Atroposelectivity of Reactions of Benzylic Metalated Thiobenzamides and Thionaphthamides

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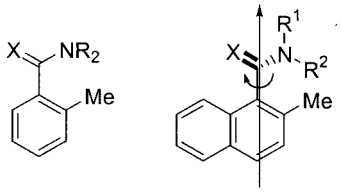
N,*N*-Dialkyl-2-methylbenzenecarbothioamides and naphthalenecarbothioamides were prepared by thionation of amides with Lawesson's reagent under unusual conditions. Their axial chirality was evidenced. Benzylic deprotonation of thioamides bearing *N*,*N*-diisopropyl groups with *sec*-butyllithium was selective. The resulting anions were reacted with prochiral electrophiles (aromatic aldehydes, an unsaturated aldehyde or ketone, and an imine) to afford diastereomeric adducts (up to 88:12 *dr*). This is the first report on atroposelective C–C bond formation in the benzylic position of thioamides.

Introduction

Molecules bearing an aromatic nucleus conjugated to an acyclic π-system are not necessarily flat. Constraints to a favorable complete orbital overlap with a planar arrangement are encountered, for instance by introduction of an *ortho*-substituent on the aromatic ring.[1–4] For 2-methylbenzamides **1** or naphthamides **3,** a noticeable angle is observed between the planes of the aromatic ring and that of the amide.[5,6] We have shown[7] recently that this is increased in the sulfur series: *ortho*-substituted *N*-thionaphthamides **4** (R^1 = H; R^2 = Me) exhibit almost complete orthogonality between the two planes (Scheme 1). A structural consequence is the axial chirality along the C_{Ar}–C(=S) bond. If the rotation barrier is high enough, enantiomers will be observed.



1 X = O
2 X = S

3 X = O
4 X = S

R^2, R^1 = Me, Et, *i*Pr

Scheme 1. Atropisomeric amides and thioamides

We have wished to investigate this possibility in the sulfur series. Our interest arose from the need to explore new structures as chiral auxiliaries for asymmetric syntheses and the observation that the axially chiral compounds available so far are almost all of the biaryl structure. Recent investigations have brought the first successes with non-biaryl compounds.[3,6,8–14] A great deal of information on atropisomeric naphthamides is available from the work of Clayden and his group.[6,15–19] This has constituted the starting point of our investigation. We have anticipated that thioamides might bring advantages or differences over the oxygen analogues: (i) marked orthogonality, (ii) enhanced barriers of rotation as suggested by data reported by Mannschreck and co-workers,[20,21] (iii) easy benzylic metallation and stabilization of the anions formed (polarizability of sulfur), (iv) specific behavior of the thioamide group present in the products for further uses.

In a previous article,[7] we have reported an approach with secondary thiobenzamides and thionaphthamides. Their geometrical structure was studied and their benzylic metallation was selectively achieved, but no atroposelectivity could be observed. We now report our results with racemic tertiary thioamides.

Synthesis and Structure of Thiobenzamides and Thionaphthamides

The most usual preparation of tertiary thioamides[22–24] involves thionation of the amides with P=S compounds, either P_4S_{10} or the Lawesson's reagent,[25] which is more soluble in organic solvents. With this latter reagent, we have attempted to prepare thioamides **12**–**18**. The failures that we have met revealed that the sulfurization reactions are sensitive to steric hindrance, and this obliged us to undertake an optimization work (Table 1).

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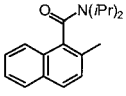
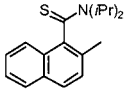
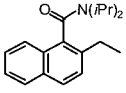
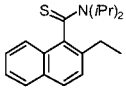
Table 1. Synthesis of thioamides **12**−**18**

Entry	Starting material	Reaction Conditions	Thioamide	Yield [%]
1	 **5**	Lawesson's reagent THF r.t., 19 h	 **12**	98
2	 **7**	Lawesson's reagent 1,2,4-Trichlorobenzene 165°C, 16 h	 **13**	90
3	 **8**	Lawesson's reagent 1,2,4-Trichlorobenzene 165°C, 24 h	 **14**	91
4	 **10**	Lawesson's reagent 1,2,4-Trichlorobenzene 165°C, 100 h	 **15**	40
5	 **11**	Lawesson's reagent 1,2,4-Trichlorobenzene 165°C, 144 h	 **16**	48
6			 **17**	80
7	+ $(Ph_3P)_2NiCl_2$ (cat.)		 **18**	71

Amides **5** and **7** were prepared by the standard reaction of acid chlorides with secondary amines (respectively dimethylamine and diisopropylamine) in quantitative yield. The crude materials were used for the next step (thionation). Amides **8**, **10** and **11** were prepared in two steps (Scheme 2): the first one involves the reaction between the benzoyl chloride or 1-naphthoyl chloride and the appropriate amine to afford amides **6** and **9**; then, the second one is an ortho-metallation with *sec*-butyllithium and subsequent alkylation with the appropriate electrophile: ethyl iodide (**6** → **8** and **9** → **11**) or methyl iodide (**9** → **10**).

Reaction of amide **5** (Table 1, Entry 1), bearing an *ortho* methyl group, with 0.6 equiv. of Lawesson's reagent in THF at room temperature overnight, afforded the thioamide **12** in 98% yield. Surprisingly, replacement of the *N*,*N*-dimethyl group by the *N*,*N*-diisopropyl one led to complete inhibition of the thionation in the previous reaction conditions. Several conditions, as well as other methods, were tested without success. Use of Lawesson's reagent in more drastic conditions finally led to the expected conversion. Sulfurization in 1,2,4−trichlorobenzene as solvent, at 165 °C, gave thioamides **13**, **14**, **15** and **16**, in acceptable yields (Table 1, Entries 2−5). Use of toluene was also efficient for the thionation reaction but only with *ortho*-unsubstituted *N*,*N*-diisopropylamide as starting material. To the best of our knowledge, they represent the first examples of *N*,*N*-diisopropylthioamides.

The difficulties to operate under classical conditions are related to the steric hindrance of the *N*,*N*-diisopropyl moiety and probably also to the geometrical structure of the starting material. The carbonyl group becomes less accessible when its plane becomes more orthogonal to the arene ring, by introduction of an *ortho* substituent. Both faces of the carbonyl are strongly hindered.

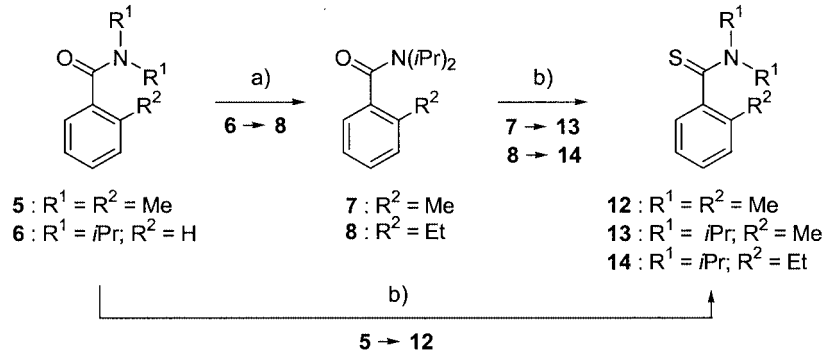
Finally, a complementary route for *N*,*N*-dimethyl and *N*,*N*-diethyl thioamides was tested according to a method reported by Fiandanese and co-workers:[26] metal-catalyzed coupling of an arylmagnesium bromide with thiocarbamoyl chlorides. We replaced [1,2-bis(diphenyl-phosphanyl)-ethane]nickel(II) dichloride by cheaper bis(triphenylphosphane)nickel(II) dichloride and achieved efficient coupling at room temperature, providing thioamides **17** and **18** in 80 and 71% yields (Table 1, Entries 6 and 7).

