Benzylic Metallation of Thiobenzamides and Thionaphthamides

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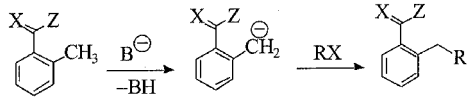
Keywords: Arenes / Axial chirality / Carbanions / Metallation / Thioamides

Various secondary thiobenzamides and thionaphthamides have been prepared, and features of their conformations [orthogonality of the arene and thioamide planes, (Z) geometries in solution etc.] have been determined. Deprotonation with *sec*-butyllithium selectively provided either the monoanion or the dianion, according to the stoichiometry of the base. The monoanion reacted with soft electrophiles (alkyl halides) through the sulfur atom and with hard electrophiles (acyl halides) through the nitrogen centre. Formation of the dianion, more reactive than the thioamide anionic moiety, allowed reaction at the benzylic centre. Addition of electrophiles allowed selective formation of C–C or C–X bonds.

Introduction

The metallation of benzylic protons provides a useful means of C−C bond formation, especially when the position is activated by an electron-withdrawing group in *ortho* position.[1] Among the array of substrates used, carbonyl compounds are strongly represented, the main class being that of amides **1** (Scheme 1).



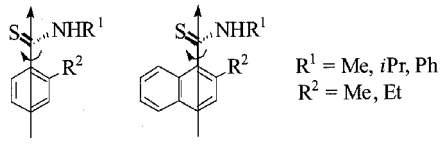
1 X = O, Z = NR_2, R, OR
2 X = S, Z = NR_2, R, SR

Scheme 1. Benzylic metallation

In contrast, lateral metallation of thiocarbonyl compounds **2** is rare.[2,3] Our experience with deprotonation of aliphatic thiocarbonyl derivatives[4,5] has shown that the sulfur atom facilitates deprotonation and stabilizes the anion to a greater extent than the oxygen atom. We anticipated that this should also be true for the species formed by deprotonation of the sulfur compounds **2**, as a result of conjugation through the arene.

A second reason to examine this chemistry was the nonplanarity of benzamides[6] and naphthamides,[7,8] which provides a potential source of axial chirality.[9] This has been used in synthesis only recently. Analogous thioamides were attractive, as we were expecting enhanced geometric features. In particular, higher barriers of rotation along the chiral axis have been reported.[10]

We decided to embark on a study of thiobenzamides and thionaphthamides (Scheme 2). In this first paper we report on the synthesis, structure and deprotonation of secondary thioamides. Little information regarding their conformations was available, and to the best of our knowledge, their axial chirality had not been investigated, nor that of their oxygen analogues. For metallation, the presence of a proton on the nitrogen atom brought with it further challenges[11] not previously clearly addressed with aromatic thioamides: the regioselectivity of deprotonation, the formation of mono- or dianions and behaviour towards electrophiles.



Scheme 2. Axial chirality of aromatic thioamides

We wish to report that selective deprotonation was achieved. The mono- or dianions could be alkylated at one of the nucleophilic sites − carbon, sulfur or nitrogen − by judicious choice of the electrophile.

Synthesis and Structure of Thioamides

The addition of Grignard reagents to isothiocyanates (R = Me, *i*Pr, Ph) is a classical method for the preparation of secondary thioamides[12,13] (Scheme 3). This reaction was carried out with isothiocyanates in THF, with subsequent hydrolysis, to give the fifteen thioamides **3**−**17** in excellent yields (Table 1). These were crystalline materials, easy and

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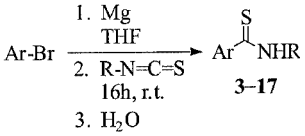
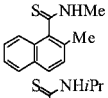
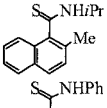
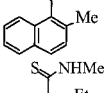
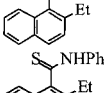
convenient to manipulate and not obnoxious like some other thiocarbonyl analogues.



Scheme 3. Synthesis of secondary thioamides

Table 1. Synthesis of thioamides **3**–**17**

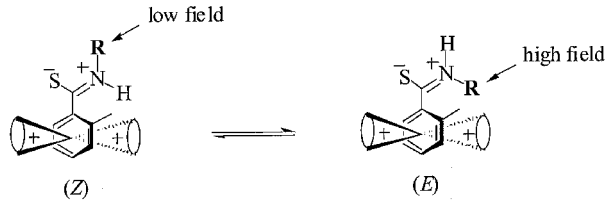
Entry	Aryl bromide	Isothiocyanate R	Thioamide		Yield [%]	(*Z*)/(*E*) ratio[a]
1	Bromobenzene	Me	**3**		98	100:0
2	1-Bromo-2-methylbenzene	Me	**4**		86	97:3
3	1-Bromo-2-methylbenzene	*i*Pr	**5**		82	96:4
4	1-Bromo-2-methylbenzene	Ph	**6**		81	70:30
5	1-Bromo-2-ethylbenzene	Me	**7**		91	98:2
6	1-Bromo-2-ethylbenzene	Ph	**8**		70	96:4
7	1-Bromo-2,6-diethylbenzene	Me	**9**		76	100:0
8	1-Bromo-2,6-diethylbenzene	Ph	**10**		73	90:10
9	1-Bromo-2-isopropylbenzene	Me	**11**		81	100:0
10	1-Bromonaphthalene	Me	**12**		85	95:5
11	1-Bromo-2-methylnaphthalene	Me	**13**		89	100:0
12	1-Bromo-2-methylnaphthalene	*i*Pr	**14**		91	0:100 to 89:11
13	1-Bromo-2-methylnaphthalene	Ph	**15**		93	80:20
14	1-Bromo-2-ethylnaphthalene	Me	**16**		45	100:0
15	1-Bromo-2-ethylnaphthalene	Ph	**17**		82	70:30

[a] Determined by ^{1}H NMR at room temp. in $CDCl_3$.

