational stability and the configuration of the lithium intermediate, at this point, were less clear.

Decarbamoylation of substituted thiocarbamates: There are various methods reported by our group for the removal of the carbamoyl moiety to generate the free hydroxy or thiol group.[7b] Thus, treatment of the substituted thiocarbamate with excess of DIBALH at 0 °C or room temperature under argon atmosphere furnished free thiols in good yields (Scheme 5, Table 1).

Configuration of alkyllithium compound 9 and stereochemical mode of electrophilic substitutions: Having explored this highly diastereoselective reaction, it was important to understand the stereochemical course of electrophilic substitution as there are very few reports on the stereochemical behavior



El-X		Yield [%]
Me_3Si-Cl	**10**	83
Ph_2MeSi-Cl	**11**	65
iPr_3Si-OTf	**12**	90
TBDMS-OTf	**13**	65
Ph_3Si-OTf	**14**	41
Me-I	**15**	83
Et-I	**16**	84
Pr-I	**17**	90
Bu-I	**18**	78
allyl-Br	**19**	89
benzyl-Br	**21**	98
R^1-Br	**22**	55
R^2-Cl	**23**	38
R^3-Br	**24**	80
R^4-Br	**25**	88

Scheme 4. Results of lithiation and electrophilic substitution of **8** with different electrophiles.

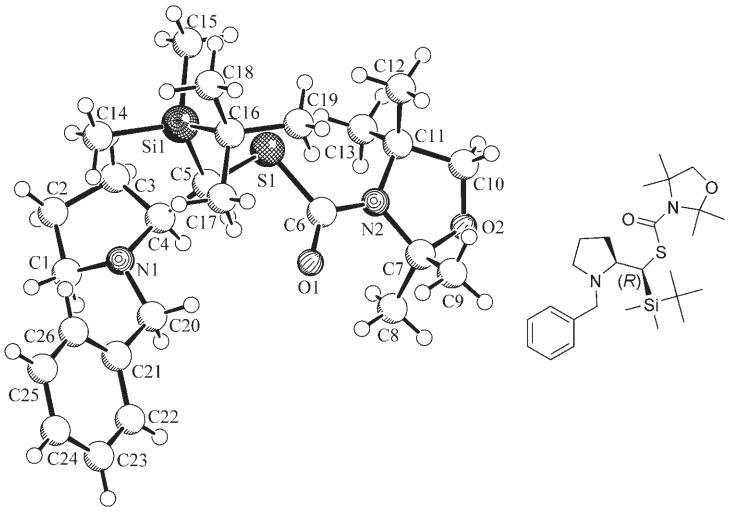


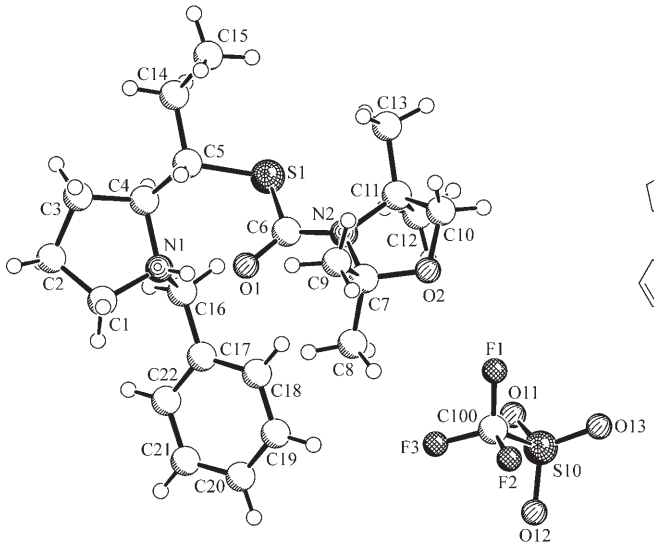
Figure 1. X-ray crystal structure of (*R*)-**13**.

of α-thiocarbanions.[5a,e,7,8] As the configurations of most of the substitution products were established, the correlation with alkyllithium derivative should clarify the stereochemical pathway. However, the alkyllithium species **9** was not crystalline and hence indirect methods had to be applied to confirm its configuration. Fortunately, a combination of NMR and quantum chemical calculations provided the answer in this case. It was observed that the two diastereotopic protons H^R and H^S of thiocarbamate **8** showed distinct chemical shifts in ^{1}H NMR spectrum at $\delta =$ 3.03 and 3.53 ppm (Figure 4).

When **8** was deprotonated followed by deuteration, the downfield signal at 3.53 ppm disappeared. As deuteration occurs with stereoretention in all known cases, assigning the chemical shifts to *pro-R* and *pro-S* protons would provide the configuration of the alkyllithium compound. Indeed, the quantum chemical calculations of the chemical shifts, details of which are provided in the following part, conclusively proved that the *pro-S* proton has a downfield chemical shift ($\delta = 3.53$ ppm) compared with the *pro-R* proton ($\delta =$ 3.03 ppm). Hence, the *pro-S* proton was removed and (*S*,*S*)-[D]-**8** was formed via intermediate **9** (Scheme 6). Further, from the configurations of silylated, alkylated and benzylated products, it is evident that these reactions occur under stereoretention.

We generally found retention in the substitution reactions of non-mesomerically stabilized sp^3-hybridized *O*-lithioalkyl carbamates.[1a,b,e] Noteworthy, the overall stereochemical course of lithiation is opposite to the reaction of the corresponding prolinol-*O*-carbamate.[15] The reasons for this are presently unknown.

Details of quantum chemical calculations: The four lowest energy conformers that resulted from a conformational search with the MMX force field[16] were taken as starting structures for geometry optimizations with the Turbomole[17] program package using density functional theory. The B-LYP functional[18] and a triple zeta valence basis set (TZVP[19]) were used, together with the RI approximation.[20] We included an empirical dispersion correction term (DFT-D[21]) that accounts for nonbonding van der Waals interactions at intermediate interatomic distances (3–4 Å).



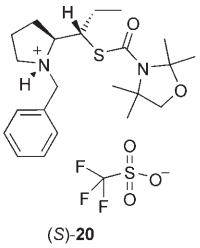
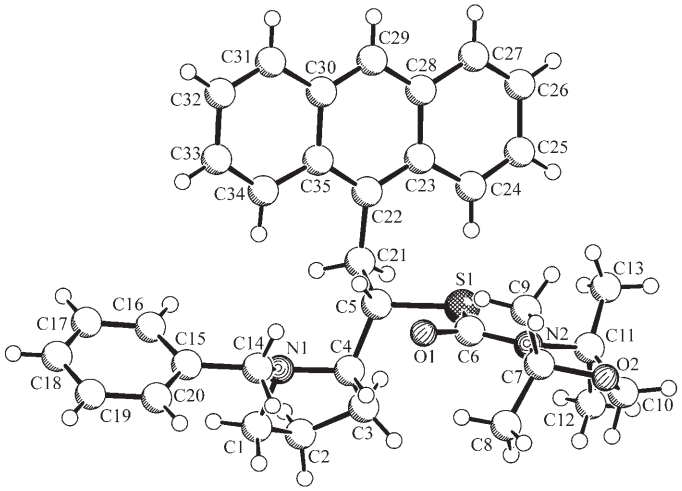


Figure 2. X-ray crystal structure of triflate salt (*S*)-**20**.[12]



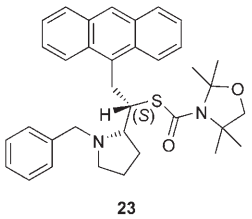
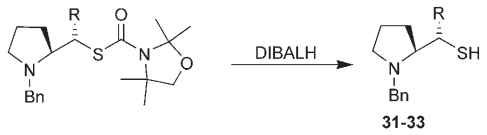


Figure 3. X-ray crystal structure of (*S*)-**23**.



Scheme 5. Decarbamoylation of substituted thiocarbamates.

Table 1. Synthesis of free thiol.

Entry	R	Yield [%]	Product
1	Et	74	**31**
2	Ph-CH_2	70	**32**
3	TBDMS	65	**33**

The two conformers lowest in energy (**A** and **B**) are shown in Figure 5. Other conformations (Table 2) were found to be at least 1.5 kcal mol^{-1} higher in energy than **B** and are not discussed here. After optimization, chemical shifts were calculated[22] on the same theoretical level with respect to tetramethylsilane as reference.

Both conformers differ in the position of the benzyl group around the C–N bond. A pronounced effect of this rotation on the chemical shift is found for H_a. The chemical shifts of the methylene group at the asymmetric center are changed to a smaller extent. The torsional angles between the *pro-S*/*pro-R* protons and atom H_a (and thus the expected ^3J coupling constants) are not influenced by the rotation of the benzyl group. We therefore conclude that the proton with the larger coupling constant and the lower chemical shift (high field signal) must be *pro-R*.

Configurational stability of intermediate alkyllithium derivative 9: As mentioned in the Introduction, there are various pathways by which the highly diastereoselective stereoinduction can occur. To know the exact pathway operating in this case, an in situ deprotonation experiment was performed on thiocarbamate **8** wherein the electrophile TBDMSOTf or TMSCl is present at the time of deprotonation (Scheme 7).