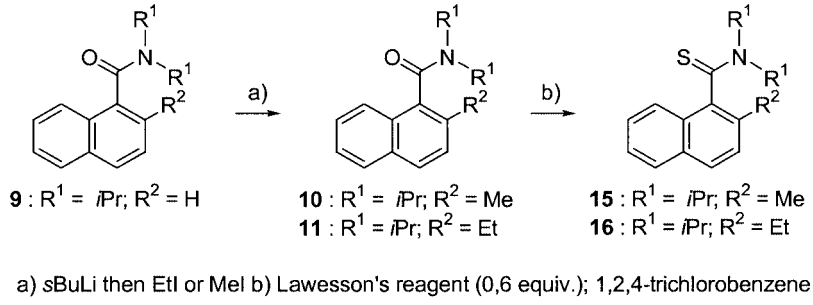
Having the expected thioamides in hands, we examined their structures. We have first shown that tertiary thioamides exhibit a chirality axis. We tested separation of enantiomers by liquid chromatography on a large variety of chiral columns (Chiracel OB and AD from Daicel, Chirose N°2 C1 from Chiralsep and Nucleodex β-OH from Macherey-Nagel), but we were unsuccessful. Then, we observed that addition of 3 equiv. of a chiral shift reagent, (+)-(*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol,[27] to thioamides **12**, **13** and **15** (and also amide **7** for comparison) effected separation of the *ortho* methyls on the aromatic ring in ^{1}H NMR (a mixture of diastereoisomer 51:49 was observed according the integration).

This prompted us to quantify the barrier to rotation along the chiral axis: the $C_{Ar}-C(=S)$. Extensive analyses have been reported for benzamides and naphthamides.[2,20,21] For thioamides, scant information[21] reveals that barriers ($\Delta G^{\neq}$) are enhanced of 30−40 kJ/mol. We have examined the ^{1}H NMR of thioamides **13** and **15** at variable temperature. The sample was heated in [D_6]DMSO until the coalescence of the two signals of the methyl group of isopropyl group. By heating at 140 °C, none of the possible rotations [$C_{Ar}-C(=S)$ and $N-C(=S)$] was attained and experimental values could not be obtained. We estimated by calculation (Mac Spartan) that the rotation barriers along the chirality axis are 115 kJ/mol for *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**) and 145 kJ/mol for the analogous naphthalenecarbothioamide **15**. The values for the corresponding amides **7** and **10** are 71 kJ/mol and 90 kJ/mol respectively. Therefore the rate of racemization is predicted to be extremely slow in the synthetic experimental conditions.

Metallation

Conditions for deprotonation were tested at −78 °C using *sec*-butyllithium (1.5 equiv.) with subsequent addition of MeI. With *N*,*N*-dimethyl-2-methylbenzenecarbothio-





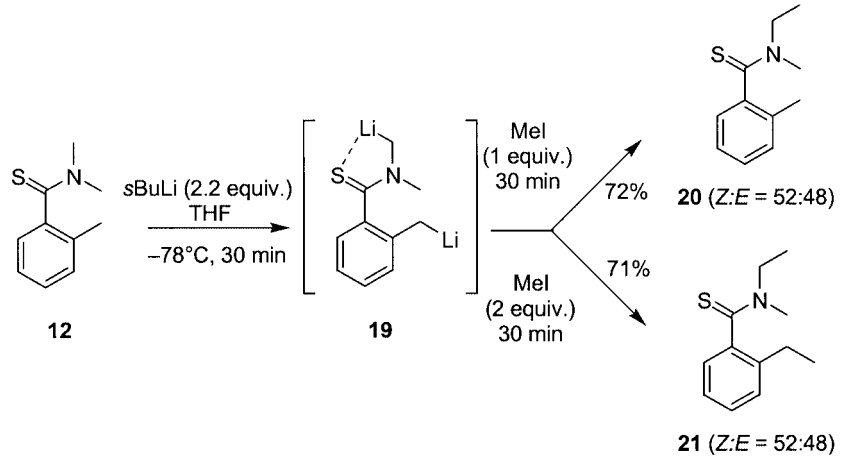
Scheme 2. Synthesis of thiobenzamides and thionaphthamides

amide (**12**), 2-ethylbenzenecarbothioamide **17** was not observed and, instead, abstraction of an *N*-methyl proton took place, to give *N*-methyl-*N*-ethyl thioamide **20** in 11% yield (Scheme 3). The yield raised to 72% using 2.2 equiv. of base and 1 equiv. of MeI. It is worthy to note that addition of 2 equiv. of MeI led to bis(alkylated) thioamide **21** in 71% yield, showing that a dianion **19** was produced. This intermediate is probably stabilized by coordination of the carbanion lithium atom with the sulfur atom of the thioamide. There are precedents for deprotonation of *N*-Me groups of amides[28,29] and some thioamides.[30,31]

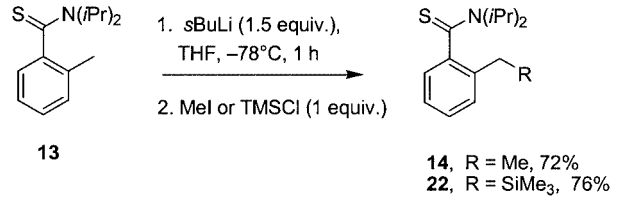
To avoid this deprotonation, the *N*-methyl groups have been replaced by *N*-isopropyl ones. Thus, using the thioamide **13,** a selective benzylic monodeprotonation was achieved and alkylation or silylation (with Me_3SiCl) afforded expected thioamides **14** and **22** (Scheme 4).

Atroposelectivity

N,*N*-Diisopropyl-2-methylbenzenecarbothioamide **13** was deprotonated under the same conditions, and was subsequently treated with a variety of prochiral electrophiles: aromatic aldehydes and Michael acceptors (Scheme 5 and

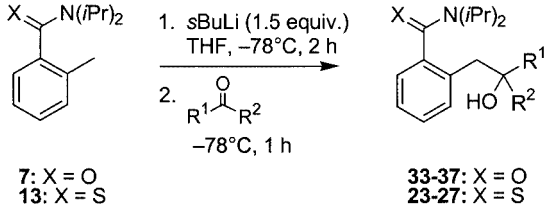


Scheme 3. Double deprotonation of *N*,*N*-dimethyl-2-methylbenzenecarbothioamide



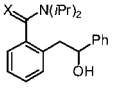
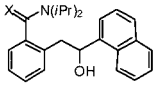
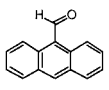
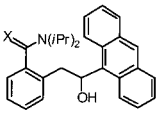
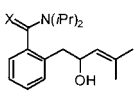
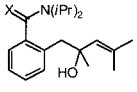
Scheme 4. Deprotonation of *N*,*N*-diisopropylthioamide **13**

Table 2). Thioamides **23−27**, bearing a hydroxy group on the newly created stereogenic center, were isolated in moderate yields (Table 2, Entries 1−5). ^{1}H NMR revealed the presence of two diastereomers with a low selectivity (*dr* 54:46 to 67:33). In order to compare with the oxygen analogues,[6,15] we have submitted amide **7** to the same sequence (Table 2). Products **33−37** were isolated in better yields and with higher diastereoselectivities (up to 88:12).

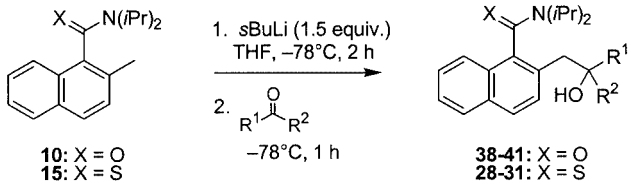


Scheme 5. Benzylic deprotonation and alkylation of benzamide **7** and thiobenzamide **13**

Table 2. Deprotonation of *N*,*N*-diisopropylthioamide **13** and amide **7** with *s*-BuLi (1.5 equiv., −78 °C, 2 h) and reaction of the anions with electrophiles (1.5 equiv., −78 °C, 1 h)

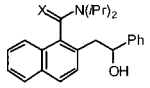
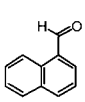
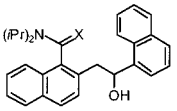
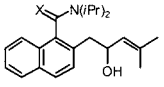
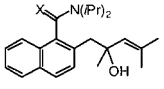
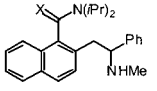
			Reaction with thioamide **13** X = S		Reaction with amide **7** X = O	
Entry	Electrophile	Product	Product Yield	d.r.	Product Yield	d.r
1			**23** 48%	55:45	**33** 79%	78:22
2			**24** 49%	58:42	**34** 91%	75:25
3			**25** 39%	57:43	**35** 72%	88:12
4			**26** 41%	54:46	**36** 62%	63:37
5			**27** 38%	67:33	**37** 80%	58:42

A second series was investigated with thionaphthamide **15** (Scheme 6 and Table 3). Aldehydes led to a very low stereoselectivity ((Table 2, Entries 1−3), whereas 4-methyl-3-penten-2-one gave a *dr* of 82:18 (Table 2, Entry 4). Comparative experiments with naphthamide **10** led to compounds **38−41** with very low selectivities in all cases.