The structures of these aromatic thioamides raised two geometrical questions: the (*E*)/(*Z*) geometry along the N−C(=S) single bond and, if the arene and the thioamide moiety were not in the same plane, axial chirality. We examined both aspects.

It has long been known[14,15] that rotation about the N−C(=S) bond is hindered. Thioamides with two different substituents on the nitrogen atom exhibit two atropisomeric forms (geometrical conformers, also known as "rotamers"), which may be observed by ^{1}H NMR. Usually, the rotation barrier in a thioamide is higher than that in the corresponding amide. Donation from the nitrogen lone pair is facilitated by the higher polarizability of the sulfur atom relative to the oxygen atom.[16]

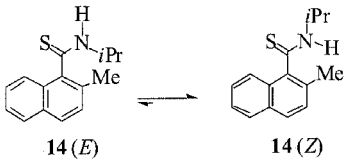
In ten cases, the ^{1}H NMR spectra of thioamides at room temperature revealed mixtures of (*E*) and (*Z*) isomers, with one being predominant (70:30 to 97:3). For six thioamides (Entries 1, 9, 11, 13, 14 and 15) we observed a single set of signals. The assignment of the (*Z*) structure to the major (or single) isomer was performed by use of the method of Mannschreck and co-workers.[17] The main anisotropic effect was the shielding of the aromatic nucleus (Scheme 4). As shown later, the orthogonality of the arene and thioamide planes brought the R groups of the (*E*) isomers close to the shielding cones of the aromatic rings, and so the R signal could be observed at high field. The shift difference was fairly significant: the *N*-methyl group of compound **11**, for instance, resonated at δ = 3.23 ppm in the (*Z*) isomer and at δ = 2.54 ppm in the (*E*) isomer.



Scheme 4. NMR shielding cones of thioamides

We propose that the (*Z*) isomer is thermodynamically favoured over the (*E*) one, which is subject to steric interaction between the two largest substituents (the R group and the arene; a monocoordinated sulfur atom is much smaller) on the N−C(=S) bond.

As this observation was carried out in solution, we were intrigued about the structure of these thioamides in the crystalline state. We could find only scant indications in the literature, with two examples[18,19] of the isolation of (*E*) and (*Z*) isomers and equilibration in solution. Further information here was provided by the thionaphthamide **14**, with an isopropyl group on the nitrogen atom. We first crystallised it (m.p. 157 °C), and then dissolved the crystals in $CDCl_3$ and immediately recorded an ^{1}H NMR spectrum. A single set of signals was observed and assigned to the (*E*) isomer. The sample was left at room temperature, and spectra were recorded to monitor any change. We observed the formation of the (*Z*) isomer (46% after 1 d) and, after a week, a (*Z*)/(*E*) ratio of 89:11 was observed with no further change (Scheme 5).



14 (*E*) **14** (*Z*)

Crystallization	100:0
Solution r.t.	100:0
1 d	54:46
2 d	34:66
7 d	11:89

Scheme 5. Isomerization of thionaphthamide **14**

This taught us that:

− the (*E*) isomer of **14** was less soluble and had crystallised out selectively,

− in solution, equilibration took place slowly, probably because of the size of the isopropyl group, to afford the thermodynamically more stable (*Z*) isomer.

The second structural feature of thioamides is their axial chirality. The challenges of asymmetric synthesis have resulted in the exploration and development of the various types of chirality. Achievements with axial chirality have been spectacular[20,21] for binaphthyl derivatives (Binol, Binap etc.). Very recently, another molecule type, aromatic amides or esters, has been explored by some groups, those of Fuji,[22,23] Clayden,[7,24−28] Curran,[29−31] Simpkins[32,33] and Taguchi.[34,35]

To the best of our knowledge, no report deals with the use of thioamides for atroposelective synthesis. Some information about the structure of thiobenzamides is available from the literature: (i) torsion angles of 10−44° between the arene and secondary thioamide planes have been measured by X-ray diffraction analysis[36−38] and (ii) the barriers to rotation about C−C(=S) are higher (30−39 kJ/mol higher $\Delta G^{\ddagger}$)[10] than those in the oxygen analogues.

To shed some light on these aspects, we examined thioamides. X-ray diffraction analysis of the *N*,2-dimethylthionaphthamide **13** was carried out on a single crystal, obtained from diethyl ether. Analysis revealed the structure shown in Figure 1, with the following features:

− the planarity of the thioamide is confirmed,

− the *N*-methyl group and the sulfur atom are in a *cis* relationship, confirming the (*Z*) NMR assignment,

− the planes of the thioamide and of the arene ring are almost perpendicular at 83°,

− the bond lengths are 1.69 Å for C=S, 1.33 Å for C−N, and 1.54 Å for C_{Ar}−C.

The requisite geometrical conditions being fulfilled, we attempted to estimate the barrier to rotation about the C_{Ar}−C bond. Very high activation energies were not expected for secondary thioamides, even though the sulfur atom was expected to increase the free energies relative to those of the oxygenated counterparts. We used two chiral shift agents[39−41] susceptible to coordination − (+)-(*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol and (+)-(*S*)-α-methoxyphenylacetic acid − to form diastereomeric complexes detectable by ^{1}H NMR. Unfortunately, no resolution was observed, even with a sixfold excess of the shift agent, or by analysis at −80 °C. A very rough estimation for the barrier to rotation was, however, made by calculation (Mac Spartan) of the energy of **4** relative to the torsion angle, which provided a ΔH value of 33 kJ/mol. Apparently, rotation was not hindered enough and the use of tertiary thioamides will probably be necessary for thermal stability in axially chiral isomers.