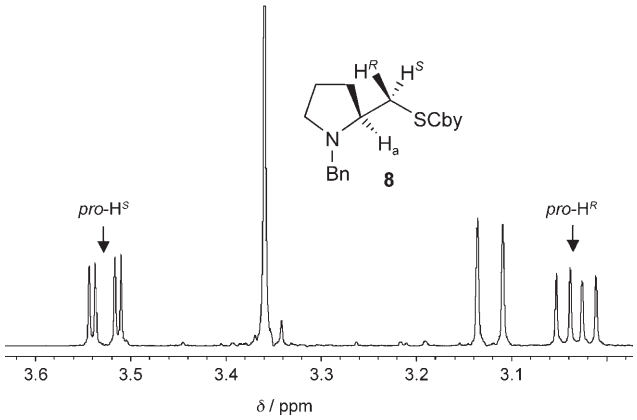
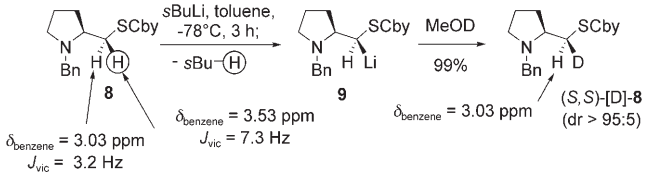


Figure 4. Distinct chemical shifts of diastereotopic protons of thiocarbamate **8** (600 MHz, C_6D_6).



Scheme 6. Deuteration experiment.

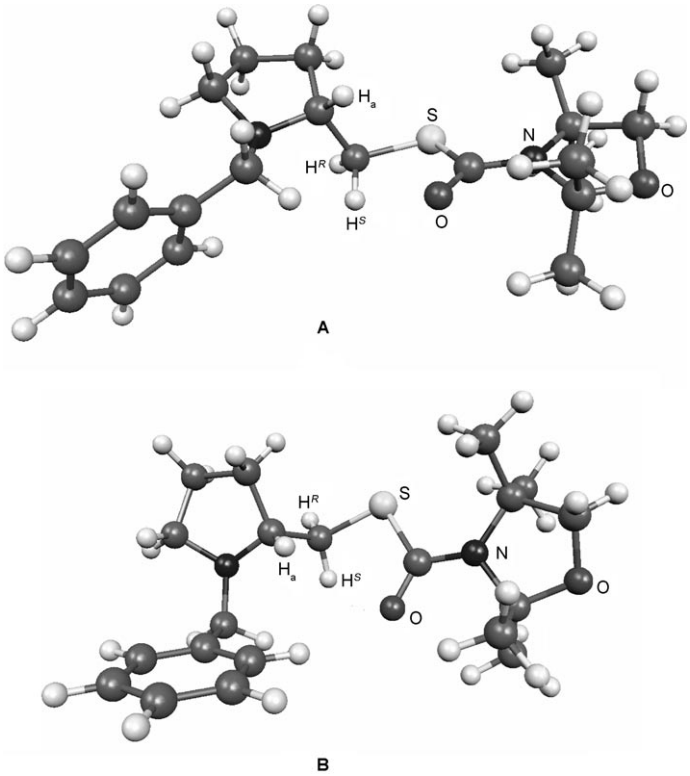


Figure 5. DFT-D optimized conformers **A** and **B** of the thiocarbamate **8**.

Table 2. Relative energies for conformers **A** and **B**, chemical shifts (vs TMS) of hydrogen atoms $H^{R/S}$ and H_a, and dihedral angles of $H^{R/S}$ with H_a.

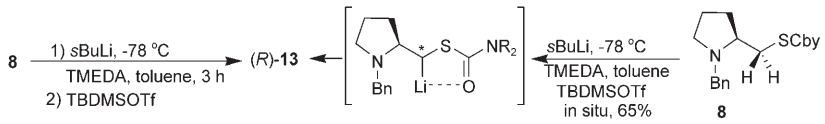
	A	**B**	Found
E_{rel} (DFT-D) [kcal mol^{-1}]	+1.2	0.0	–
σ_{calcd} (H^S) [ppm]	3.58	3.59	3.53
σ_{calcd} (H^R) [ppm]	2.28	2.07	3.03
σ_{calcd} (H_a) [ppm]	2.68	3.03	2.85
σ_{calcd} (PhCH_2) [ppm]	3.16, 4.71	3.84, 4.38	3.11, 4.12
Θ (H^S-C-C-H_a) [°]	69.1	68.5	–
Θ (H^R-C-C-H_a) [°]	−169.7	−170.5	–

Thus, the same diastereomer (*R*)-**13** is obtained from the in situ experiment, that is, formed by the standard deprotonation–substitution method. Similar results were obtained for in situ experiment with TMSCl. This fact indicates that the lithium species formed by in situ deprotonation is the same which survives after 3 h of deprotonation. However, the possibility that the alkyllithium species epimerizes before the reaction with electrophile could not be completely excluded.[3d] Thus, from this experiment, question arises: why no evidence was found for the existence of the epimeric lithium compound *epi*-**9**? Is it due to rapid equilibration or configurational stability of **9**? To answer this question, we decided to generate *epi*-**9** by deprotonation of deuterated (*S*,*S*)-[D]-**8** (Scheme 8). (*S*,*S*)-[D]-**8** was prepared by deuteration of **9** by MeOD. ^{1}H and ^{2}D NMR spectra revealed that it is not contaminated by *epi*-[D]-**8**. Due to the high H/D-isotope effect in the deprotonation reaction, which was found for alkyl carbamates[23] and alkyl thiocarbamates,[24] that should override the kinetic preference for the *pro-S* hydrogen. After deprotonation of [D]-**8** under the usual conditions, the reaction mixture was quenched with methanol. The product obtained in 99% yield was subjected to a careful ^{1}H and ^{2}H NMR analyses. It consisted of the undeuterated starting material **8** (78%), [D]-**8** (3%) and *epi*-[D]-**8** (19%). Hence, the removal of D from the preferred position proceeded approximately four times faster than the former *pro-R* position, overriding the H/D-isotope effect. Most importantly, lithium compound *epi*-[D]-**9** formed in 19% yield, isomerizes to the thermodynamically favored epimer [D]-**9** before being trapped by protonation.

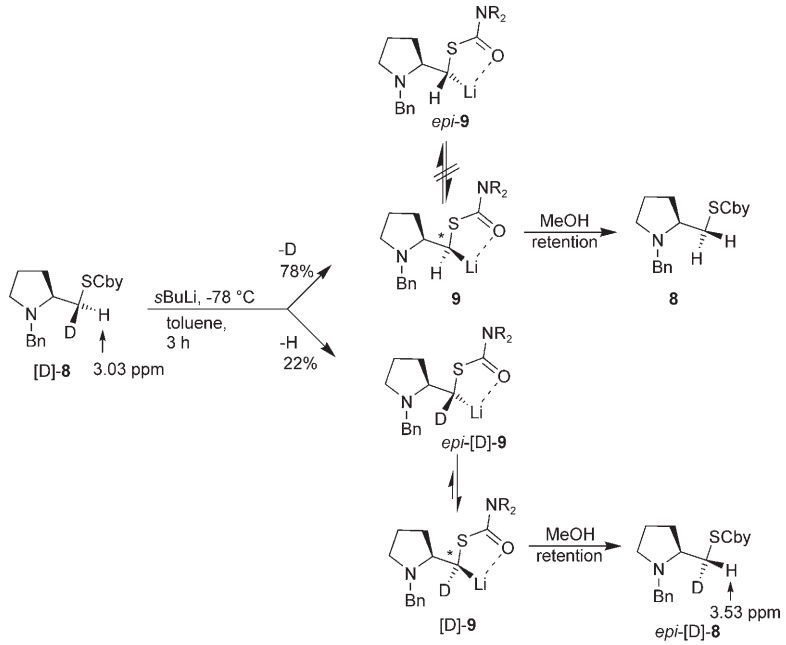
The above conclusion are supported by the NMR data as follows: The GHSQC NMR spectrum of the mixture of **8**, [D]-**8** and *epi*-[D]-**8**, as obtained above, clearly showed the presence of a methylene (CH_2) of **8** and a methyne group (CH) of *epi*-[D]-**8** correlating to the carbon signals at δ 34.6 (singlet) and 34.3 ppm (triplet, due to ^{2}H, ^{13}C coupling) (cf. Supporting Information). In addition, it was clearly visible that in [D]-**8** and *epi*-[D]-**8**, the protons on the D-bearing carbon atom show different chemical shifts for example, in former; the proton in discussion was observed at δ 3.03, while in latter case at 3.53 ppm. This is possible only if the intermediate lithium compound *epi*-[D]-**9** had undergone epimerization before adding the proton from the opposite face.

We attempted to trap the unfavored lithium species *epi*-[D]-**9** (formed in 22% yield) by TMSCl. For this purpose, [D]-**8** was deprotonated in presence of 10 equivalents of TMSCl and the product obtained was subjected to careful NMR analysis. The analyses showed the presence of a single diastereomer of silane, indicating that the barrier of inversion for *epi*-[D]-**9** is lower than the barrier for its reaction with TMSCl (Scheme 9).

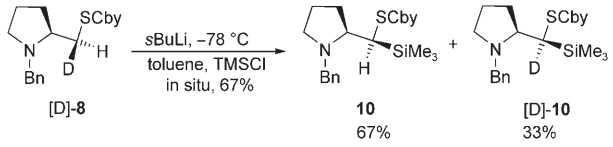
From these experiments, it must be concluded: Lithium compound **9** (which also is formed more rapidly from **8**) is



Scheme 7. In situ deprotonation–silylation experiments with **8**.