Scheme 6. Deprotonation and carbonyl compounds addition in the naphthalene series

Table 3. Deprotonation of *N*,*N*-diisopropylthioamide **15** and amide **10** with *s*-BuLi (1.5 equiv., −78 °C, 2 h) and reaction of the anions with electrophiles (1.5 equiv., −78 °C, 1 h)

			Reaction with thioamide **15** X = S		Reaction with amide **10** X = O	
Entry	Electrophile	Product	Product Yield	d.r.	Product Yield	d.r
1			**28** 49%	60:40	**38** 51% [a]	56:44 [a]
2			**29** 79%	57:43	**39** 82%	52:48
3			**30** 70%	55:45	**40** 90%	52:48
4			**31** 71%	82:18	**41** 83%	52:48
5			**32** 70%	65:35	**42** 74% [a]	>99:1 [a]

[a] Ref.[15]

We could separate a few pure diastereomers by chromatography (**28, 31**) or by crystallization (minor **29** from ethyl acetate). An interesting observation was made with thioamides **28** and **29**. The isolated major diastereoisomers were placed in $CDCl_3$ solutions and monitored by ^{1}H NMR at room temperature. A slow isomerization was observed for **28**: a *dr* of 84:16 was monitored after 36 d and 59:41 after 62 d. The epimerization of **29** was even slower.

Another type of electrophile was used by Clayden and co-workers,[15] leading to an excellent stereocontrol: imines. *N*-Benzylidene-*N*-methylamine was reacted with the anion of thioamide **15**. It gave a good yield of amine **32** but a largely decreased *dr* 65:35 (Table 3, Entry 5).

As this was the first time that some degree of atroposelectivity was observed for thioamides, we have attempted to

determine the relative configuration of the major diastereomers (determined by the Clayden group[15] for amino naphthamides **42**, but not for hydroxy naphthamide **38**). Unfortunately, single crystals of pure diastereomers and suitable for X-ray diffraction analysis have not been available.

Conclusion

This study and the previous one have demonstrated, for the first time, that tertiary thioamides are prone to atroposelectivity.

Thiobenzamides and thionaphthamides were prepared by thionating the amides with Lawesson's reagent and conditions were adapted for the hindered examples, bearing *N*,*N*-diisopropyl groups. The enantiomeric forms could be monitored by complexation with a chiral shift agent. The rotation barriers along the chirality axis were estimated to be very high.

Selective abstraction of the benzylic proton required the use of *N*,*N*-diisopropylthioamides and was achieved in both thiobenzamide and thionaphthamide series.

A number of prochiral electrophiles were reacted with the intermediate anions: aromatic aldehydes, α-unsaturated aldehydes and a ketone, and an imine. C−C Bond formations were achieved.

The atroposelectivity varied to a large extent: from 55:45 up to 82:18. Despite some exceptions, the selectivity was poorer as compared to the amide series.

Though the selectivities are not high, this is the first report on atroposelective reactions with thioamides in a benzylic position.

Experimental Section

General Remarks: NMR spectra were measured in $CDCl_3$. The ^1H NMR spectra were recorded at 250 MHz (Bruker DPX 250) and the ^{13}C NMR spectra at 62.9 MHz (Bruker DPX 250). The chemical shifts are expressed in ppm relative to tetramethylsilane as an internal standard. The coupling constants *J* are in Hz. The FTIR spectra were recorded with a Perkin−Elmer 16 PC FTIR spectrometer. Mass spectra were determined with a Nermag Riber R 10 RH spectrometer (ISMRA, Caen) or a JEOL AX 500 spectrometer (IRCOF, Rouen). Elemental analyses were carried out by ICSN (CNRS, Gif-sur-Yvette) and by ISMRA (Caen). Melting points were measured with a digital IA 9000 Electrothermal instrument. All reactions were carried out under nitrogen. Tetrahydrofuran (THF) was distilled from sodium/benzophenone, and petroleum ether from P_2O_5. Commercial solutions of sec-butyllithium were titrated before use, according to ref.[32] Isomer ratios were determined by ^1H NMR of the crude product. The preparation of thioamides **14**, **16**, **17**, **18**, and amides **33**−**41** is reported in the Supporting Information (see footnote on the first page of this article).

***N*,*N*,2-Trimethylbenzenecarbothioamide (12):** A stirred solution of Lawesson's reagent (14.868 g, 36.8 mmol, 0.6 equiv.) in THF (340 mL). was added cautiously to *N*-dimethyl-2-methylbenzamide (**5**, 10.009 g, 61.3 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 19 h. Purification by silica gel chromatography (R_f = 0.3) with petroleum ether/ethyl acetate (8:2) afforded 10.774 g (98%) of compound **12**. After crystallization from ethyl acetate, green crystals were obtained. M.p. 60 °C. ^1H NMR: δ = 2.24 (s, 3 H, ArMe), 3.04 (s, 3 H, NMe_2), 3.61 (s, 3 H, NMe_2), 7.11−7.22 (m, 4 H, Ar-H) ppm. ^{13}C NMR: δ = 18.9 (ArMe), 42.3 (NMe_2), 42.8 (NMe_2), 125.2 (Ar−H), 126.2 (Ar−H), 128.1 (Ar−H), 130.4 (Ar−H), 131.5 (Ar-Me), 143.3 (Ar−C=S), 201.1 (C=S) ppm. MS (EI): *m*/*z* (%) = 179 (100) [M^+·], 164 (33), 1135 (57), 91 (21).

***N*,*N*-Diisopropyl-2-methylbenzenecarbothioamide (13):** A stirred solution of Lawesson's reagent (11.065 g, 27.4 mmol, 0.6 equiv.) in 1,2,4-trichlorobenzene (60 mL) was added cautiously to *N*,*N*-diisopropyl-2-methylbenzamide (**7**, 10.000 g, 45.6 mmol, 1 equiv.). The reaction mixture was stirred at 165 °C for 16 h. Purification by silica gel chromatography (R_f = 0.3) with petroleum ether/ethyl acetate (9:1) afforded 9.653 g (90%) of amide **13**. After crystallization from hexane, a yellow powder was obtained. M.p. 140 °C. ^1H NMR: δ = 1.12 [d, *J* = 6.7 Hz, 3 H, N(CH*Me*$_2$)$_2$], 1.21 [d, *J* = 6.7 Hz, 3 H, N(CH*Me*$_2$)$_2$], 1.82 [br. s, 6 H, N(CH*Me*$_2$)$_2$], 2.30 (s, 3 H, ArMe), 3.96−4.02 [m, 2 H, N(C*H*Me$_2$)$_2$], 6.94−6.99 (m, 1 H, Ar-H), 7.14−7.18 (m, 3 H, Ar-H) ppm. ^{13}C NMR: δ = 19.3 (CH*Me*), 19.6 (CH*Me*), 20.0 (CH*Me*), 20.7 (CH*Me*), 51.2 (*C*HMe), 56.9 (*C*HMe), 124.3 (Ar−H), 126.4 (Ar−H), 127.6 (Ar−H), 131.0 (Ar−H), 131.5 (*Ar*-Me), 145.3 (*Ar*−C=S), 199.7 (C=S). IR (KBr): $\tilde{\nu}$ = 2968, 1494, 1376, 1342, 1244, 1144 ($\nu_{C=S}$), 1116, 754 cm^{-1}. MS (EI): *m*/*z* (%) = 235 (21) [M^+·], 192 (10), 135 (100), 118 (25), 91 (10), 75 (32), 43 (17). $C_{14}H_{21}NS$ (235.38): calcd. C 71.43, H 8.99, N 5.95; found C 71.31, H 9.06, N 5.92.