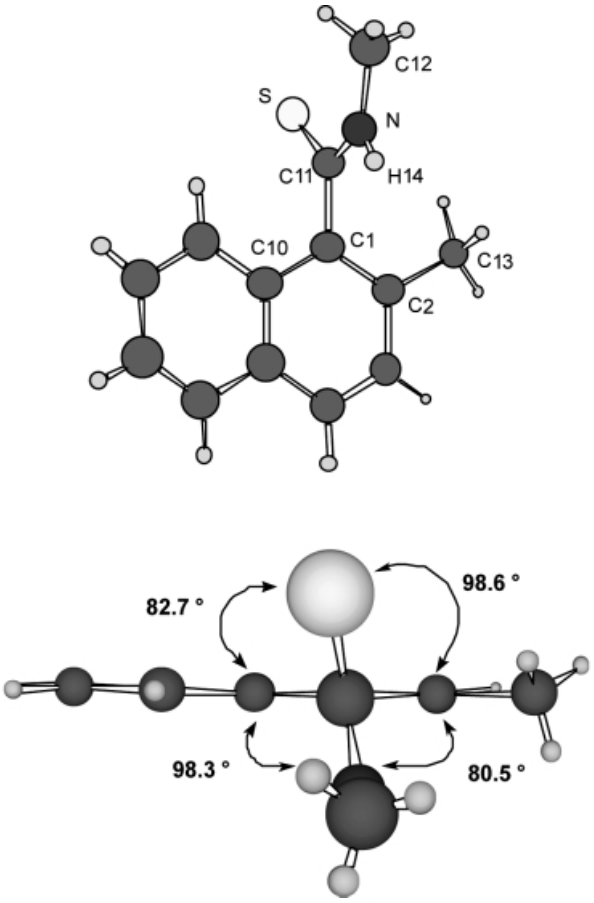


Figure 1. Structure of the *N*,2-dimethylthionaphthamide **13**; selected interatomic distances [Å] and bond angles [°]: S−C11 1.688 (3), C1−C2 1.386 (5), C1−C10 1.403 (5), C1−C11 1.536 (4), C2−C13 1.472 (8), C11−N 1.334 (3), N−C12 1.493 (5), N−H14 0.89 (3); C2−C1−C10 118.2 (3), C2−C1−C11 123.1 (3), C10−C1−C11 118.7 (3), C1−C2−C13 118.8 (3), S−C11−C1 122.0 (19), S−C11−N 121.8, C1−C11−N 116.2, C11−N−C12 126.3, C11−N−H14 110.2 (18), C12−N−H14 123.5

Metallation of Thiobenzamides and Thionaphthamides

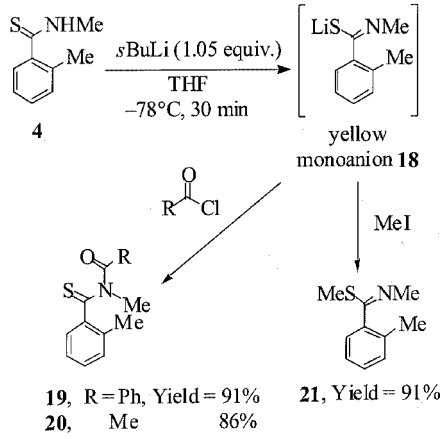
No extensive study of benzylic deprotonation of aromatic thiocarbonyl compounds is available. Hartke and his group reported[2] that the deprotonation of methyl 2-alkyldithiobenzoates did not result in abstraction of the benzylic proton, but afforded dimeric products after alkylation. The formation of these compounds was explained in terms of

single electron transfer reduction and subsequent coupling of radical anions. Fitt and Gschwend have reported[3] the deprotonation of a secondary thioamide, *N*,2-dimethylthiobenzamide, by *n*-butyllithium (2 equiv.), followed by addition of a ketone to give an adduct at the benzylic position.

For our investigation, we examined the metallation of thiobenzamides **4** and **7** and thionaphthamides **13**, **15** and **16**, with a variety of bases, stoichiometries, and subsequent addition of electrophiles.

Monodeprotonation

The typical base used was secondary butyllithium. Addition of 1 equiv. to thiobenzamides **4** at −78 °C provided a yellow solution, which was treated with two types of electrophiles (Scheme 6, Table 2). Benzoyl and propanoyl chlorides (Entries 1 and 2) afforded the *N*-acylthioamides **19** and **20**, respectively, in 91 and 86% yields [as single (*Z*) isomers]. Methyl iodide gave a 91% yield of thioimido ester **21** (Entry 3).



Scheme 6. Metallation of thiobenzamide **4**

This showed that the monoanion **18** was formed readily. It was an ambident nucleophile, hard electrophiles such as acyl halides reacting at its hard terminus, the nitrogen atom, whereas the soft electrophile methyl iodide attacked the soft sulfur atom.

An analogous study was carried out with thionaphthamide **13**, and gave comparable results (Table 2, Entries 4 and 5).

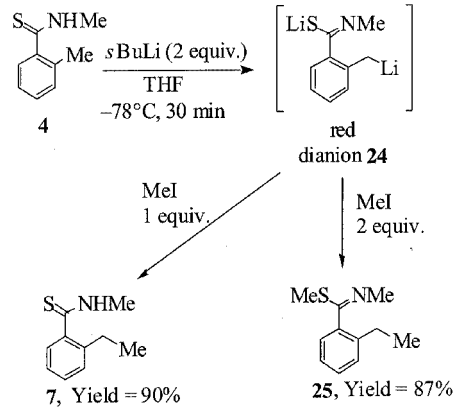
In both cases, mixtures of (*Z*)- and (*E*)-thioimido esters (1:2 ratio) were obtained on treatment with methyl iodide (Entries 3 and 5), showing either unselective *S*-alkylation or subsequent equilibration.