Scheme 8. Dedeuteration/deprotonation–protonation of **8**.



Scheme 9. In situ dedeuteration/deprotonation–silylation of [D]-**9**.

thermodynamically more stable than *epi*-**9**. Assuming the ratio **10**/*epi*-**10** is in the magnitude 98:2 or higher (according to the level of detection), $\Delta\Delta G^{\neq}$ amounts to at least 1.5 kcal mol^{-1} estimated from the equation $\Delta G = -RT\ln K$.

Conclusion

In summary, a new class of unbranched, non-mesomerically stabilized, lithiated α-thiocarbanions has been discovered. Its (*S*,*S*)-diastereomer **9** is formed with high, kinetically and thermodynamically controlled, substrate-induced diastereoselectivity. Alkyllithium species **9** formed after deprotonation is persistent under the reaction conditions, due to its high thermodynamic stability in comparison with *epi*-**9**. The alkyllithium **9** undergoes substitution reactions with various classes of electrophiles with retention of configuration to furnish the products in good to excellent yields and high diastereoselectivity. The pathway of diastereoselectivity and the stereochemical course of electrophilic substitution reactions were elucidated using a combination of X-ray crystal structure analysis, NMR studies, deuteration and dedeuteration experiments, and quantum chemical calculations. Facile decarbamoylation of so obtained products gives access to α-branched chiral amino thiols.

Experimental Section

General remarks: All solvents were dried and purified prior to use. Diethyl ether and toluene were distilled over sodium/benzophenone, THF over potassium/benzophenone, and CH_2Cl_2 was distilled over CaH_2. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA). TMSCl and NEt_3 were distilled from powdered CaH_2 and stored under argon. EA refers to ethyl acetate, CH: cyclohexane, E: Et_2O, P: pentane. All reactions were performed under argon atmosphere in flame-dried glassware using septum and syringe techniques. Flash column chromatography (FCC) was performed on Merck 60 silica gel, 0.040–0.063 mm using an argon pressure of 1.2–1.4 bar, and monitored by thin-layer chromatography (TLC) on Merck 60 F_{254} silica gel. Gas chromatography was performed on Agilent 6890 plus, Agilent, Böblingen. HP-5 was used as an achiral column (30 m long, 0.32 mm diameter, 0.25 μm thick stationary phase, N_2 as the mobile phase, 106 kPa pressure, 290 °C injection temperature, 300 °C detector temperature, program: 50 °C start temperature, 10 °C min^{-1} heating rate, 300 °C final temperature for 15 min). Melting points were measured on an SMP3 melting point apparatus purchased from Stuart Scientific, UK (uncorrected values). The optical rotations were measured in a 10 cm cuvette on a polarimeter 341 purchased from Perkin-Elmer. Unless otherwise stated, ^{1}H and ^{13}C NMR data were recorded on Bruker ARX 300, AM 360, AMX 400 or Varian Associated Unity Plus 600; spectra were obtained from solutions in $CDCl_3$ ($\delta_C = 77.0$ ppm) and were calibrated relative to residual content of $CHCl_3$ ($\delta_H = 7.24$ ppm) or $SiMe_4$ ($\delta_H = 0.0$ ppm). Elemental analyses were performed at the Microanalytical Section of the Organisch-Chemisches Institut, WWU Münster, on a Vario El III, purchased from Elementar Analysen Systeme, Hanau (Germany). Mass spectrometric data were obtained on Finnigan MAT 8230 (EI); Micromass Quattro LCZ (ESI), Micromass MAT 8200 (GC-TOF/HRMS).

Synthesis of starting material 8

(*S*)-S-[(1-Benzylpyrrolidin-2-yl)methyl] ethanethioate (6):[12] Anhydrous triethylamine (3.90 g, 39.1 mmol, 1.5 equiv) was added to a solution of *N*-benzyl prolinol[11] (5.0 g, 26.1 mmol, 1.0 equiv) in dichloromethane (40 mL). This solution was stirred at room temperature for 10 min then cooled to −78 °C and a solution of methanesulfonyl chloride (3.5 g, 30.7 mmol, 1.2 equiv) in anhydrous dichloromethane (10 mL) was added. This mixture was stirred for 1 h. Afterwards, the solvent was removed under vacuum to obtain a pale yellow semisolid. A solution of potassium thioacetate (5 g, 43.8 mmol, 1.6 equiv) in water (50 mL) was added and the resulting solution was stirred at room temperature for 2 h. Afterwards, the reaction mixture was poured into dichloromethane (100 mL), the layers were separated and the aqueous layer was washed with dichloromethane (3×25 mL). The combined organic layer was dried with anhydrous magnesium sulfate and evaporated under reduced pressure. The residue was purified by column chromatography (EA/CH 1:6) to afford the desired thioester as an yellow oil (5.0 g, 20 mmol, 77 %). R_f = 0.60 (EA/CH 1:1); $[\alpha]_D^{20} = -111.0$ ($c = 1.25$, $CHCl_3$); ^{1}H NMR (400 MHz): δ = 1.42–1.80 (m, 3H, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-2a}}$), 1.85 (m, 1H, $CH_{2\text{-pyrro-2b}}$), 2.12 (ddd, 1H, $CH_{2\text{-pyrro-4a}}$), 2.28 (s, 3H, CH_3), 2.67 (m, 1H, $CH_{\text{pyrro-1}}$), 2.92 (m, 2H, $CH_{2\text{-pyrro-4b}}$, $CH_{2\text{-pyrro-5a}}$), 3.29(dd, ^3J=3.0 Hz, 2H), 4.05 (d, ^2J= 13.3 Hz,1H, CH_2-Ph), 7.24 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz):δ = 22.3, 29.9, 30.5, 33.1, 54.23, 58.4, 62.5, 126.8, 128.5, 128.7, 139.7 (Ph), 195.8 ppm (C=O); elemental analysis calcd (%) for $C_{14}H_{19}NOS$ (249.1):

C 67.43, H 7.68, N 5.92; found C 67.52, H 7.72, N 6.04; MS (ESI): *m/z*: 250.1279 $[M+H]^+$.

(*S*)-S-[(1-Benzylpyrrolidin-2-yl)methyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (8): A solution of thioester **6**, obtained as above, (5.0 g, 20 mmol, 1.0 equiv) in Et_2O (40 mL) was added in a dropwise manner at 0 °C to a well stirred suspension of $LiAlH_4$ (1.1 g, 30 mmol, 1.5 equiv) in Et_2O (50 mL). The resulting solution was stirred at 0 °C for 30 min and at room temperature for an additional hour. Afterwards, the reaction flask was cooled to 0 °C and the reaction was quenched by careful addition of water (10 mL). After filtration of the aluminum salts followed by evaporation of solvent from filtrate, the crude thiol was obtained as a colorless liquid. The thiol was used in the subsequent step without further purification.

A solution of crude thiol in anhydrous THF (20 mL) was added to a stirred suspension of NaH (60 % in mineral oil, 1.2 g, 30 mmol, 1.5 equiv) in anhydrous THF (40 mL). The resulting solution was stirred at room temperature for 15 min and then a solution of CbyCl (5.74 g, 30 mmol, 1.5 equiv) in anhydrous THF (25 mL) was added. This mixture was stirred at room temperature for 24 h. Afterwards, the reaction flask was cooled to 0 °C and water (10 mL) was slowly injected into the flask. The layers were separated and the aqueous layer was extracted with Et_2O (3×25 mL). The collective organic phase along with washing was dried over anhydrous $MgSO_4$, filtered through glass wool, and concentrated under reduced pressure to get the crude thiocarbamate which was subjected to column chromatography (E/P 1:4) to furnish the desired thiocarbamate **8** as a colorless, viscous oil (5.5 g, 15.2 mmol, 76 % based on **6**). R_f = 0.58 (E/P 1:1); $[\alpha]_D^{20} = -78.9$ (c = 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6): δ = 1.37 (s, 6H, 2×CH_3-Cby), 1.47–1.86 (m, 10H, 2×CH_3-Cby, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-4}}$), 1.95 (m, 1H, $CH_{pyrro\text{-}5}$), 2.67 (m, 1H, $CH_{pyrro\text{-}5}$), 2.84 (tt, ^3J = 1.8, ^3J = 8.2 Hz, 1H, $CH_{pyrro\text{-}2}$), 3.03 (dd, ^3J = 7.6, ^2J = 13.1 Hz 1H, S-CH_2-pro-H^R), 3.12 (d, ^2J = 13.4 Hz, 1H, CH_2-Ph), 3.36 (s, 2H, Cby-CH_2), 3.53 (dd, ^3J = 3.2, ^2J = 13.1 Hz, 1H, S-CH_2-pro-H^S), 7.05–7.23 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz): δ = 22.4, 24.7, 25.7, 30.0, 34.2, 54.0, 54.1, 58.8, 62.9, 77.2, 96.0; 126.6, 128.1, 128.7, 139.4 (Ph), 163.8 (C=O); elemental analysis calcd (%) for $C_{20}H_{30}N_2O_2S$ (362.2): C 66.26, H 8.34, N 7.73; found C 66.11, H 8.37, N 7.62; MS (ESI): *m/z*: 363.2064 $[M+H]^+$, 385.1870 $[M+Na]^+$.