General Procedure for the Preparation of Thioamides 14, 15 and 16:

Preparation of the Amides 8, 10 and 11: A solution of benzoyl chloride or 1-naphthoyl chloride (1 equiv.) in diethyl ether was cooled to 0 °C. A solution of the appropriate amine (2.5 equiv.) in diethyl ether was added dropwise. The reaction mixture was stirred at room temperature for 16 h. After completion of the reaction, the mixture was quenched with water. The organic phase was washed twice with a aqueous solution of HCl (1 M) and then with brine. The organic phase was dried with magnesium sulfate and after filtration the solvent was removed under reduced pressure. The amide was obtained sufficiently pure for immediate further use (quantitative yield).

A solution of the previous amide (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium in cyclohexane (1.1 equiv.) was then added dropwise. The reaction mixture was stirred at −78 °C for 1 h. The appropriate electrophile (ethyl or methyl iodide) (1.1 equiv.) was added dropwise, and the resulting mixture was stirred at −78 °C for 30 min. After completion of the reaction, the mixture was quenched with a saturated aqueous solution of ammonium chloride. The mixture was extracted twice with dichloromethane. The combined organic phases were then washed with brine and dried with magnesium sulfate. After filtration, the solvent was removed under reduced pressure and a solid was obtained. The amide was obtained sufficiently pure for immediate further use.

Thionation of the Amides 8, 10 and 11: To a stirred solution of Lawesson's reagent (0.6 equiv.) in 1,2,4-trichlorobenzene was added caustiously the amide (1 equiv.). The reaction mixture was stirred at 165 °C for 24−144 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography with petroleum ether/ethyl acetate as eluent.

***N*,*N*-Diisopropyl-2-methyl-1-naphthalenecarbothioamide (15):** The general procedure of thionation was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarboxamide (**10**, 2.301 g, 8.5 mmol), Lawesson's reagent (2.075 g, 5.1 mmol) and 1,2,4-trichlorobenzene (20 mL). Reaction time at 165 °C: 100 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (9:1) afforded 0.976 g (40%) of compound **15**. After crystallization from chloroform/hexane, a yellow solid was obtained. M.p. 151 °C. R_f = 0.6 (petroleum ether/ethyl acetate, 8:2). ^{1}H NMR: δ = 1.04 [d, 3 H, *J* = 6.6 Hz, N(CH*Me*$_2$)$_2$], 1.16 [d, 3 H, *J* = 6.6 Hz, N(CH*Me*$_2$)$_2$], 1.97−2.07 [2 br. s, 6 H, N(CH*Me*$_2$)$_2$], 2.47 (s, 3 H, ArMe), 3.88−4.15 [m, 2 H, N(C*H*Me$_2$)$_2$], 7.28−7.81 (m, 6 H, Ar-H) ppm. ^{13}C NMR: δ = 19.8 (Ar*Me*), 20.0, 20.5, 20.9 [N(CH*Me*$_2$)$_2$], 51.4, 57.7 [N(C*H*Me$_2$)$_2$], 125.2, 125.7, 126.9, 127.4, 128.3, 128.4, 129.0, 129.4, 132.6, 140.3, 198.4 (C=S) ppm. IR (KBr): ṽ = 2966, 1455, 1376, 1138 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 285 (8) [M$^+$·], 242(7), 200 (11), 185 (100), 168 (54), 115 (27). $C_{18}H_{23}NS$ (285.45): calcd. C 75.74, H 8.12, N 4.91, S 11.23; found C 75.40, H 8.09, N 5.41, S 10.98.

General Procedure for Single Deprotonation of Thioamides 12 and 13, and then Treatment with Electrophiles (Compounds 20−22): A solution of thioamides **12** or **13** (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium in cyclohexane (1.5−2.4 equiv.) was then added dropwise. The reaction mixture was stirred at −78 °C for 30−60 min. The appropriate electrophile (methyl iodide or trimethylsilyl chloride) was added dropwise and the resulting mixture was stirred at −78 °C for 30 min. After addition of a saturated aqueous ammonium chloride solution, the mixture was extracted twice with dichloromethane. The combined organic phases were washed with brine and dried with magnesium sulfate. After filtration, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography with petroleum ether/ethyl acetate as eluent.

***N*-Ethyl-*N*-methyl-2-methylbenzenecarbothioamide (20):** The general procedure was applied to *N*,*N*-dimethyl-2-methylbenzenecarbothioamide **12** (98 mg, 0.55 mmol), *s*BuLi (1 mL of a 1.2 M solution in cyclohexane, 1.20 mmol), methyl iodide (27 μL, 0.44 mmol) and THF (5 mL). Reaction time after addition of base: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 76 mg (yield: 72%) of compound **20** as a green oil. R_f = 0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 52:48. ^{1}H NMR [(*Z*) isomer]: δ = 1.11 (t, *J* = 7.1 Hz, 3 H, NCH$_2$*Me*), 2.26 (s, 3 H, ArMe), 3.55 (s, 3 H, NMe), 3.31−3.49 (m, 2 H, NC*H*$_2$Me), 7.02−7.21 (m, 4 H, Ar-H) ppm. ^{1}H NMR [(*E*) isomer]: δ = 1.37 (t, *J* = 7.1 Hz, 3 H, NCH$_2$*Me*), 2.23 (s, 3 H, ArMe), 2.97 (s, 3 H, NMe), 3.97−4.05 (m, 1 H, NC*H*$_2$Me), 4.33−4.41 (m, 1 H, NC*H*$_2$Me), 7.07−7.21 (m, 4 H, Ar-H) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 9.5, 12.1 (NCH$_2$*Me*), 17.6, 17.9 (ArMe), 38.3, 38.8 (NMe), 47.5, 48.9 (N*C*H$_2$Me), 123.7, 123.9, 124.9, 125.2, 126.8, 129.3, 130.1, 130.5, 141.9, 199.2, 199.3 (C=S) ppm. MS (EI): *m*/*z* (%) = 193 (89) [M$^+$·], 178 (36), 135 (100), 91 (37), 58 (40). HMRS calcd. for $C_{11}H_{15}NS$: 193.0925; found 193.0938.

***N*,2-Diethyl-*N*-methylbenzenecarbothioamide (21):** The general procedure was applied to *N*,*N*-dimethyl-2-methylbenzenecarbothioamide **12** (100 mg, 0.56 mmol), *s*BuLi (1.12 mL of a 1.2 M solution in cyclohexane, 1.34 mmol), methyl iodide (70 μL, 1.12 mmol) and THF (4 mL). Reaction time after addition of base: 30 min. Purification by silica gel chromatography (R_f = 0.5) with petroleum ether/ethyl acetate (8:2) afforded 83 mg (yield: 71%) of compound **21** as a green oil. (*Z*)/(*E*) ratio = 52:48. ^{1}H NMR [(*Z*) isomer]: δ = 1.11 (t, *J* = 7.1 Hz, 3 H, NCH$_2$*Me*), 1.24 (t, *J* = 7.5 Hz, 3 H, ArCH$_2$*Me*), 2.56−2.63 (m, 2 H, ArC*H*$_2$Me), 3.55 (s, 3 H, NMe), 3.26−3.35 (m, 1 H, NC*H*$_2$Me), 3.42−3.51 (m, 1 H, NC*H*$_2$Me), 7.02−7.26 (m, 4 H, Ar-H) ppm. ^{1}H NMR [(*E*) isomer]: δ = 1.37 (t, *J* = 7.1 Hz, 3 H, NCH$_2$*Me*), 1.24 (t, *J* = 7.5 Hz, 3 H, ArCH$_2$*Me*), 2.56−2.63 (m, 2 H, ArC*H*$_2$Me), 2.96 (s, 3 H, NMe), 4.01−4.10 (m, 1 H, NC*H*$_2$Me), 4.31−4.40 (m, 1 H, NC*H*$_2$Me), 7.02−7.26 (m, 4 H, Ar-H) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 10.9, 13.7 (NCH$_2$*Me*), 14.7, 14.8 (ArCH$_2$*Me*), 25.6, 25.9 (Ar*C*H$_2$Me), 39.9, 40.8 (NMe), 49.0, 50.7 (N*C*H$_2$Me), 125.2, 125.4, 126.3, 126.5, 128.5, 128.8, 128.9, 137.7, 138.0, 142.8, 143.2, 200.4, 200.7 (C=S) ppm. MS (EI): *m*/*z* (%) = 207 (82) [M$^+$·], 193 (20), 174 (100), 149 (44), 134 (68), 115 (66), 105 (15), 91 (28), 58 (66). HMRS calcd. for $C_{12}H_{17}NS$: 207.1082; found 207.1089.