Double Deprotonation of Thiobenzamides

Addition of 2 equiv. of *s*BuLi to thiobenzamide **4** resulted in a red coloration (Scheme 7). The nature of the intermediate **24** could be determined by quenching with 2 equiv. of methyl iodide and the isolation of the thioimido

Table 2. Deprotonation of thioamides **4** and **13** with 1.05 equiv. of *s*BuLi (−78 °C, 30 min to 1 h) and treatment of the monoanions with electrophiles (−78 °C, 30 min)

Entry	Thioamide	Electrophile	Product	Yield [%]	(*Z*)/(*E*) ratio
1	**4**	PhCOCl	**19**	91	100:0
2	**4**	EtCOCl	**20**	86	100:0
3	**4**	MeI	**21**	91	37:63
4	**13**	PhCOCl	**22**	73	100:0
5	**13**	MeI	**23**	85	34:66



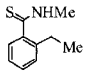
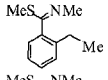
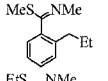
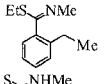
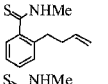
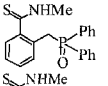
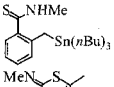
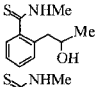
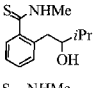
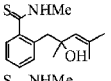
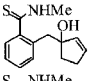
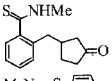
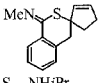
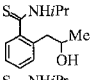
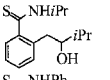
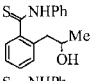
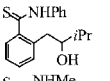
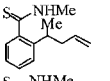
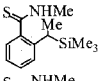
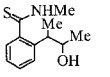
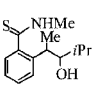
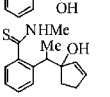
Scheme 7. Double metallation of thioamide **4**

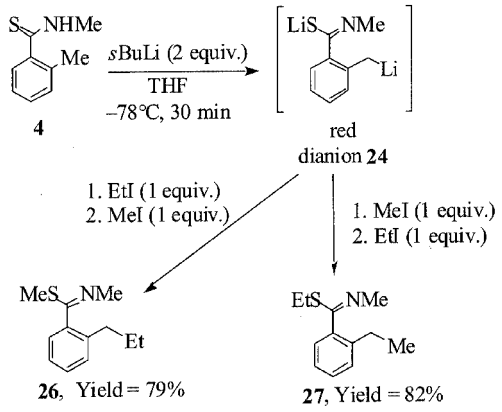
ester **25** in 87% yield (Table 3, Entry 2). This compound was the result of alkylation at two centres, the sulfur atom and the benzylic carbon atom. Thus, the dianion **24** had been formed in the first step.

An interesting observation was made when only 1 equiv. of methyl iodide was added to the red dianion **24**, thioamide **7** being isolated in 90% yield (Table 3, Entry 1). Thus, the benzylic site was much more reactive than the thioamide anion part. This behaviour followed the rule of thumb for dianions, the site of the second deprotonation being the more reactive one.

This attractive selectivity was exploited for a double alkylation with two *different* alkyl halides (Scheme 8). Addition of 1 equiv. of *ethyl* iodide to the dianion, followed by treatment with 1 equiv. of *methyl* iodide selectively gave the thioimido ester **26** (Entry 3). The reverse order of addition afforded the thioimido ester **27**, with no crossover product (Entry 4).

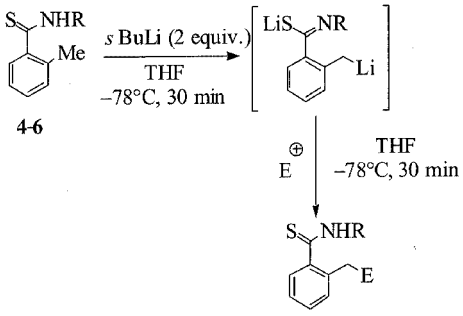
Table 3. Deprotonation of thiobenzamides **4**–**7** with 2 equiv. of *s*BuLi (−78 °C, 1−2 h) and treatment of the dianions with electrophiles (−78 °C, 30 min to 1 h)

Entry	Thio-amide	Electrophile(s)	Equiv-alent	Product	Yield [%]	(*Z*)/(*E*) ratio
1	**4**	MeI	1	**7** 	90	98:2
2	**4**	MeI	2	**25** 	87	29:71
3	**4**	EtI then MeI	1 1	**26** 	79	34:66
4	**4**	MeI then EtI	1 1	**27** 	82	24:76
5	**4**	Allyl iodide	1.2	**28** 	74	100:0
6	**4**	Ph_2PCl	1.1	**29** 	23	100:0
7	**4**	nBu_3SnCl	1.1	**30** 	61	100:0
8	**4**	MeCOCl	3	**31** 	93	
9	**4**	MeCHO	5	**32** 	76	100:0
10	**4**	*i*PrCHO	3	**33** 	79	100:0
11	**4**	4-Methyl-3-penten-2-one 	1.2	**34** 	66	100:0
12	**4**	2-Cyclopentenone	1	**35** 	16	100:0
				36 	34	100:0
				37 	8	
13	**5**	MeCHO	10	**38** 	88	100:0
14	**5**	*i*PrCHO	1.5	**39** 	80	100:0
15	**6**	MeCHO	6	**40** 	77	100:0
16	**6**	*i*PrCHO	1.4	**41** 	68	100:0
17	**7**	Allyl iodide	1.1	**42** 	48	100:0
18	**7**	Me_3SiCl	2	**43** 	30	100:0
19	**7**	MeCHO	1.5	**44** 	71	100:0 dr 57:43
20	**7**	*i*PrCHO	3	**45** 	73	100:0 dr 50:50
21	**7**	2-Cyclopentenone	1.3	**46** 	46	100:0 dr 81:19 After cryst.: dr 100:0



Scheme 8. Sequential alkylation of dianion **24**

Other electrophiles were tested with the dianion **24** (Scheme 9); 1 equiv. of allyl iodide produced the 2-(but-3-enyl)-*N*-methylthiobenzamide **28** (Entry 5). Chlorodiphenylphosphane reacted at the benzylic site to give the phosphane oxide **29**, after air oxidation (Entry 6).