General procedure for the deprotonation and electrophilic substitution: Thiocarbamate **8** (100 mg, 0.27 mmol, 1.0 equiv) was dissolved in toluene (5 mL). TMEDA (37 mg, 0.32 mmol, 1.2 equiv) was added and the reaction flask was cooled to −78 °C. Afterwards, *s*BuLi (1.36 M, 0.23 mL, 0.32 mmol, 1.2 equiv) was injected in a dropwise manner and the reaction mixture was stirred at −78 °C for 3 h. Then appropriate electrophile (0.81 mmol, 3.0 equiv) injected and the reaction mixture stirred for 1–12 h until no more of the starting material could be detected by TLC. The reaction was quenched with water (2 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3×10 mL). The collective organic phase was dried over anhydrous $MgSO_4$, filtered through glass wool, and concentrated under reduced pressure to get the crude product. The crude product was subjected to column chromatography (Et_2O/pentane or ethyl acetate/cyclohexane) to obtain the pure substitution product.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-1-(trimethylsilyl)methyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (10): Colorless oil; yield: 83 %; R_f = 0.55 (EA/CH 1:4); t_R = 20.4 min (HP-5); $[\alpha]_D^{20} = -81.5$ (c = 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.18 (s, 9H, $Si(CH_3)_3$), 1.60–1.80 (m, 15H, 4×CH_3-Cby, $CH_{pyrro\text{-}3a}$, $CH_{2\text{-pyrro-4}}$), 1.95 (m, 1H, $CH_{pyrro\text{-}3b}$), 2.07 (m, 1H, $CH_{pyrro\text{-}5a}$), 2.83 (m, 1H, $CH_{pyrro\text{-}5b}$), 2.89 (m, 1H, $CH_{pyrro\text{-}2}$), 3.23 (d, 1H, $^2J_{H,H}$ = 13.2 Hz, Ph-CH_2), 3.35 (d, ^3J = 4.2 Hz, 1H, CH-$SiMe_3$), 3.75 (s, 2H, Cby-CH_2), 4.30 (d, $^2J_{H,H}$ = 13.2 Hz, 1H, Ph-CH_2), 7.30–7.55 (m, 5H, Ph); ^{13}C NMR (100 MHz): δ = 0.01 ($Si(CH_3)_3$), 22.7, 24.7, 25.7, 30.2, 33.2, 54.0, 54.1, 58.8, 68.1, 77.2, 96.0, 126.6, 128.1, 128.7, 139.4, 164.3 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2963, 2926, 2868 (s, C-H_{ali}), 1630 (s, C=O), 1452 (s), 1368 (s), 1334 (s), 1310 (s), 1247 (s), 1202 (s), 1081 (s), 920 (s), 837 (s), 797 cm^{-1} (s); elemental analysis calcd (%) for $C_{23}H_{38}N_2O_2SSi$ (434.7): C 63.54, H 8.81, N 6.44; found: C 63.43, H 8.88, N 6.22; MS (ESI): *m/z*: 434.2477 $[M+H]^+$, 457.2335 $[M+Na]^+$.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-1-(methyldiphenylsilyl)methyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (11): Colorless oil; yield: 65 %; R_f = 0.62 (E/P 1:2); t_R = 26.2 min (HP-5); $[\alpha]_D^{20} = -46.2$ (c = 0.58, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (s, 3H, Si-CH_3), 1.70–1.98 (m, 13H, 4×CH_3-Cby, $CH_{pyrro\text{-}4a}$), 2.15 (m, 1H, $CH_{pyrro\text{-}4b}$), 2.40 (m, 1H, $CH_{pyrro\text{-}3a}$), 3.15 (m, 3H, $CH_{pyrro\text{-}3b}$, $CH_{2\text{-pyrro-5}}$), 3.22 (m, 1H, $CH_{pyrro\text{-}2}$), 3.35 (d, ^2J = 13.8 Hz, 1H, CH_2-Ph), 3.95 (s, 2H, Cby-CH_2), 4.35 (d, ^3J = 4.6 Hz, 1H, Ph_2MeSi-CH), 4.50 (d, ^2J = 13.8 Hz, 1H; CH_2-Ph), 7.30–7.55 ppm (m, 15H, Ph); ^{13}C NMR (100 MHz): δ = −1.23 (Si-CH_3), 23.1, 24.4, 25.6, 30.7, 32.3, 53.8, 59.4, 67.5, 76.7, 126.6, 127.8, 128.6, 129.0, 129.7, 133.9, 134.7, 135.0, 136.5, 137.1 (Ph), 164.0 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2962, 2942, 2865 (s, C-H_{ali}), 1630 (s, C=O), 1490 (s), 1368 (s), 1333 (s), 1309 (s), 1247 (s), 1203 (s), 1081 (s), 920 (s), 824 (s), 791 cm^{-1} (s); elemental analysis calcd (%) for $C_{33}H_{42}N_2O_2SSi$ (558.8): C 70.92, H 7.58, N 5.01; found: C 70.69, H 7.58, N 4.88; MS (ESI): *m/z*: 559.2859 $[M+H]^+$, 581.2643 $[M+Na]^+$.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-1-(triisopropylsilyl)methyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (12): Colorless oil; yield: 90 %; R_f = 0.62 (E/P 1:1), t_R = 23.7 min (HP-5); $[\alpha]_D^{20} = -66.1$ (c = 1.23, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98–1.32 (m, 21H, Si(CH-$(CH_3)_2)_3$), 1.50–1.80 (m, 15H, 4×CH_3-Cby, $CH_{pyrro\text{-}3a}$, $CH_{2\text{-pyrro-4}}$), 1.87–2.17 (m, 2H, $CH_{pyrro\text{-}3b}$, $CH_{pyrro\text{-}5a}$), 2.88 (m, 2H, $CH_{pyrro\text{-}2}$, $CH_{2\text{-pyrro-5b}}$), 3.33 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 3.55 (d, ^3J = 5.1 Hz, 1H, iPr$_3$Si-CH), 3.68 (s, 2H, Cby-CH_2), 4.20 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 7.00–7.45 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ = 12.7 ($Si(CH(CH_3)_2)_3$), 19.7 ($Si(CH-(CH_3)_2))_3$), 22.7, 25.2, 26.2, 31.6, 32.3, 54.1, 54.1, 60.9, 68.2, 77.2, 96.0, 126.6, 128.2, 128.9, 140.7 (Ph), 164.3 (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2962, 2942, 2865 (s, C-H_{ali}), 1630 (s, C=O), 1490 (s), 1368 (s), 1333 (s), 1309 (s), 1247 (s), 1203 (s), 1081 (s), 920 (s), 824 (s), 791 cm^{-1} (s); elemental analysis calcd (%) for $C_{29}H_{50}N_2O_2SSi$ (518.8): 67.13, H 9.71, N 5.40; found: C 67.02, H 10.08, N 4.99; MS (ESI): *m/z*: 519.3418 $[M+H]^+$.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-1-(*tert*-butyldimethylsilyl)methyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (13): Colorless solid; yield: 65 %; R_f = 0.62 (E/P 1:2); t_R = 23.7 min (HP-5); $[\alpha]_D^{20} = -88.0$ (c = 0.96, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3H, Si-CH_3a), 0.12 (s, 3H, Si-CH_3b), 0.08 (s, 9H, Si-$C(CH_3)_3$), 1.40–1.60 (m, 15H, 4×CH_3-Cby, $CH_{pyrro\text{-}3a}$, $CH_{2\text{-pyrro-4}}$), 1.95 (m, 2H, $CH_{pyrro\text{-}3b}$, $CH_{pyrro\text{-}5a}$), 2.53 (m, 1H, , $CH_{2\text{-pyrro-5b}}$), 2.75 (m, 1H, $CH_{pyrro\text{-}2}$), 3.0 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 3.45 (d, ^3J = 4.2 Hz, 1H, TBDMS-CH), 3.58 (s, 2H, Cby-CH_2), 4.20 (d, 1H, ^2J = 13.2 Hz, 1H, CH_2-Ph), 7.00–7.35 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ = −3.4 (Si-CH_3a), −3.1 (Si-CH_3b), 18.1 (Si-*C*-$(CH_3)_3$), 22.6, 25.3, 26.2, 27.4, 30.6, 30.6, 54.0, 54.4, 59.6, 70.2, 77.2, 98.0, 126.7, 128.3, 129.0, 140.7 (Ph), 164.5 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2952, 2935, 2796 (s, C-H_{ali}), 1626 (s, C=O), 1457 (s), 1362 (s), 1332 (s), 1308 (s), 1244 (s), 1200 (s), 1153 (s), 916 (s), 837 (s), 828 cm^{-1} (s); elemental analysis calcd (%) for $C_{26}H_{44}N_2O_2SSi$ (476.2): C 65.50, H 9.30, N 5.88; found: C 65.19, H 9.56, N 5.51; MS (ESI): *m/z*: 477.2933 $[M+H]^+$, 499.2747 $[M+Na]^+$.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-1-(triphenylsilyl)methyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (14): Colorless oil; yield: 41 %; R_f = 0.87 (E/P 1:1); t_R = 30.2 min (HP-5); $[\alpha]_D^{20} = -17.1$ (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10–1.90 (m, 15H, 4×CH_3-Cby, $CH_{pyrro\text{-}3a}$, $CH_{2\text{-pyrro-4}}$), 2.05 (m, 1H, $CH_{pyrro\text{-}3b}$), 2.15 (m, 1H, $CH_{pyrro\text{-}5a}$), 2.69 (m, 1H, $CH_{pyrro\text{-}5b}$), 3.10 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 3.60 (s, 2H, Cby-CH_2), 3.85 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 4.25 (d, ^3J = 4.2 Hz, 1H, Ph_3Si-CH), 6.80–7.85 ppm (m, 20H, Ph); ^{13}C NMR (75 MHz): δ = 23.9, 24.9, 25.4, 32.1, 33.7, 53.8, 54.0, 60.1, 67.4, 77.2, 96.0, 126.6, 127.9, 128.0, 129.1, 129.6, 135.2, 136.8, 140.2 (Ph), 164.4 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2962, 2942, 2865 (s, C-H_{ali}), 1630 (s, C=O), 1490 (s), 1368 (s), 1333 (s), 1309 (s), 1247 (s), 1203 (s), 1081 (s), 920 (s), 824 (s), 791 cm^{-1} (s); HR MS (ESI): *m/z*: calcd for $C_{38}H_{44}N_2O_2SSi$: 621.2971; found: 621.2973 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)ethyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (15): Colorless oil; yield: 83 %; R_f = 0.45 (E/P 1:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.29–1.80 (m, 16H, 4×CH_3-Cby, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-4}}$), 2.10 (m, 1H, $CH_{pyrro\text{-}5a}$), 2.83 (m, 2H, $CH_{pyrro\text{-}2}$, $CH_{pyrro\text{-}5b}$), 3.23 (d, ^2J = 13.5 Hz, 1H, CH_2Ph), 3.67 (s,