***N*,*N*-Diisopropyl-2-ethylbenzenecarbothioamide (14):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 103 mg, 0.44 mmol), *s*BuLi (404 μL of a 1.3 M solution in cyclohexane, 0.53 mmol), methyl iodide (33 μL, 0.53 mmol) and THF (5 mL). Reaction time after addition of base: 1 h. Purification by silica gel chromatography (R_f = 0.3 as starting material) with petroleum ether/ethyl acetate (9:1) afforded 79 mg (yield: 72%) of compound **14** as a yellow powder. The spectroscopic data were identical to those previously reported.

***N*,*N*-Diisopropyl-2-(1-trimethylsilylmethyl)-1-benzenecarbothioamide (22):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 285 mg, 1.21 mmol), *s*BuLi (1.4 mL of a 1.3 M solution in cyclohexane, 1.81 mmol), trimethylsilyl chloride (310 μL, 2.42 mmol) and THF (7 mL). Reaction time after addition of base: 1 h. Purification by silica gel chromatography (R_f = 0.7) with petroleum ether/ethyl acetate (8:2) afforded 281 mg (yield: 76%) of compound **22** as a green oil. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.09 (s, 9 H, Si*Me*$_3$), 1.00 [d, *J* = 6.7 Hz, 3 H, N(CH*Me*$_2$)$_2$], 1.12 [d, *J* = 6.7 Hz, 3 H, N(CH*Me*$_2$)$_2$], 1.72 [br. s, 6 H, N(CH*Me*$_2$)$_2$], 1.88−1.95 (AB, *J* = 13.7 Hz, 2 H, CH$_2$), 3.81−3.99 [m, 2 H, N(C*H*Me$_2$)$_2$], 6.88−7.01 (m, 4 H, Ar-H) ppm. ^{13}C NMR: δ = 0.3, 0.4, 1.6 (SiMe$_3$), 19.3, 20.1, 20.6 [N(CH*Me*$_2$)$_2$], 23.1 (*C*H$_2$), 51.0, 56.6 [N(*C*HMe$_2$)$_2$], 124.8, 125.2, 127.2, 129.3, 134.8, 144.4, 200.1 (C=S) ppm. IR (KBr): ṽ = 3028, 1522, 1343, 1252 (ν_{Si-Me}), 1154 ($\upsilon_{C=S}$), 846 (ν_{Si-Me}) cm^{-1}. MS (EI): *m*/*z* (%) = 307 (6) [M$^+$·], 292 (5), 264 (6), 207 (7), 222 (4), 207 (7), 174 (4), 135 (10), 117 (15), 73 (24), 45 (73), 43 (100).

General Procedure for Single Deprotonation of Thioamides 13, 15 and Amides 7, 10 then treatment with Electrophiles (Compounds 23−41): A solution of compounds **7**, **10**, **13** or **15** (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium in cyclohexane (1.2−2 equiv.) was then added dropwise. The reaction mixture was stirred at −78 °C for 2 h. The appropriate electrophile was added dropwise, and the resulting mixture was stirred at −78 °C for 1 h. After addition of a saturated aqueous ammonium chloride solution, the mixture was extracted twice with dichloromethane. The combined organic phases were washed with brine and dried with magnesium sulfate. After filtration, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography with petroleum ether/ethyl acetate as eluent.

***N*,*N*-Diisopropyl-2-(2-hydroxyphenylethyl)benzenecarbothioamide (23):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide **13** (212 mg, 0.90 mmol), *s*BuLi (960 μL of a 1.4 M solution in cyclohexane, 1.35 mmol), benzaldehyde (138 μL, 1.35 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 55:45). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2 then 6:4) afforded 147 mg (yield: 48%) of compound **23**. After crystallisation

from chloroform/hexane, a yellow solid was obtained. Minor and major diastereoisomers were not separated by chromatography or crystallisation. M.p. 113 °C. R_f = 0.3 (petroleum ether/ethyl acetate, 8:2). ^{1}H NMR [major diastereoisomer]: δ = 1.07−1.14 (m, 6 H, NCHMe_2), 1.85 (br. s, 6 H, NCHMe_2), 2.71−3.01 (m, 2 H, CH_2), 3.92−4.09 [m, 2 H, N(CHMe$_2$)$_2$], 5.38 (dd, J = 2.6, J = 9.5 Hz, 1 H, CHOH), 6.98−7.47 (m, 9 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.07−1.14 (m, 6 H, NCHMe_2), 1.85 (br. s, 6 H, NCHMe_2), 2.71−3.01 (m, 2 H, CH_2), 3.92−4.09 [m, 2 H, N(CHMe$_2$)$_2$], 4.96 (dd, J = 5.4, J = 9.0 Hz, 1 H, CHOH), 6.98−7.47 (m, 9 H, Ar-H) ppm. ^{13}C NMR [mixture of diastereoisomers]: δ = 20.62, 20.8, 21.1, 21.8, 22.8 [N(CHMe_2)$_2$], 44.6, 44.8 (CH_2), 52.8, 58.6 [N(CHMe$_2$)$_2$], 74.4 [CHOH, (major)], 77.2 [CHOH, (minor)], 125.6, 125.9, 127.1, 127.3, 128.3, 128.5, 128.7, 128.8, 129.5, 129.9, 130.0, 130.1, 131.6, 132.7, 133.1, 133.9, 146.6, 147.1, 200.5 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3368 (ν_{OH}), 2968, 2930, 2364, 1494, 1446, 1376, 1342, 1246, 1144 ($\nu_{C=S}$) cm^{-1}. MS (CI): m/z (%) = 342 (100) [M + H]$^+$, 324 (18), 308 (20). HMRS calcd. for $C_{21}H_{28}NOS$: 342.1892; found 342.1900.

***N*,*N*-Diisopropyl-2-(2-hydroxynaphthylethyl)benzenecarbothioamide (24):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 253 mg, 1.1 mmol), *s*BuLi (1.0 mL of a 1.3 M solution in cyclohexane, 1.30 mmol), 1-naphthaldehyde (440 μL, 3.2 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 58:42). Purification by silica gel chromatography (R_f = 0.4) with petroleum ether/ethyl acetate (8:2) afforded 206 mg (yield: 49%) of compound **24** as a white solid. Minor and major diastereoisomers were not separated by chromatography. M.p. 72 °C. ^{1}H NMR [major diastereoisomer]: δ = 0.99−1.09 (m, 6 H, NCHMe_2), 1.79 (br. s, 6 H, NCHMe_2), 2.74 (br. s, 1 H, OH), 2.90−3.22 (m, 2 H, CH_2), 3.92−3.98 [m, 2 H, N(CHMe$_2$)$_2$], 6.02−6.11 (m, 1 H, CHOH), 7.01−7.87 (m, 11 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 0.99−1.09 (m, J = 6.7 Hz, 6 H, NCHMe_2), 1.79 (br. s, 6 H, NCHMe_2), 2.90−3.22 (m, 2 H, CH_2), 3.92−3.98 [m, 2 H, N(CHMe$_2$)$_2$], 4.35 (d, J = 4.5 Hz, 1 H, OH), 5.71−5.83 (m, 1 H, CHOH), 7.01−7.87 (m, 11 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 19.6, 20.0, 20.1, 20.6 [N(CHMe_2)$_2$], 42.3 (CH_2), 51.5, 57.7 [N(CHMe$_2$)$_2$], 69.9 [CHOH, (major)], 73.7 [CHOH, (minor)], 123.5, 123.7, 123.8, 124.3, 124.6, 125.8, 125.9, 126.0, 126.2, 126.3, 126.5, 127.3, 127.4, 127.5, 128.0, 128.4, 129.1, 129.4, 130.2, 130.7, 130.8, 131.9, 132.4, 133.0, 134.1, 134.2, 141.0, 141.5, 145.3, 145.6, 199.3 [(C=S), (minor)], 202.1 [(C=S), (major)] ppm. IR (KBr): $\tilde{\nu}$ = 3372 (ν_{OH}), 2968, 2928, 1494, 1340, 1246, 1144 ($\nu_{C=S}$) cm^{-1}. MS (EI): m/z (%) = 391 (33) [M^{+}·], 358 (59), 235 (94), 220 (45), 192 (81), 135 (93), 43 (100). $C_{25}H_{29}NOS$ (391.57): calcd. C 76.68, H 7.46, S 8.19; found C 76.71, H 7.55, S 7.63.