Scheme 9. Benzylic electrophilic addition of thiobenzamide dianions

Treatment with tri-*n*-butyltin chloride was intriguing, as the favourable S−Sn bond formation might have competed with *C*-alkylation. However, the same orientation was again observed, with the formation of thioamide **30** (Entry 7).

Acylation of the dianion **24** resulted in the formation of **31**, with ring closure (Entry 8). This compound was the product of the addition of acetyl chloride at one of the two reactive centres (carbon or sulfur) and subsequent attack of the other anionic site on the carbonyl group with ensuing dehydration.

The dianion **24** was also treated with various aldehydes and ketones. Ethanal and 2-methylethanal provided good yields of the monoalcohols **32** and **33**, respectively, generated by addition of the benzylic anion to the carbonyl moiety (Entries 9 and 10). A single set of peaks was observed by ^1H and ^{13}C NMR, consistently with two features: (i) a single (*Z*)-thioamide rotamer, and (ii) no evidence of atropisomers along the $C_{Ar}-C(=S)$ bond, which would have produced diastereoisomers with the newly created stereogenic carbon centre.

We were also interested in the behaviour of dianion **24** with ambident Michael acceptors. Treatment with mesityl

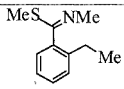
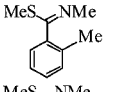
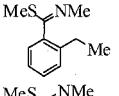
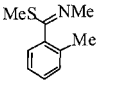
oxide (Entry 11) gave a single regioisomer **34** arising from 1,2-addition, as a result of steric hindrance to 1,4-attack. 2-Cyclopentenone is known for its propensity towards conjugate addition; we obtained the 1,4 adduct **36** as the major compound (Entry 12). It was accompanied by the 1,2-regioisomer **35** and the cyclic compound **37** (arising from **35**, as shown by isolation of **37** on heating of **35**). The 1,4/1,2 addition ratio was therefore 34:24, showing a moderately soft character of the dianion **24**.

Treatment of dianions from thioamides **5** and **6**, bearing different substituents on the nitrogen atom (*i*Pr, Ph), with aldehydes afforded compounds **38**−**41**, products of benzylic attack (Entries 13−16).

We then investigated thiobenzamide **7**, bearing a lateral ethyl group rather than a methyl group. In other series, this structural change had tended to hinder deprotonation. Here, with the same base, we were able to introduce a variety of substituents in the benzylic position by treatment with allyl iodide, Me_3SiCl and aldehydes (Entries 17−20). With 2-cyclopentenone (Entry 21), a single 1,2-regioisomer **46** was isolated. The two preceding reactions with carbonyl compounds (Entries 19 and 20) had not resulted in any diastereoselectivity along the newly created C−C bond. With cyclopentenone, however, we found a *dr* of 81:19, and crystallization furnished a pure diastereomer (Entry 21).

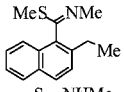
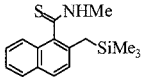
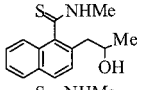
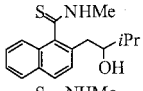
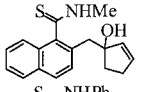
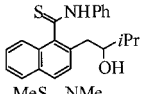
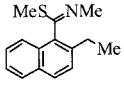
The base used had so far been *sec*-butyllithium. We wished to investigate other organolithium compounds. The test reaction involved addition of 2.3 equiv. of base and subsequent treatment with 2.3 equiv. of methyl iodide (Table 4). At −78 °C, *n*-butyllithium and LDA effected only single deprotonation. At 0 °C, double proton abstraction was achieved selectively with *n*-butyllithium and unselectively with LDA.

Table 4. Deprotonation of thiobenzamide **4** with 2.3 equiv. of various bases and quenching with 2.3 equiv. of MeI

Entry	Base	Deprotonation conditions [°C]	Alkylation conditions(s) [°C]	Product	Formation [%]
1	*s*BuLi	−78	−78	**25** 	95
2	*n*BuLi	−78	−78 or 0	**21** 	99
3	*n*BuLi	0	0	**25** 	94
4	LDA	−78	−78	**21** 	98
5	LDA	0	0	**21** + **25**	66 :34 ratio

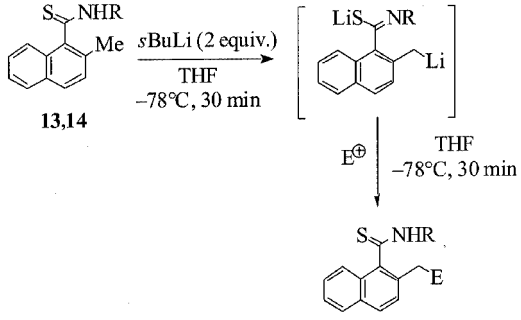
The stronger basic character of *s*BuLi is therefore confirmed; to achieve a result similar to that obtained with that base at −78 °C, a temperature of 0 °C had to be applied with *n*BuLi.

Table 5. Deprotonation of thionaphthamides **13**, **14** and **17** with 2 equiv. of *s*BuLi (−78 °C, 1−2 h) and treatment of the dianions with electrophiles (−78 °C, 30 min to 1 h)

Entry	Thioamide	Electrophile	Equivalent	Product	Yield [%]	(*Z*)/(*E*) ratio
1	**13**	MeI	2.5	**47** 	87	24:76
2	**13**	Me_3SiCl	2.5	**48** 	91	100:0
3	**13**	MeCHO	3	**49** 	81	64:36
4	**13**	*i*PrCHO	3	**50** 	71	67:33
5	**13**	2-Cyclopentenone	1.2	**51** 	60	64:36
6	**15**	*i*PrCHO	3	**52** 	65	71:29
7	**16**	MeI (using 5 equiv. of *s*BuLi)	7	**47** 	65	76:24

Thionaphthamides

Addition of 2 equiv. of base to thionaphthamide **13**, followed by 2 equiv. of methyl iodide, gave the thioimido ester **47** (Table 5, Entry 1). A dianion had been formed and doubly alkylated (Scheme 10).