2H, Cby-CH_2), 3.90 (m, 1H, C*H*-SCby), 4.11 (d, ^2J=13.5 Hz, 1H, CH_2-Ph), 7.10–7.45 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ=15.1, 23.7, 25.2, 26.1, 28.2, 41.8, 53.0, 54.7, 58.9, 67.0, 77.2, 94.0 (C-7), 124.4, 126.9, 128.7, 140.0 (Ph), 164.1 (C=O); elemental analysis calcd (%) for $C_{21}H_{32}N_2O_2S$ (376.2): C 66.98, H 8.57, N 7.44; found C 67.12 H 8.65, N 7.30; MS (ESI): *m/z*: 377.2257 $[M+H]^+$, 399.2046 $[M+Na]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)propyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (16): Colorless oil; R_f = 0.36 (E/P 1:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.27 (t, ^3J=7.5 Hz 3H, CH_3-CH_2), 1.60–1.95 (m, 17H, 4×CH_3-Cby, C$H_2$$CH_3$, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 2.10 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.41 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 3.14 (m, 2H, $CH_{2\text{-pyrro-5b}}$, $CH_{pyrro\text{-}2}$), 3.54 (d, ^2J= 13.5 Hz, 1H, CH_2Ph), 3.95 (m, 3H, Cby-CH_2, CH-SCby), 4.45 (d, ^2J= 13.5 Hz, 1H, CH_2Ph), 7.30–7.55 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ=12.7, 21.8, 23.8, 25.2, 26.2, 27.5, 50.0, 54.8, 59.1, 67.6, 77.2, 96.0; 126.9, 128.4, 129.0, 140.6 (Ph), 164.4 ppm (C=O); elemental analysis calcd (%) for $C_{22}H_{34}N_2O_2S$ (390.2): C 67.65, H 8.77, N 7.17; found C 67.70, H 8.82, N 7.04; MS (ESI): *m/z*: 391 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-(1-Benzylpyrrolidin-2-yl)butyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (17): Colorless oil; yield: 90%; R_f = 0.38 (E/P 1:2); t_R = 20.3 min (HP-5); $[\alpha]_D^{20}$=−77.4 (*c*=1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, ^3J=7.0 Hz, 3H, CH_3), 1.37–1.70 (m, 17H, 4×CH_3-Cby, CH_2C$H_2$$CH_3$, $CH_{2\text{-pyrro-4a}}$), 1.81 (m, 2H, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4b}}$), 2.01 (m, 2H, $CH_{2\text{-pyrro-3b}}$, $CH_{2\text{-pyrro-5a}}$), 2.84 (m, 2H, $CH_{2\text{-pyrro-5b}}$, $CH_{pyrro\text{-}2}$), 3.23 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 3.65 (s, 2H, Cby-CH_2), 3.75 (m, 1H, C*H*-SCby), 4.13 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 7.05–7.36 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ = 14.5, 23.7, 25.2, 26.2, 27.3, 28.5, 30.4, 47.4, 53.0, 54.8, 59.0, 67.8, 77.2, 99.7, 126.9, 128.4, 129.0, 140.4 (Ph), 164.3 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2968, 2919, 2863 (s, C-H_{ali}), 1629 (s, C=O), 1454 (s), 1369 (s), 1335 (s), 1310 (s), 1268 (s), 1212 (s), 1082 (s), 918 (s), 837 (s), 791 cm^{-1} (s); elemental analysis calcd (%) for $C_{23}H_{36}N_2O_2S$ (404.5): C 68.27, H 8.97, N 6.92; found: C 68.30, H 9.15, N 7.09; MS (ESI): *m/z*: 405.5 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)pentyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (18): Colorless oil; yield: 78%; R_f = 0.40 (E/P 1:2); t_R = 20.8 min (HP-5); $[\alpha]_D^{20}$=−64.6 (*c*=1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.81 (t, ^3J=7.0 Hz, 3H, CH_3), 1.15–1.70 (m, 20H, 4×CH_3-Cby, CH_2CH_2CH_2 $CH_{2\text{-pyrro-4}}$), 1.80 (m, 1H, $CH_{2\text{-pyrro-3a}}$), 2.10 (m, 2H, $CH_{2\text{-pyrro-3b}}$, $CH_{2\text{-pyrro-5a}}$), 2.82 (m, 2H, $CH_{2\text{-pyrro-5b}}$, $CH_{2\text{-pyrro-2}}$), 3.23 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 3.62 (s, 2H, Cby-CH_2), 3.79 (m, 1H, *CH*-SCby), 4.15 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 7.10–7.39 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz): δ=14.0, 22.5, 23.1, 24.7, 25.7, 26.8, 27.5, 29.7, 47.2, 53.0, 54.3, 58.5, 67.2, 77.2, 96.7, 126.4, 127.8, 128.5, 140.1 (Ph), 163.8 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2968, 2919, 2863 (s, C-H_{ali}), 1629 (s, C=O), 1454 (s), 1369 (s), 1335 (s), 1310 (s), 1268 (s), 1212 (s), 1082 (s), 918 (s), 837 (s), 791 cm^{-1} (s); elemental analysis calcd (%) for $C_{24}H_{38}N_2O_2S$ (418.6): C 68.86, H 9.15, N 6.69; found: C 68.90, H 9.24, N 6.54; MS (ESI): *m/z*: 419.2708 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)but-3-enyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (19): Colorless oil; yield: 89%; R_f = 0.54 (E/P 1:2); t_R = 20.0 min (HP-5); $[\alpha]_D^{20}$=−31.9 (*c*=0.99, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.25–1.70 (m, 15H, 4×CH_3-Cby, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 1.80 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.15 (m, 2H, $CH_{2\text{-pyrro-5}}$), 2.83 (m, 3H, $CH_{pyrro\text{-}2}$, CH_2-CH=CH_2), 3.23 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 3.60 (s, 2H, Cby-CH_2), 3.82 (m, 1H, C*H*-SCby), 4.15 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 5.00 (dd, $^3J_{cis}$=4.8, $^3J_{trans}$=10.3 Hz, 2H, CH_2-CH=CH_2), 5.80 (m, 1H, CH_2-C*H*=CH_2), 7.05–7.41 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ=23.8, 25.2, 26.2, 27.6, 33.5, 47.4, 53.0, 54.8, 59.1, 67.1, 77.2, 94.0, 116.5, 126.9, 128.4, 128.9, 137.1 (Ph), 140.4, 164.1 ppm (C=O); IR (film): $\tilde{\nu}$ = 3079, 2978 (m, C-H_{aro}), 2931, 2869, 2782 (s, C-H_{ali}), 1634 (s, C=O), 1449 (s), 1340 (s), 1311 (s), 1239 (s), 1268 (s), 1202 (s), 1079 (s), 920 (s), 826 (s), 793 cm^{-1} (s); elemental analysis calcd (%) for $C_{23}H_{34}N_2O_2S$ (402): C 68.62, H 8.51, N 6.96; found C 68.68, H 8.53, N 6.72; MS (ESI): *m/z*: 403.5 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-phenylethyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (21): Colorless oil; R_f = 0.50 (E/P 1:2); $[\alpha]_D^{20}$=−4.7 (*c*=1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.25–1.70 (m, 15H, 4×CH_3-Cby, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 1.90 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.15 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.61 (m, 1H, $CH_{2\text{-pyrro-4b}}$), 2.91 (m, 1H, $CH_{2\text{-pyrro-2}}$), 3.25 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 3.45 (dd, ^2J=14.5, ^3J=2.9 Hz 1H, CH-CH_{2a}Ph), 3.60 (s, 2H, Cby-CH_2), 4.10 (dd, ^2J=14.5, ^3J=2.9 Hz, 1H, CH-CH_{2b}Ph), 4.25 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 7.07–7.41 ppm (m, 10H, Ph); ^{13}C NMR (100 MHz): δ=23.4, 24.8, 25.5, 29.5, 34.8, 49.0, 53.0, 54.4, 58.7, 66.9, 77.2, 94.0, 125.7, 126.5, 127.9, 128.0, 128.5, 129.1, 129.4, 139.9 (Ph), 163.0 ppm (C=O); elemental analysis calcd (%) for $C_{27}H_{36}N_2O_2S$ (452.2): C 71.64, H 8.02, N 6.19; found C 71.46, H 8.22, N 5.96; MS (ESI): *m/z*: 453.25 $[M+H]^+$, 475.23 $[M+Na]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-(naphthalen-1-yl)ethyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (22): Colorless oil; yield: 55%; R_f = 0.50 (E/P 1:1); t_R = 26.9 min (HP-5); $[\alpha]_D^{20}$=+37.3 (*c*=1.12, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.25–1.70 (m, 12H, 4×CH_3-Cby), 1.55–1.90 (m, 4H, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-4}}$), 2.18 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.71 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 2.96 (m, 1H, $CH_{pyrro\text{-}2}$), 3.35 (d, ^2J=13.5 Hz, 1H, CH_2Ph), 3.50 (s, 2H, Cby-CH_2), 3.60 (dd, ^3J=2.9, ^2J=14.5 Hz, 1H, Nap-CH_{2a}), 4.15 (dd, ^3J=2.9, ^2J=14.5 Hz, 1H, Nap-CH_{2b}), 4.25 (d, ^2J= 13.5 Hz, 1H, CH_2Ph), 7.07–7.91 ppm (m, 12H, Ar); ^{13}C NMR (75 MHz): δ=24.0, 24.9, 25.9, 27.8, 35.7, 49.5, 53.0, 55.0, 59.3, 67.5, 77.2, 94.0, 125.4, 126.0, 127.0, 127.8, 128.3, 128.6, 129.0, 132.5, 133.8, 138.0, 140.5 (Ar), 163.2 ppm (C=O); IR (film): $\tilde{\nu}$ = 3088, 3055 (s, C-H_{aro}), 2979, 2866, 2790 (s, C-H_{ali}), 1626 (s, C=O), 1599, 1514 (s), 1496 (s), 1454 (s), 1334 (s), 1309 (s), 1309 (s), 1264 (s), 1220 (s), 1058 (s), 917 (s), 826 (s), 784 cm^{-1} (s); elemental analysis calcd (%) for $C_{31}H_{38}N_2O_2S$ (502.2): C 74.06, H 7.62, N 5.57; found: C 74.04, H 7.88, N 5.25; MS (ESI): *m/z*: 503.2726 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-(anthracen-9-yl)ethyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (23): Yellow crystalline solid; yield: 38%; R_f = 0.51 (E/P 1:1); m.p. 160.1 °C; t_R = 31.6 min (HP-5); $[\alpha]_D^{20}$=+74.2 (*c*=1.01, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.60–1.25 (m, 12H, 4×CH_3-Cby), 1.65–2.16 (m, 4H, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-4}}$), 2.24 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 3.15(m, 2H, $CH_{2\text{-pyrro-5b}}$, $CH_{pyrro\text{-}2}$), 3.35 (s, 2H, Cby-CH_2), 3.48 (d, ^2J=14.4 Hz, 1H, CH_2-Ph), 3.75 (m, 1H, CH-SCby), 4.31 (dd, ^3J=2.5 Hz, 2H, Anthra-CH_2), 4.52 (d, ^2J=14.4 Hz, 1H, CH_2-Ph), 7.10–8.40 ppm (m, 14H, Ar); ^{13}C NMR (150 MHz): δ=24.2, 25.1, 25.3, 26.9, 48.7, 54.8, 55.0, 59.2, 64.2, 68.4, 76.9, 93.6, 124.2, 124.5, 124.8, 125.0, 125.2, 126.0, 126.5, 128.2, 128.3, 128.8, 130.6, 131.0, 131.3, 131.4, 132.1, 133.9 (Ar), 162.1 ppm (C=O); IR (KBr): $\tilde{\nu}$ = 3088, 3055 (s, C-H_{aro}), 2979, 2866, 2790 (s, C-H_{ali}), 1626 (s, C=O), 1599 (s), 1514 (s), 1496 (s), 1454 (s), 1334, 1309 (s), 1309 (s), 1264 (s), 1220 (s), 1058 (s), 917 (s), 826 (s), 784 cm^{-1} (s); elemental analysis calcd (%) for $C_{35}H_{40}N_2O_2S$ (552.2): C 76.05, H 7.29, N 5.07; found C 75.83, H 7.19, N 4.70. MS (ESI): *m/z*: 553.2889 $[M+H]^+$, 575.2704 $[M+Na]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-(3-bromo-5-fluorophenyl)ethyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (24): Colorless oil; yield: 80%; R_f = 0.55 (E/P 1:1); t_R = 24.4 min (HP-5); $[\alpha]_D^{20}$=+5.4 (*c*= 1.05, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.47–1.89 (m, 14H, 4× CH_3-Cby, $CH_{2\text{-pyrro-4}}$), 2.19 (m, 1H, $CH_{2\text{-pyrro-3a}}$), 2.40 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.68 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.99 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 3.15 (m, 3H, $CH_{pyrro\text{-}2}$, CbyS-C*H*-CH_{2a}-Ph), 3.53 (d, ^2J=13.3 Hz, 1H, CH_2Ph), 3.60 (dd, ^3J=3.6, ^2J=13.4 Hz, 1H, CbyS-CH-CH_{2b}-Ph), 3.92 (s, 2H, Cby-CH_2), 4.36 (d, ^2J= 13.4 Hz, 1H, CH_2Ph), 7.29–7.60 ppm (m, 8H, Ph); ^{13}C NMR (75 MHz): δ=24.7, 25.7, 27.0, 30.1, 34.2, 47.0, 54.0, 54.2, 58.6, 67.0, 77.2, 97.0, 126.6, 127.9, 128.0, 128.9, 129.1, 129.5, 131.1, 139.5, 139.7, 145.4 (Ar), 163.8 ppm (C=O); ^{19}F NMR (282.4 MHz): δ=114.87 ppm; IR (film): $\tilde{\nu}$ =3029, 2964 (s, C-H_{aro}), 2934, 2873, 2789 (s, C-H_{ali}), 1625 (s, C=O), 1496 (s), 1454 (s), 1370 (s), 1336 (s), 1309 (s), 1260 (s), 1202 (s), 1058 (s), 917 (s), 826 (s), 784 cm^{-1} (s); elemental analysis calcd (%) for $C_{27}H_{34}BrFN_2O_2S$ (550.1): C 59.01, H 6.24, N 5.10; found: C 59.34, H 6.41, N 4.78. MS (ESI): *m/z*: 551.1575 $[M+H]^+$, 573.1385 $[M+Na]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-(biphenyl-2-yl)ethyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (25): Colorless oil; yield: 88%; R_f = 0.44 (E/P 1:1); t_R = 26.9 min (HP-5); $[\alpha]_D^{20}$=−11.6 (*c*=1.11, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.25–1.70 (m, 15H, 4×CH_3-Cby, $CH_{2\text{-pyrro-4}}$, $CH_{2\text{-pyrro-3a}}$), 1.98 (m, 1H, $CH_{2\text{-pyrro-3a}}$), 2.25 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.90 (dd, ^3J=4.1, ^2J=11.9 Hz, 1H, Ph-Ph-CH_{2a}), 3.00 (m, 2H, $CH_{pyrro\text{-}2}$, $CH_{2\text{-pyrro-5b}}$), 3.24 (d, ^2J=13.5 Hz, 1H, CH_2-Ph), 3.65 (dd, ^3J=4.1, ^2J= 11.9 Hz, 1H, Ph-Ph-CH_{2b}), 3.90 (s, 2H, Cby-CH_2), 4.00 (d, ^2J=13.5 Hz, 1H, CH_2-Ph), 4.28 (m, 1H, C*H*-SCby), 7.25–7.60 ppm (m, 14H, Ph); ^{13}C NMR (75 MHz): δ=23.4, 25.2, 26.4, 27.8, 31.9, 48.5, 54.6, 58.8, 67.3,