***N*,*N*-Diisopropyl-2-(2-hydroxyanthrylethyl)benzenecarbothioamide (25):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 263 mg, 1.11 mmol), *s*BuLi (1.2 mL of a 1.4 M solution in cyclohexane, 1.67 mmol), 9-anthraldehyde (346 mg, 1.67 mmol) and THF (15 mL). The crude product contained two diastereoisomers (*dr* = 57:43). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 191 mg (yield: 39%) of compound **25**. After crystallisation from ethyl acetate, a yellow solid was obtained. Minor and major diastereoisomers were not separated by chromatography or crystallisation. R_f = 0.3 (petroleum ether/ethyl acetate, 8:2). ^{1}H NMR [major diastereoisomer]: δ = 1.04−1.14 (m, 6 H, NCHMe_2), 2.02 (br. s, 6 H, NCHMe_2), 3.05−3.21 (m, 2 H, CH_2), 4.01−4.11 [m, 2 H, N(CHMe$_2$)$_2$], 6.81−6.92 (m, 1 H, CHOH), 7.12−8.43 (m, 13 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.04−1.14 (m, 6 H, NCHMe_2), 1.79 (br. s, 6 H, NCHMe_2), 3.63−3.78 (m, 2 H, CH_2), 4.01−4.11 [m, 2 H, N(CHMe$_2$)$_2$], 6.61−6.65 (m, 1 H, CHOH), 7.12−8.43 (m, 13 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 19.6, 20.0, 20.5, 20.8, 20.9 [N(CHMe_2)$_2$], 40.7, 40.8 (CH_2), 50.9, 57.2 [N(CHMe$_2$)$_2$], 69.4 [CHOH, (major)], 73.0 [CHOH, (minor)], 124.7, 124.8, 125.3, 125.6, 127.1, 127.2, 127.8, 127.9, 128.2, 129.0, 129.1, 129.2, 129.3, 129.4, 134.6, 135.0, 140.7, 145.4, 198.2 [(C=S), (minor)], 199.6 [(C=S), (major)] ppm. IR (KBr): $\tilde{\nu}$ = 3305 (ν_{OH}), 2968, 2928, 1489, 1347, 1264, 1152 ($\nu_{C=S}$) cm^{-1}. MS (EI): m/z (%) = 441 (19) [M^{+}·], 423 (42), 407 (36), 306 (100), 235 (60), 192 (95), 135 (55). HMRS calcd. for $C_{29}H_{31}NOS$: 441.2126; found 441.2130.

***N*,*N*-Diisopropyl-2-(2-hydroxy-4-methylpent-3-enyl)benzenecarbothioamide (26):** The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 180 mg, 0.76 mmol), *s*BuLi (820 μL of a 1.4 M solution in cyclohexane, 1.14 mmol), distilled 3-methyl-2-propenal (220 μL, 2.28 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 54:46). Purification by silica gel chromatography (R_f = 0.2) with petroleum ether/ethyl acetate (8:2) afforded 100 mg (yield: 41%) of compound **26** as a yellow oil. Minor and major diastereoisomers were not separated by chromatography. ^{1}H NMR [major diastereoisomer]: δ = 1.07 (d, J = 6.7 Hz, 3 H, NCHMe_2), 1.11 (d, J = 6.7 Hz, 3 H, NCHMe_2), 1.72 (br. s, 6 H, CH=CMe_2), 1.74−1.80 (br. s, 6 H, NCHMe_2), 2.54−2.84 (m, 2 H, CH_2), 3.96−4.02 [m, 2 H, N(CHMe$_2$)$_2$], 4.69 (td, J = 8.7, 5.0 Hz, 1 H, CHOH), 5.24−5.26 (m, 1 H, CH=CMe$_2$), 6.95−7.34 (m, 4 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.18 (d, J = 6.7 Hz, 3 H, NCHMe_2), 1.19 (d, J = 6.7 Hz, 3 H, NCHMe_2), 1.65 (m, 6 H, CH=CMe_2), 1.74−1.80 (br. s, 6 H, NCHMe_2), 2.54−2.84 (m, 2 H, CH_2), 3.96−4.02 [m, 2 H, N(CHMe$_2$)$_2$], 4.95 (td, J = 8.8, 4.5 Hz, 1 H, CHOH), 5.28−5.29 (m, 1 H, CH=CMe$_2$), 6.95−7.34 (m, 4 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 18.6, 18.9, 20.7, 26.1 (CH=CMe_2), 19.7, 20.0, 20.7 [N(CHMe_2)$_2$], 41.0, 41.2 (CH_2), 51.4, 57.1 [N(CHMe$_2$)$_2$], 68.0 [(CHOH, (major)], 70.3 [(CHOH, (minor)], 124.5, 124.9, 126.9, 127.1, 127.5, 127.9, 128.0, 128.7, 130.6, 131.3, 132.0, 132.6, 134.7, 135.0, 145.4, 145.6 ppm. IR (NaCl, film): $\tilde{\nu}$ = 3381 (ν_{OH}), 1530, 1447, 1395, 1212, 1181 ($\nu_{C=S}$), 813 cm^{-1}. MS (CI): m/z (%) = 320 (81) [M + H]$^+$, 302 (100), 286 (44). HMRS calcd. for $C_{19}H_{3O}NOS$: 320.2048 found 320.2050.

2-(2-Hydroxy-2,4-dimethylpent-3-enyl)-*N*,*N*-diisopropylbenzenecarbothioamide (27): The general procedure was applied to *N*,*N*-diisopropyl-2-methylbenzenecarbothioamide (**13**, 124 mg, 0.53 mmol), *s*BuLi (568 μL of a 1.4 M solution in cyclohexane, 0.80 mmol), distilled 4-methyl-3-propen-2-one (121 μL, 1.05 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 67:33). Purification by silica gel chromatography (R_f = 0.4) with petroleum ether/ethyl acetate (8:2) afforded 67 mg (yield: 38%) of compound **27** as a yellow oil. Minor and major diastereoisomers were not separated by chromatography. ^{1}H NMR [major diastereoisomer]: δ = 1.08 (d, J = 6.6 Hz, 6 H, NCHMe_2), 1.09 (d, J = 6.6 Hz, 6 H, NCHMe_2), 1.41 [s, 3 H, C(OH)Me], 1.71 (m, 6 H, CH=CMe_2), 1.76−1.87 (br. s, 6 H, NCHMe_2), 2.83 and 2.90 (AB, J = 13.8 Hz, 2 H, CH_2), 3.46 (s, 1 H, OH), 3.89−4.00 [m, 2 H, N(CHMe$_2$)$_2$], 5.29 (br. s, 1 H, CH=CMe$_2$), 6.97−7.89 (m, 4 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.17 (d, J = 6.6 Hz, 6 H, NCHMe_2), 1.19 (d, J = 6.6 Hz, 6 H, NCHMe_2), 1.38 [s, 3 H, C(OH)Me], 1.74 (m, 3 H, CH=CMe_2), 1.76−1.87 (br. s, 6 H, NCHMe_2), 1.88 (m, 3 H, CH=CMe_2), 2.79 and 2.99 (AB, J = 14.1 Hz, 2 H, CH_2), 3.37 (s, 1 H, OH), 3.89−4.00 [m, 2 H, N(CHMe$_2$)$_2$], 5.42 (br. s, 1 H, CH=CMe$_2$), 6.97−7.89 (m, 4 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 19.2,

19.3, 19.4, 20.0, 20.6 [N(CH*Me*$_2$)$_2$], 19.0, 27.9, 28.0 (CH=C*Me*$_2$), 29.6, 32.3 [C(OH)*Me*], 45.4, 45.8 (CH_2), 51.4, 56.2 [N(*C*HMe$_2$)$_2$], 73.3 [*C*(OH)Me, (minor)], 74.3 [*C*(OH)Me, (major)], 124.6, 125.1, 126.9, 127.0, 127.4, 127.5, 131.2, 131.6, 131.9, 132.0, 132.6, 133.2, 133.5, 145.7 ppm. IR (NaCl, film): $\tilde{\nu}$ = 3348 (ν_{OH}), 3041, 2966, 2854, 1487, 1464, 1321, 1221, 1135 ($\nu_{C=S}$) cm^{-1}. MS (CI): *m*/*z* (%) = 334 (41) [M + H]$^+$, 3316 (100), 300 (27), 236 (16), 99 (12). HMRS calcd. for $C_{20}H_{32}NOS$: 334.2205 found 334.2201.