Scheme 10. Benzylic electrophilic addition of thionaphthamide dianions

Addition of trimethylsilyl chloride to the dianion afforded the thioamide **48**, with the TMS group attached to the benzylic carbon atom (Entry 2). The actual product of the reaction was probably the bis(silylated) compound (on both carbon and nitrogen atoms), which then underwent desilylation of the nitrogen atom upon hydrolytic workup.

Addition of aldehydes (Entries 3, 4 and 6) resulted in the efficient formation of thioamides **49**, **50** and **52**, containing alcohol moieties. 2-Cyclopentenone reacted in a selective nonconjugate manner to give alcohol **51** (Entry 5). It is

worth noting that the dianion **24** of thiobenzamide **4** afforded a mixture of 1,2- and 1,4 adducts (Table 3, Entry 12). Thus, the thionaphthamide dianion showed an unexpected harder character.

Double deprotonation of thionaphthamide **16**, bearing an ethyl lateral group, was not achieved even under forcing conditions (Entry 7). The monoanion was formed instead, as shown by the formation of thioimido ester **47**, the result of single methyl incorporation, on addition of MeI.

Conclusion

Our study has shown that secondary thioamides have interesting structural features and potential for synthesis.

X-ray diffraction revealed that a thionaphthamide bearing a (small) methyl group on the nitrogen atom exhibited an almost perpendicular arrangement between the plane of the arene and that of the thioamide group. The second condition for axial chirality, however, was not fulfilled at room temperature, as the barrier to rotation was too low. More suitable $\Delta G^{\ddagger}$ values, relating to tertiary thioamides bearing two large substituents on the nitrogenatom, will be reported soon.

For secondary thiobenzamides and thionaphthamides, the (*Z*) structure was the main one observed in solution, and appeared to be thermodynamically favoured. This configuration places the two larger substituents, aryl and methyl, on opposite sides of the N−C(=S) bond. The (*Z*)/(*E*) equilibrium could be established in one example, in which the (*E*) isomer was isolated on crystallization. It must be noted that the solubilities were dependent upon the structure; with N−*i*Pr the (*E*) isomer of **14** crystallised, whereas for **13** (N−Me) it was the (*Z*) isomer that crystallised.

As an extension of a single example[3] of regioselective lateral deprotonation of a secondary thioamide, we observed that both metallation and alkylation could be made selective in most cases. The first proton to be abstracted by alkyllithium compounds was the one of the NH group. The pK_a of thiobenzamide, 16.9 in DMSO,[42] corresponds to a much higher acidity than seen in the benzamide oxygen analogue (23.3). This reflects the greater ability of the sulfur atom to accommodate a negative charge, and the lower electronegativity. The second deprotonation also took place readily at low temperature in the presence of a strong base.

The selective routes to both the mono- and the dianions allowed us to investigate their chemistry. Although some of the reactions observed here had been reported in the literature, no general and comparative studies were available. There are precedents for *S*-alkylation of secondary thiobenzamides under basic conditions with alkyl iodides,[43,44] a sulfenyl chloride[45] and a phosphinoyl chloride.[46] For the reaction with acyl halides, both regioselectivities − acylation of the sulfur atom[47] or of the nitrogen atom[48,49] − have been reported. Our results are clear-cut. The monoanions reacted on the sulfur terminus with alkyl halides and on the nitrogen atom with acyl halides.

The behaviour of the dianions was also selective. Addition of 1 equiv. of electrophile (alkyl iodide, trialkylsilyl chloride) resulted in attack at the benzylic position. This regioselectivity is potentially useful for synthesis. A second equivalent of electrophile resulted in a reaction at the thioamide moiety. As previously shown for monoanions, treatment with alkyl iodides (soft reagents) afforded *S*-alkylation products. The attack on the two anionic moieties of the dianion can be conveniently controlled simply by the order of addition, as shown with ethyl and methyl iodides (or vice versa).

A variety of compounds was synthesised by exploitation of the higher reactivity of the benzylic centre of the dianions. C−C bonds were created with alkyl halides, aldehydes and ketones. C−heteroatom bonds were formed by addition of stannyl, silyl and phosphonoyl chlorides. Some observations on the soft/hard character of the intermediates were evidenced with ambident Michael acceptors.

The easy preparation and manipulation of secondary thiobenzamides and naphthamides make them attractive compounds. The aromatic products formed are potentially useful. The thioamide moiety exhibits specific or enhanced reactivity[5] in comparison with that of the carbonyl derivatives: high nucleophilicity, Eschenmoser reaction, Michael addition (NH) etc.

The second aspect of our study deals with the use of axially chiral thiobenzamides or thionaphthamides for atroposelective reactions and will be reported in due course.

Experimental Section

General Remarks: NMR spectra were measured in $CDCl_3$. The ^{1}H NMR spectra were recorded at 250 MHz (Bruker DPX 250), the ^{13}C NMR spectra at 62.9 MHz (Bruker DPX 250) and the ^{31}P NMR spectra at 101.3 MHz (Bruker AC 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 butyllithium were titrated before use, according to ref.[50] Isomer ratios were determined by ^{1}H NMR. The preparation of thioamides **3**−**17** is reported in the Supporting Information (see footnote on the first page of this article).