77.1, 126.1, 126.8, 127.1, 127.3, 128.3, 129.1, 129.8, 130.9, 137.6, 140.2, 142.3, 143.1 (Ph), 163.4 ppm (C=O); IR (film): $\tilde{\nu}$ = 3058, 2964 (s, C-H_{aro}), 2962, 2863, 2784 (s, C-H_{ali}), 1632 (s, C=O), 1496 (s), 1478 (s), 1449 (s), 1370 (s), 1333 (s), 1309 (s), 1263 (s), 1199 (s), 1062 (s), 923 (s), 824 (s), 724 cm^{-1} (s); elemental analysis calcd (%) for $C_{33}H_{46}N_2O_2S$ (528.7): C 74.96, H 7.63, N 5.30; found: C 74.76, H 7.71, N 5.16; MS (ESI): *m*/*z*: 529.5 $[M+H]^+$, 551.5 $[M+Na]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-2-hydroxy-2,2-diphenylethyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (26): Colorless oil; yield: 78%; R_f = 0.46 (E/P 1:1); t_R = 26.9 min (HP-5); $[\alpha]_D^{20}$ = +18.5 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20–1.55 (m, 12H, 4 × CH_3-Cby), 1.60–1.85 (m, 3H, $CH_{2\text{-pyrro-4}}$, $CH_{2\text{-pyrro-3a}}$), 2.05 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.55 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.81 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 2.91 (m, 1H, $CH_{pyrro\text{-}2}$), 3.15 (d, *J* = 13.5 Hz, 1H, CH_2-Ph), 3.05 (d, *J* = 13.5 Hz, 1H, CH_2-Ph), 3.55 (s, 2H, Cby-CH_2), 4.87 (d, ^3J = 3.5 Hz, 1H, C*H*-SCby), 7.0–7.80 (m, 15H, Ph), 9.29 ppm (br s, 1H, OH); ^{13}C NMR (75 MHz): δ = 23.3, 24.2, 25.2, 29.1, 51.3, 57.6, 60.5, 67.9, 77.2, 82.8, 98.0, 125.1, 125.8, 126.3, 126.9, 127.7, 127.9, 128.1, 128.9, 129.2, 138.6, 148.5, 148.1 (Ph), 164.6 ppm (C=O); IR (film): $\tilde{\nu}$ = 3463 (b, OH), 3058, 3023, 2978 (s, C-H_{aro}), 2939, 2867 (s, C-H_{ali}), 1621 (s, C=O), 1499 (s), 1453 (s), 1349 (s), 1315 (s), 1309 (s), 1265 (s), 1239 (s), 1204 (s), 1082 (s), 921 (s), 826 (s), 784 cm^{-1} (s); elemental analysis calcd (%) for $C_{23}H_{40}N_2O_3S$ (544.7): C 72.26, H 7.04, N 5.14; found: C 72.32, H 7.41, N 4.68; MS (ESI): *m*/*z*: 545.2853 $[M+H]^+$, 567.2654 $[M+Na]^+$.