2-(2-Hydroxyphenylethyl)-*N*,*N*-diisopropyl-1-naphthalenecarbothioamide (28): The general procedure was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarbothioamide (**15**, 69 mg, 0.24 mmol), *s*BuLi (230 μL of a 1.2 M solution in cyclohexane, 0.28 mmol), benzaldehyde (25 μL, 0.24 mmol) and THF (5 mL). The crude product contained two diastereoisomers (*dr* = 60:40). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 46 mg (yield: 49%) of compound **28**. Minor (R_f = 0.2, colourless oil) and major (R_f = 0.3, white solid, M.p. 123 °C.) diastereoisomers were separated by chromatography. ^{1}H NMR [major diastereoisomer]: δ = 1.02 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.09 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.96 (br. s, 3 H, NCH*Me*$_2$), 2.07 (br. s, 3 H, NCH*Me*$_2$), 2.92 (dd, *J* = 13.8, 9.0 Hz, 1 H, CH_2), 3.20 (dd, *J* = 13.8, 2.8 Hz, 1 H, CH_2), 3.81−4.21 [m, 2 H, N(C*H*Me$_2$)$_2$], 5.52 (dd, *J* = 9.0, 2.8 Hz, 1 H, C*H*OH), 6.75−7.91 (m, 11 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.04 (d, *J* = 6.5 Hz, 3 H, NCH*Me*$_2$), 1.06 (d, *J* = 6.5 Hz, 3 H, NCH*Me*$_2$), 1.99 (br. s, 3 H, NCH*Me*$_2$), 2.06 (br. s, 3 H, NCH*Me*$_2$), 3.03 (dd, *J* = 13.8, 3.9 Hz, 1 H, C*H*$_2$), 3.21 (dd, *J* = 13.8, 10.6 Hz, 1 H, C*H*$_2$), 3.81−3.88 [m, 1 H, [N(C*H*Me$_2$)$_2$], 4.29 [br. s, 1 H, [N(C*H*Me$_2$)$_2$], 5.09−5.13 (m, 1 H, C*H*OH), 7.28−7.87 (m, 11 H, Ar-H) ppm. ^{13}C NMR [major diastereoisomer]: δ = 19.4, 20.0, 20.1, 20.4 [N(CH*Me*$_2$)$_2$], 43.6 (*C*H$_2$), 51.0, 57.4 [N(*C*HMe$_2$)$_2$], 72.9 (*C*HOH), 125.0, 125.6, 125.9, 126.6, 126.7, 126.9, 127.1, 127.9, 128.0, 128.3, 128.4, 128.6, 129.0, 132.7, 140.4, 145.2 ppm. ^{13}C NMR [minor diastereoisomer]: δ = 20.1 [N(CH*Me*$_2$)$_2$], 43.8 (*C*H$_2$), 75.5 (*C*HOH), 51.4, 60.0 [N(*C*HMe$_2$)$_2$], 124.9, 125.6, 125.8, 126.0, 126.9, 127.1, 127.2, 128.0, 128.2, 128.3, 128.4, 128.9, 132.5, 145.9 ppm. IR (KBr): $\tilde{\nu}$ = 3318 (ν_{OH}), 3050, 2966, 1492, 1374, 1338, 1208, 1148 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 391 (28) [M$^{+\cdot}$], 285 (63), 242 (60), 185 (28), 105 (60), 77 (86), 43 (100). HMRS calcd. for $C_{25}H_{29}NOS$: 391.1970 found 391.1902.

2-(2-Hydroxynaphthylethyl)-*N*,*N*-diisopropyl-1-naphthalenecarbothioamide (29): The general procedure was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarbothioamide (**15**, 165 mg, 0.58 mmol), *s*BuLi (490 μL of a 1.3 M solution in cyclohexane, 0.63 mmol), 1-naphthaldehyde (118 μL, 0.87 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 57:43). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 201 mg (yield: 79%) of compound **29**. Minor and major diastereoisomers were not separated by chromatography. After crystallisation from ethyl acetate, the minor diastereoisomer was obtained as a white solid. Minor Diastereoisomer: M.p. 203 °C. R_f = 0.3 (petroleum ether/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.96 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.04 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.96 (br. s, 6 H, NCH*Me*$_2$), 2.07 (br. s, 6 H, NCH*Me*$_2$), 3.28−3.34 (m, 2 H, CH_2), 3.71−4.17 [m, 2 H, N(C*H*Me$_2$)$_2$], 4.55 (br. s, 1 H, OH), 5.91 (m, 1 H, C*H*OH), 7.28−7.88 (m, 13 H, Ar-H) ppm. ^{13}C NMR: δ = 18.8, 19.1, 19.5, 20.1 [N(CH*Me*$_2$)$_2$], 42.6 (*C*H$_2$), 51.4, 57.8 [N(*C*HMe$_2$)$_2$], 73.3 (*C*HOH), 123.0, 125.4, 125.9, 126.0, 126.1, 126.2, 126.9, 127.0, 128.1, 128.2, 128.3, 128.6, 129.2, 129.4, 129.7, 130.2, 132.6, 133.8, 141.0, 141.2, 197.7 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3362 (ν_{OH}), 3046, 2966, 1496, 1464, 1372, 1206, 1140 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 441 (4) [M$^{+\cdot}$], 308 (11), 285 (60), 242 (42), 185 (36), 166 (51). HMRS calcd. for $C_{29}H_{31}NOS$: 441.2126; found 441.2154.

2-(2-Hydroxy-4-methylpent-3-enyl)-*N*,*N*-diisopropyl-1-naphthalenecarbothioamide (30): The general procedure was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarbothioamide (**15**, 160 mg, 0.56 mmol), *s*BuLi (650 μL of a 1.3 M solution in cyclohexane, 0.84 mmol), distilled 3-methyl-2-propenal (86 μL, 0.84 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 55:45). Purification by silica gel chromatography (R_f = 0.3) with petroleum ether/ethyl acetate (8:2) afforded 147 mg (yield: 70%) of compound **30** as a yellow oil. Minor and major diastereoisomers were not separated by chromatography. ^{1}H NMR [major diastereoisomer]: δ = 1.12 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.15 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.76 (s, 3 H, CH=C*Me*$_2$) 1.77 (s, 3 H, CH=C*Me*$_2$), 1.90−1.96 (br. s, 6 H, NCH*Me*$_2$), 2.75 (dd, *J* = 13.7, 9.0 Hz, 1 H, C*H*$_2$), 2.96 (dd, *J* = 13.7, 3.6 Hz, 1 H, C*H*$_2$), 3.85−4.20 [2 br. s, 2 H, N(C*H*Me$_2$)$_2$], 5.09 (td, *J* = 9.0, 3.6 Hz, 1 H, C*H*OH), 5.34−5.37 (m, 1 H, C*H*=CMe$_2$), 7.43−7.52 (m, 3 H, Ar-H), 7.71−7.79 (m, 3 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.02 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.04 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.70 (s, 3 H, CH=C*Me*$_2$), 1.71 (s, 3 H, CH=C*Me*$_2$), 1.97−2.05 (br. s, 6 H, NCH*Me*$_2$), 2.78 (dd, *J* = 13.7, 4.4 Hz, 1 H, C*H*$_2$), 3.03 (dd, *J* = 13.7, 9.5 Hz, 1 H, C*H*$_2$), 3.85−4.20 [2 br. s, 2 H, N(C*H*Me$_2$)$_2$], 4.81 (td, *J* = 9.5, 4.4 Hz, 1 H, C*H*OH), 5.34−5.37 (m, 1 H, C*H*=CMe$_2$), 7.43−7.52 (m, 3 H, Ar-H), 7.71−7.79 (m, 3 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 18.2, 18.6 (CH=C*Me*$_2$), 19.3, 19.9, 20.1 [N(CH*Me*$_2$)$_2$], 25.7, 25.8 (CH=C*Me*$_2$), 41.2 (CH_2), 51.0, 51.2, 57.4, 57.6 [N(*C*HMe$_2$)$_2$], 67.7 [CHOH, (minor)], 69.8 [CHOH, (minor)], 125.0, 125.1, 125.7, 125.9, 126.5, 126.7, 126.9, 127.5, 127.6, 128.0, 128.5, 128.9, 129.0, 132.4, 132.5, 134.0, 134.6, 140.5, 140.7, 127.8, 127.9, 128.6, 128.7, 197.4 (C=S) ppm. MS (EI): *m*/*z* (%) = 369 (28) [M$^{+\cdot}$], 285 (13), 269 (29), 242 (25), 141 (24), 43 (100). $C_{23}H_{31}NOS$ (369.56): calcd. C 74.75, H 8.45, N 3.79, S 8.67; found C 74.85, H 8.51, N 4.19, S 8.49. IR (KBr): $\tilde{\nu}$ = 3418 (ν_{OH}), 2966, 2926, 1490, 1144 ($\nu_{C=S}$) cm^{-1}.