General Procedure for Single Deprotonation of Thioamides 4 and 13 and Treatment with Electrophiles (Compounds 19−23): A solution of thioamide **4** or **13** (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium (1.05 equiv.) in cyclohexane was added dropwise. The reaction mixture was stirred at −78 °C for 30−60 min. The appropriate electrophile 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 or-

ganic 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*-Methyl-*N*-[(2-methylphenyl)carbonothioyl]benzamide (19):** The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 561 mg, 3.4 mmol), *s*BuLi (2.6 mL of a 1.4 M solution in cyclohexane, 3.57 mmol), benzoyl chloride (435 μL, 3.74 mmol) and THF (15 mL). Reaction time after addition of base: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 832 mg (yield: 91%) of compound **19** as an orange solid. M.p. 66 °C. R_f = 0.53 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 2.24 (s, 3 H, ArMe), 3.86 (s, 3 H, NMe), 6.84−7.40 (m, 9 H, Ar-H) ppm. ^{13}C NMR: δ = 20.2 (Ar*Me*), 40.9 (NMe), 125.8, 128.4, 128.6, 128.7, 129.0, 129.3, 129.5, 131.0, 132.9, 134.0, 136.1, 145.2, 175.0 (C=O), 208.8 (C=S) ppm. MS (EI): *m*/*z* (%) = 269 (1) [M$^+$], 105(100), 77 (56), 51 (21) ppm. IR (neat): $\tilde{\nu}$ = 3058 cm^{-1}, 1692 ($\nu_{C=O}$), 1272, 1166 ($\nu_{C=S}$) cm^{-1}. $C_{16}H_{15}NSO$ (269.36): calcd. C 71.35, H 5.61, N 5.20, S 11.90; found C 71.54, H 5.63, N 5.33, S 11.72.

***N*-Methyl-*N*-[(2-methylphenyl)carbonothioyl]acetamide (20):** The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 669 mg, 4.05 mmol), *s*BuLi (3.1 mL of a 1.4 M solution in cyclohexane, 4.25 mmol), propanoyl chloride (400 μL, 4.46 mmol) and THF (15 mL). Reaction time after addition of base: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 281 mg (yield: 86%) of compound **20** as an orange oil. R_f = 0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.94 (t, *J* = 7.4 Hz, 3 H, CH_2*Me*), 2.18 (q, *J* = 7.4 Hz, 2 H, C*H*$_2$Me), 2.26 (s, 3 H, ArMe), 3.70 (s, 3 H, NMe), 7.14−7.29 (m, 4 H, Ar-H) ppm. ^{13}C NMR: δ = 9.8 (CH_2*Me*), 19.5 (ArMe), 32.5 (*C*H$_2$Me), 126.2, 127.4, 129.5, 132.8, 145.6, 178.2 (C=O), 209.2 (C=S) ppm. IR (neat): $\tilde{\nu}$ = 3062 cm^{-1}, 2940, 1712 ($\nu_{C=O}$), 1456, 1418, 1334, 1264, 1148 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 221 (77) [M$^+$], 206 (67), 164 (100), 135 (58), 132 (84), 116 (20), 89 (19), 65 (22). $C_{12}H_{15}NSO$ (221.32): calcd. C 65.12, H 6.83, N 6.33, found C 64.80, H 6.86, N 6.61.

Methyl *N*,2-Dimethylbenzenecarbimidothioate (21): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 489 mg, 2.96 mmol), *s*BuLi (2.39 mL of a 1.3 M solution in cyclohexane, 3.11 mmol), methyl iodide (155 μL, 3.25 mmol) and THF (13 mL). Reaction time after addition of base: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 482 mg (yield: 91%) of compound **21** as a yellow oil. R_f = 0.4−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 37:63. ^{1}H NMR [(*E*) isomer]: δ = 2.23 (s, 3 H, ArMe), 2.40 (s, 3 H, SMe), 3.01 (s, 3 H, NMe), 7.06−7.23 (m, 4 H, Ar-H) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 1.91 (s, 3 H, SMe), 2.30 (s, 3 H, ArMe), 3.37 [s, 3 H, NMe, (*Z*)], 7.06−7.23 (m, 4 H, Ar-H) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 13.5 [SMe, (*E*)], 15.2 [SMe, (*Z*)], 19.1 [ArMe, (*E*)], 19.3 [ArMe, (*Z*)], 40.5 [NMe, (*Z*)], 40.8 [NMe, (*E*)], 126.3, 127.3, 127.9, 129.0, 129.4, 130.5, 130.7, 135.0, 137.0, 167.2, 168.3 (C=N) ppm.

***N*-Methyl-*N*-[(2-methyl-1-naphthalene)carbonothioyl]benzamide (22):** The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 187 mg, 0.87 mmol), *s*BuLi (730 μL of a 1.25 M solution in cyclohexane, 0.91 mmol), benzoyl chloride (111 μL, 0.97 mmol) and THF (11 mL). Reaction time after addition of base: 1 h. Silica gel chromatographic separation with petroleum ether/ethyl acetate (8:2) afforded 201 mg (yield: 73%) of compound **22** as an orange oil. R_f = 0.5 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 2.36 (s, 3 H, ArMe), 3.95 (s, 3 H, NMe), 6.95−7.91 (m, 11 H, Ar-H) ppm. ^{13}C NMR: δ = 20.4 (Ar*Me*), 40.1 (NMe), 125.2, 126.4, 127.4, 127.6, 127.7, 128.0, 128.2, 128.9, 129.0, 129.7, 131.1, 131.6, 131.8, 133.9, 139.9, 174.0 (C=O), 205.9 (C=S) ppm. IR (neat): $\tilde{\nu}$ = 3060 cm^{-1}, 1663 ($\nu_{C=O}$), 1268, 1179 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 319 (4) [M$^+$], 200(100), 164 (47).