[1*R*,1(2*S*),2*R*]- and [1*R*,1(2*S*),2*S*]-S-[(1-Benzylpyrrolidin-2-yl)-2-(4-bromophenyl)-2-hydroxyethyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate (27 and *epi*-27 [mixture] dr 68:32): Colorless oil; yield: 76%; R_f = 0.22 (E/P 1:1); t_R = 20.5 and 22.5 min (HP-5); $[\alpha]_D^{20}$ = +29.05 (*c* = 1.0, CH_2Cl_2) of the above diastereomeric mixture; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24–1.59 (m, 12H, 4 × CH_3-Cby), 2.00 (m, 2H, $CH_{2\text{-pyrro-4}}$), 2.23 (m, 2H, $CH_{2\text{-pyrro-3}}$), 2.38 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 3.11 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 3.46 (m, 2H, $CH_{pyrro\text{-}2}$, C*H*-SCby), 3.79 (s, 2H, Cby-CH_2), 4.51 (d, ^2J = 12.8 Hz, 1H, CH_2-Ph), 4.73 (d, ^2J = 12.8 Hz, 1H, CH_2-Ph), 5.10 (d, ^{3}J = 10.6 Hz, 1H, C*H*-OH), 7.36–7.63 (m, 9H, Ph), 8.62 ppm (br s, 1H, OH); ^{13}C NMR (75 MHz): δ = 23.2, 24.8, 25.2, 26.4, 47.4, 53.5, 58.8, 65.6, 68.6, 75.5, 76.5, 127.3, 128.4, 128.9, 129.8, 130.5, 137.5, 141.3 (Ph), 160.5 ppm (C=O); IR (film): $\tilde{\nu}$ = 3463 (b, OH), 3058, 3023, 2978 (s, C-H_{aro}), 2939, 2867 (s, C-H_{ali}), 1621 (s, C=O), 1499 (m), 1453 (s), 1349 (m), 1315 (s), 1309 (s), 1265 (s), 1239, 1204 (s), 1082 (s), 921 (s), 826 (s), 784 cm^{-1} (s); elemental analysis calcd (%) for $C_{27}H_{35}BrN_2O_3S$ (547.5): C 59.23, H 6.44, N 5.12; found: C 59.28, H 6.40, N 4.94. MS (ESI): *m*/*z*: 549.1623 $[M+H]^+$.

[(1*R*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-3,3-dimethyl-2-oxobutyl] 2,2,4,4-tetramethyloxazolidine-3-carbothioate (28): Colorless oil; yield: 76%; R_f = 0.60 (E/P 1:2); t_R = 14.2 min (HP-5); $[\alpha]_D^{20}$ = −1.4 (*c* = 1.12, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9H, C(CH_3)$_3$), 1.55–1.70 (m, 15H, 4 × CH_3-Cby, $CH_{2\text{-pyrro-4}}$, $CH_{2\text{-pyrro-3a}}$), 1.90 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.31 (m, 1H, $CH_{2\text{-pyrro-4a}}$), 2.91 (m, 1H, $CH_{pyrro\text{-}2}$), 3.40 (m, 2H, $CH_{2\text{-pyrro-4b}}$, CH_2-Ph), 3.80 (s, 2H, Cby-CH_2), 4.15 (d, ^2J = 12.9 Hz, 1H, CH_2-Ph), 5.12 (d, $^3J_{1,6}$ = 7.0 Hz, 1H, C*H*-SCby), 7.14–7.51 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz): δ = 25.2, 26.0, 26.8, 27.2, 31.6, 41.0, 49.3, 51.1, 55.2, 61.7, 66.1, 77.2, 98.0, 128.2, 129.5, 130.5, 140.1 (Ph), 163.0 (C=O), 214.9 ppm (O=C-*t*Bu); IR (film): $\tilde{\nu}$ = 3029, 2962 (s, C-H_{aro}), 2928, 2864, 2793 (s, C-H_{ali}), 1696, 1639 (s, C=O), 1493 (s), 1452 (s), 1339 (s), 1309 (s), 1267 (s), 1245 (s), 1200 (s), 1059 (s), 922 (s), 824 (s), 787 cm^{-1} (s); HR MS (ESI): *m*/*z*: calcd for $C_{25}H_{38}N_2O_3S$: 447.2694; found: 447.2681 $[M+H]^+$.

[(1*S*),1(2*S*)]-S-[(1-Benzylpyrrolidin-2-yl)-deuteriomethyl] 2,2,4,4-tetramethyl-oxazolidine-3-carbothioate ([D]-8): Colorless oil; yield: 99%; R_f = 0.42 (E/P 1:2); t_R = 20.39 min (HP-5); $[\alpha]_D^{20}$ = −69.5 (*c* = 0.63, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.80 (m, 15H, 4 × CH_3-Cby, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 1.90 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.12 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.65 (m, 1H, $CH_{pyrro\text{-}2}$), 2.85 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 3.03 (d, ^3J = 6.9 Hz, 1H, C*H*D), 3.12 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 3.65 (s, 2H, Cby-CH_2), 4.05 (d, ^2J = 13.2 Hz, 1H, CH_2-Ph), 7.11–7.45 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz): δ = 22.4, 24.7, 25.7, 30.0, 34.2, 54.0, 54.1, 58.8, 62.9, 77.2, 96.0, 126.6, 128.1, 128.7, 139.4 (Ph), 163.8 ppm (C=O); IR (film): $\tilde{\nu}$ = 3064, 3030 (m, C-H_{aro}), 2974, 2926, 2869 (s, C-H_{ali}), 1632 (s, C=O), 1690 (s), 1458 (s), 1364 (s), 1267 (s), 1241 (s), 1076 (s), 919 (s), 885 (s), 799 cm^{-1} (s); elemental analysis calcd (%) for $C_{20}H_{30}DN_2O_2S$ (363.2): C 66.08, H 8.59, N 7.71; found: C 66.11, H 8.37, N 7.62; MS (ESI): *m*/*z*: 364.2170 $[M+H]^+$.

Dedeuteration experiment: According to the general experimental procedure, the deprotonation was carried out with [D]-**8** (100 mg, 0.27 mmol, 1.0 equiv) dissolved in toluene (5 mL). TMEDA (37 mg, 0.32 mmol, 1.2 equiv) was added and the reaction flask was cooled to −78°C. Afterwards, *s*BuLi (1.36 M, 0.23 mL, 0.32 mmol, 1.2 equiv) was injected in a dropwise manner and the reaction mixture was stirred at −78°C for 3 h. Then MeOD (2.70 mmol, 10.0 equiv) was injected and the reaction mixture stirred for 15 min. To the reaction mixture then anhydrous $MgSO_4$ was added, the mixture filtered through glass wool and washed several times with Et_2O. The collective organic phase was concentrated under reduced pressure to get the crude product. The crude product was passed through a short column (Et_2O), concentrated, dried, and subjected to analyses. From NMR and mass spectral analyses, it was found to be a mixture of **8** (78%), [D]-**8** (3%), and *epi*-[D]-**8** (19%). Colorless oil; yield: 98%; R_f = 0.42 (E/P 1:2); ^{1}H NMR (600 MHz, C_6D_6): δ = 1.37 (s, 6H, 2 × CH_3-Cby), 1.51–185 (m, 10H, 2 × CH_3-Cby, $CH_{2\text{-pyrro-3}}$, $CH_{2\text{-pyrro-4}}$), 1.95 (m, 1H, $CH_{2\text{-pyrro-5a}}$,), 2.68 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 2.84 (m, 1H, $CH_{pyrro\text{-}2}$), 3.03 (dd, ^3J = 7.3, ^2J = 13.6 Hz; 1H), 3.12 (d, ^2J = 13.2 Hz, 2H, CH_2Ph), 3.36 (s, 2H, Cby-CH_2), 3.52 (dd, *J* = 3.2, 13.6 Hz, 1H), 4.12 (d, ^2J = 13.2 Hz, 1H), 7.07–7.21 ppm (m, 5H, Ph); ^{2}H NMR [in C_6H_6 with a trace of C_6D_6 for reference (600 MHz)]: δ = 3.03 (85%), 3.53 ppm (15%); MS (ESI): *m*/*z*: 363.2101 $[M-D+H]^+$ (78%), 364.2170 $[M_D+H]^+$(22%).