2-(2-Hydroxy-2,4-dimethylpent-3-enyl)-*N*,*N*-diisopropyl-1-naphthalenecarbothioamide (31): The general procedure was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarbothioamide (**15**, 128 mg, 0.45 mmol), *s*BuLi (450 μL of a 1.3 M solution in cyclohexane, 0.58 mmol), distilled 4-methyl-3-propen-2-one (129 μL, 1.12 mmol) and THF (10 mL). The crude product contained two diastereoisomers (*dr* = 82:18). Purification by silica gel chromatography (R_f = 0.4) with petroleum ether/ethyl acetate (8:2) afforded 122 mg (yield: 71%) of compound **31** as a yellow oil. IR (KBr): $\tilde{\nu}$ = 3362 (ν_{OH}), 3046, 2966, 1496, 1464, 1372, 1206, 1140 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 383 (3) [M$^{+\cdot}$], 365 (15), 322 (21), 285 (30), 185 (12), 43 (100). HMRS calcd. for $C_{24}H_{33}NOS$: 383.2283; found 383.2205. Minor diastereoisomer and major diastereoisomer were separated by chromatography. ^{1}H NMR [major diastereoisomer]: δ = 1.01 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.11 (d, *J* = 6.7 Hz, 3 H, NCH*Me*$_2$), 1.48 [s, 3 H, C(OH)*Me*], 1.73 (d, *J* = 1.1 Hz, 3 H, CH=C*Me*$_2$), 1.79 (d, *J* = 0.7 Hz, 3 H, CH=C*Me*$_2$), 1.85−1.94 (br. s, 6 H, NCH*Me*$_2$), 3.00−3.11 (m, 2 H, CH_2), 3.78 [br. s, 2 H, N(C*H*Me$_2$)$_2$], 5.38 (br. s, 1 H, C*H*=CMe$_2$), 7.43−7.80 (m, 6 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 0.98 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.13 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.48 [s, 3 H, C(OH)*Me*], 1.74 (br. s, 3 H, CH=C*Me*$_2$), 1.88−2.09 (m, 6 H, NCH*Me*$_2$), 1.93 (br. S, 3 H, CH=C*Me*$_2$), 2.93 and 3.24 (AB, *J* = 14.0 Hz, 2 H, CH_2), 3.75 [br. s, 2 H, N(C*H*Me$_2$)$_2$], 5.50 (br. s, 1 H, C*H*=CMe$_2$), 7.44−7.53 (m, 3 H, Ar-H), 7.71−7.82 (m, 3 H, Ar-H) ppm. ^{13}C NMR [major diastereoisomer]: δ = 19.2 (CH=

C*Me*$_2$), 19.3, 19.5, 20.0, 20.6 [N(CH*Me*$_2$)$_2$], 28.0 (CH=C*Me*$_2$), 32.9 [CH(OH)*Me*], 46.0 (CH_2), 51.7, 51.8 [N(*C*HMe$_2$)$_2$], 74.6 [*C*(OH)Me], 125.5, 126.0, 126.8, 127.0, 128.4, 128.7, 128.9, 130.0, 132.0, 132.9, 133.0, 141.1, 199.0 (C=S) ppm. ^{13}C NMR [minor diastereoisomer]: δ = 18.9 (CH=C*Me*$_2$), 19.4, 19.5, 20.6, 21.1 [N(CH*Me*$_2$)$_2$], 27.4 (CH=C*Me*$_2$), 29.4 [CH(OH)*Me*], 45.9 (CH_2), 51.1, 51.9 [N(*C*HMe$_2$)$_2$], 73.2 [*C*(OH)Me], 125.2, 125.4, 125.8, 126.5, 126.6, 126.8, 127.9, 128.0, 128.8, 132.5, 133.5, 140.9, 198.2 (C=S) ppm.

***N*,*N*-Diisopropyl-2-[2-(*N*-methylamino)phenylethyl)-1-naphthalenecarbothioamide (32):** The general procedure was applied to *N*,*N*-diisopropyl-2-methyl-1-naphthalenecarbothioamide (**15**, 77 mg, 0.27 mmol), *s*BuLi (260 μL of a 1.2 M solution in cyclohexane, 0.32 mmol), distilled *N*-benzylidene-methanimine (44 μL, 0.35 mmol) and THF (5 mL). The crude product contained two diastereoisomers (*dr* = 65:35). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2 then 5:5) afforded 71 mg (yield: 65%) of compound **32**. After crystallisation from ethyl acetate a white solid was obtained. Minor and major diastereoisomers were not separated by chromatography or crystallisation. M.p. 182 °C. ^{1}H NMR [major diastereoisomer]: δ = 1.00 (d, *J* = 6.6 Hz, 6 H, NCH*Me*$_2$), 1.86−1.94 (br. s, 6 H, NCH*Me*$_2$), 2.18 (s, 3 H, NH*Me*), 2.76−2.89 (m, 2 H, CH_2), 3.72−3.89 [br. s, 2 H, N(C*H*Me$_2$)$_2$], 4.08−4.12 (m, 1 H, C*H*), 7.06−7.53 (m, 11 H, Ar-H) ppm. ^{1}H NMR [minor diastereoisomer]: δ = 1.08 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.09 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.97−2.14 (br. s, 6 H, NCH*Me*$_2$), 2.26 (s, 3 H, NH*Me*), 3.08−3.24 (m, 2 H, CH_2), 3.91−4.12 [br. s, 2 H, N(C*H*Me$_2$)$_2$], 4.47−4.50 (s, 1 H, CH), 7.06−7.53 (m, 11 H, Ar-H) ppm. ^{13}C NMR [major + minor diastereoisomers]: δ = 19.4, 20.1, 20.5 [N(CH*Me*$_2$)$_2$], 34.6, 34.9 (NH*Me*), 41.8, 43.3 (CH_2), 50.9, 57.3 [N(*C*HMe$_2$)$_2$], 63.7, 66.2 (CH), 125.8, 125.9, 126.6, 126.7, 126.9, 127.1, 127.2, 127.5, 127.7, 127.9, 128.0, 128.4, 128.5, 128.6, 132.7, 140.6, 140.7, 144.2, 197.5, 198.2 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3362 (ν_{OH}), 3046, 2966, 1496, 1464, 1372, 1206, 1140 ($\nu_{C=S}$), 808 cm^{-1}. MS (EI): *m*/*z* (%) = 404 (11) [M^{+}·], 285 (100), 270 (33), 242 (34), 185 (51), 120 (74). HMRS calcd. for $C_{26}H_{32}N_2S$: 404.2286; found 404.2200.

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