In situ trapping with TMSCl-**10** and [D]-**10**: According to the general experimental procedure, the deprotonation was carried out with [D]-**8** (100 mg, 0.27 mmol, 1.0 equiv), dissolved in toluene (5 mL). TMEDA (37 mg, 0.32 mmol, 1.2 equiv) and TMSCl (291 mg, 2.70 mmol, 10 equiv) was added and the reaction flask was cooled to −78°C. Afterwards, *s*BuLi (1.36 M, 0.23 mL, 0.32 mmol, 1.2 equiv) was injected in a dropwise manner and the reaction mixture was stirred at −78°C till no starting material could be detected by TLC. Standard workup, followed by column chromatography (E/P) afforded the product which was found to be a 67:33 mixture of **10** and [D]-**10**. (cf. Supporting Information).

General experimental procedure for the decarbamoylation of substituted thiocarbamates: Under argon atmosphere, appropriately substituted thiocarbamate (1.0 equiv) was treated with diisobutylaluminium hydride (DIBALH, 1 M solution in hexanes, 20 equiv) at room temperature for 1–3 h (TLC monitor). The reaction mixture was then cooled to 0°C and worked up according to the Fieser procedure[25] by adding calculated amounts of water, 15% NaOH and water with several minutes of stirring in between (for *n* g of metal hydride, successive addition of *n* mL of water, *n* mL of 15% NaOH and 3*n* mL of water is required). The resulting aluminium salts were filtered through a short silica gel column under vacuum and the solvent from the filtrate was evaporated to get the crude thiol which was subjected to column chromatography.

(*S*)-1-[(*S*)-1-Benzylpyrrolidin-2-yl]propane-1-thiol (31): Colorless oil; yield: 84%; R_f = 0.50 (E/P 1:1); $[\alpha]_D^{20}$ = −73.0 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (300 MHz; $CDCl_3$): δ = 0.92 (t, ^3J = 7.5 Hz, 3H, CH_2-CH_3), 1.55–1.68 (m, 5H, CH_2-CH_3, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 1.83 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.16 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.18 (dt, *J* = 7.5 Hz, 1H, $CH_{2\text{-pyrro-5b}}$), 2.64 (m, 1H, $CH_{pyrro\text{-}2}$), 2.71 (m, 1H, C*H*-SH), 3.28 (d, ^2J = 13.3 Hz, 1H, CH_2-Ph), 3.92 (d, ^2J = 13.3 Hz, 1H, CH_2-Ph), 7.14–7.26 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz): δ = 12.6, 23.5, 26.0, 27.2, 46.6, 55.0, 59.9, 69.6, 126.7, 128.1, 128.3, 140.1 ppm (Ph); IR (film): $\tilde{\nu}$ = 3064, 3030 (w, C-H_{aro}), 2962, 2929, 2873 (s, C-H_{ali}), 1494 (s), 1453 (s), 1374 (s), 1215 (s), 1131 (s), 1072 (s), 918 (s), 847 (s), 751 (s), 698 cm^{-1} (s); HR MS (ESI): calcd for $C_{14}H_{21}NS$: 236.1467; found: 236.1459 $[M+H]^+$.

(*S*)-1-[(*S*)-1-Benzylpyrrolidin-2-yl]-2-phenylethanethiol (32): Colorless oil; yield: 50%; R_f = 0.37 (E/P 1:2); $[\alpha]_D^{20}$ = −67.5 (*c* = 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64 (m, 2H, $CH_{2\text{-pyrro-4}}$), 1.78 (m, 1H, $CH_{2\text{-pyrro-3a}}$), 1.88 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 2.16 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.22 (m, 1H, $CH_{2\text{-pyrro-5b}}$), 2.84 (m, 1H, $CH_{pyrro\text{-}2}$), 3.07 (m, 1H, C*H*-SH), 3.16 (d, ^2J = 13.3 Hz, 1H, N-CH_2-Ph), 3.44 (m, 2H, HS-CH-CH_2-Ph, N-CH_2Ph), 3.99 (d, ^2J = 13.3 Hz, 1H, CH_2-Ph), 7.03–7.38 ppm (m, 10H, Ph); ^{13}C NMR (100 MHz): δ = 22.6, 25.9, 37.8, 44.6, 54.1, 58.7, 68.0; 125.1, 125.8, 127.1, 127.3, 127.5, 128.2, 139.0, 139.2 ppm (Ph); IR (film): $\tilde{\nu}$ = 3064, 3030 (w, C-H_{aro}), 2962, 2929, 2873 (s, C-H_{ali}), 2571 (w), 1494 (s),

1453 (s), 1374 (s), 1215 (s), 1131 (s), 1072 (s), 918 (s), 847 (s), 751 (s), 698 cm^{-1} (s); HR MS (ESI): *m/z*: calcd for $C_{19}H_{23}NS$: 298.1624; found: 298.1614 $[M+H]^+$.

(*R*)-[(*S*)-1-Benzylpyrrolidin-2-yl](*tert*-butyldimethylsilyl)-methanethiol (33): Colorless oil; yield: 80%; R_f = 0.38 (E/P 1:2); $[\alpha]_D^{20} = -139.3$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.10 (s, 3H, Si-CH_{3a}), 0.10 (s, 3H, Si-CH_{3b}), 0.90 (s, 9H, SiC(CH_3)$_3$; 155–1.62 (m, 3H, $CH_{2\text{-pyrro-3a}}$, $CH_{2\text{-pyrro-4}}$), 1.85 (m, 1H, $CH_{2\text{-pyrro-3b}}$), 1.95 (m, 1H, $CH_{2\text{-pyrro-5a}}$), 2.05 (m, 1H, $CH_{pyrro\text{-}2}$), 2.24 (d, ^3J = 4.1 Hz, 1H, HS-C*H*-TBDMS), 2.74 (m, 2H, $CH_{2\text{-pyrro-5b}}$, S*H*), 3.10 (d, ^2J = 13.3 Hz, 1H, CH_2Ph), 3.96 (d, ^2J = 13.3 Hz, 1H, CH_2Ph), 7.10–7.26 ppm (m, 5H, Ph); ^{13}C NMR (100 MHz): δ = −5.3, −4.2, 17.5, 23.1, 25.7, 27.2, 31.2, 54.0, 60.4, 69.7; 126.7, 128.1, 128.5, 139.9 ppm (Ph); IR (film): $\tilde{\nu}$ = 3062, 3029 (w, C-H_{aro}), 2962, 2929, 2873 (s, C-H_{ali}), 2569 (w), 1494 (s), 1453 (s), 1374 (s), 1215 (s), 1131 (s), 1072 (s), 918 (s), 847 (s), 751 (s), 698 cm^{-1} (s); HR MS (ESI): calcd for $C_{18}H_{31}NSSi$: 322.2019; found: 322.2019 $[M+H]^+$.

Crystallographic data: Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN,[26], absorption correction Denzo,[27] structure solution SHELXS-97,[28] structure refinement SHELXL-97,[29] graphics SCHAKAL.[30]

X-ray crystal structure analysis for (*R*)-**13**:[31] formula $C_{26}H_{44}N_2O_2SSi$, M = 476.78, colorless crystal 0.35 × 0.15 × 0.05 mm, a = 7.811(1), b = 17.453(1), c = 21.319(1) Å, V = 2906.3(4) Å^3, ρ_{calcd} = 1.090 g cm^{-3}, μ = 1.55 mm^{-1}, empirical absorption correction (0.613 ≦ T ≦ 0.927), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 293 K, ω and ϕ scans, 9760 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.60 Å^{-1}, 4636 independent (R_{int} = 0.058) and 3666 observed reflections [I ≧ 2 $\sigma(I)$], 289 refined parameters, R = 0.070, wR^2 = 0.201, Flack parameter 0.05(4), max. residual electron density 0.32 (−0.22) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

X-ray crystal structure analysis for (*S*)-**23**:[31] formula $C_{35}H_{40}N_2O_2S{\cdot}CHCl_3$, M = 672.12, colorless crystal 0.20 × 0.10 × 0.10 mm, a = 11.331(1), b = 14.506(1), c = 21.213(1) Å, V = 3486.7(4) Å^3, ρ_{calcd} = 1.280 g cm^{-3}, μ = 3.20 mm^{-1}, empirical absorption correction (0.567 ≦ T ≦ 0.740), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 293 K, ω and ϕ scans, 46664 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.60 Å^{-1}, 6181 independent (R_{int} = 0.075) and 4842 observed reflections [I ≦ 2 $\sigma(I)$], 412 refined parameters, R = 0.077, wR^2 = 0.227, Flack parameter 0.02(3), max. residual electron density 0.28 (−0.63) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

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