Methyl *N*,2-Dimethyl-1-naphthalenecarbimidothioate (23): The general procedure was applied with *N*-methyl-2-methylthionaphthamide (**13**, 206 mg, 0.96 mmol), *s*BuLi (777 μL of a 1.3 M solution in cyclohexane, 1.01 mmol), methyl iodide (50.5 μL, 1.06 mmol) and THF (12 mL). Reaction time after addition of the base: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 187 mg (yield: 85%) of compound **23** as an orange oil. R_f = 0.5−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 34:66. ^{1}H NMR (*E* isomer): δ = 2.37 (s, 3 H, ArMe), 2.46 (s, 3 H, SMe), 2.94 (s, 3 H, NMe), 7.30−7.83 (m, 6 H, Ar-H) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 1.67 (s, 3 H, SMe), 2.40 (s, 3 H, ArMe), 3.50 (s, 3 H, NMe), 7.30−7.83 (m, 6 H, Ar-H) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 12.9, 13.9 (SMe), 19.1, 19.4 (Ar*Me*), 40.2, 40.3 (NMe), 124.1, 124.5, 125.2, 125.4, 126.7, 126.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.8, 129.5, 131.6, 132.4, 132.5 (Ar−H), 166.5, 167.4 (C=N) ppm. MS (EI): *m*/*z* (%) = 230 (76) [MH$^+$], 192 (100), 168 (14), 105 (53). HMRS calcd. for $C_{14}H_{15}NS$: 230.1004; found 230.1003.

General Procedure for Double Deprotonation of Thioamides 4−7 and Treatment with Electrophiles (Compounds 25−46): A solution of thioamide **4**, **5**, **6** or **7** (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium in cyclohexane (2−2.5 equiv.) was then added dropwise. The reaction mixture was stirred at −78 °C for 1−2 h.

− Addition of 1 electrophile (1−10 equiv.): The electrophile was added dropwise and the resulting mixture was stirred at −78 °C for 30 min−1 h.

− Addition of 2 different electrophiles: The first electrophile (1 equiv.) was added slowly and the mixture was stirred at −78 °C for 30 min. The second electrophile (1 equiv.) was then added dropwise and the reaction mixture was stirred for 30 min at the same temperature.

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 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.

Methyl 2-Ethyl-*N*-methylbenzenecarbimidothioate (25): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 73 mg, 0.41 mmol), *s*BuLi (658 μL of a 1.3 M solution in cyclohexane, 0.86 mmol), methyl iodide (41 μL, 0.86 mmol) and THF (6 mL). Reaction time after addition of base: 1 h, after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 91 mg (yield: 87%) of compound **25** as a colourless oil. R_f = 0.4−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 29:71. ^{1}H NMR [(*E*) isomer]: δ = 1.22 (t, *J* = 7.6 Hz, 3 H, CH_2*Me*), 2.40 (s, 3 H, SMe), 2.55 (q, *J* = 7.6 Hz, 2 H, C*H*$_2$Me), 3.01 (s, 3 H, NMe), 7.03−7.32 (m, 4 H, Ar) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 1.20 (t, *J* = 7.6 Hz, 3 H, CH_2*Me*), 1.91 (s, 3 H, SMe), 2.65 (q, *J* = 7.6 Hz, 2 H, C*H*$_2$Me), 3.36 (s, 3 H, NMe), 7.03−7.32 (m, 4 H, Ar) ppm. ^{13}C NMR [(*E*)

isomer]: δ = 13.2 (SMe), 15.0 (CH_2*Me*), 25.5 (*C*H_2Me), 40.7 (NMe), 125.9, 127.1, 128.4, 129.2, 135.9, 140.8 (Ar−H), 168.0 (C=N) ppm. ^{13}C NMR [(*Z*) isomer]: δ = 14.9 (SMe), 15.1 (CH_2*Me*), 25.4 (*C*H_2Me), 40.1 (NMe), 125.8, 127.7, 128.6, 128.8, 137.0, 141.0 (Ar−H), 166.7 (C=N) ppm. MS (EI): *m*/*z* (%) = 194 (100) [M$^+$ H]$^+$, 160 (88), 146 (71), 132 (16). HMRS calcd. for $C_{11}H_{16}NS$: 194.1003; found 194.1000.

Methyl *N*-Methyl-2-propylbenzenecarbimidothioate (26): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 208 mg, 1.27 mmol) in THF (6 mL), *s*BuLi (2.5 mL of a 1.3 M solution in cyclohexane, 3.19 mmol) and ethyl iodide (103 μL, 1.27 mmol) and methyl iodide (79 μL, 1.27 mmol), respectively. Reaction time after addition of base: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 280 mg (yield: 79%) of compound **26** as a colourless oil. R_f = 0.4−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 34:66. ^{1}H NMR [(*E*) isomer]: δ = 0.95 (t, *J* = 7.2 Hz, 3 H, CH_2*Me*), 1.60−1.73 (m, 2 H, CH_2CH_2Me), 2.42 (s, 3 H, SMe), 2.49−2.64 (m, 2 H, C$H_2$$CH_2$Me), 3.00 (s, 3 H, NMe), 7.03−7.30 (m, 4 H, Ar-H) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 0.96 (t, *J* = 7.2 Hz, 3 H, CH_2*Me*), 1.60−1.73 (m, 2 H, CH_2CH_2Me), 1.94 (s, 3 H, SMe), 2.49−2.64 (m, 2 H, C$H_2$$CH_2$Me), 3.35 (s, 3 H, NMe), 7.07−7.21 (m, 4 H, Ar-H) ppm. ^{13}C NMR [(*E*) isomer]: δ = 15.5 (SMe), 14.7 (CH_2*Me*), 24.2 (CH_2CH_2Me), 35.1 (*C*$H_2$$CH_2$Me), 41.2 (NMe), 126.3, 127.7, 129.4, 129.5, 136.6, 139.7, 167.5 (C=N) ppm. ^{13}C NMR [(*Z*) isomer]: δ = 13.7 (SMe), 14.6 (CH_2*Me*), 24.1 (CH_2CH_2Me), 35.0 (*C*$H_2$$CH_2$Me), 40.5 (NMe), 126.2, 128.2, 128.9, 129.7, 137.5, 140.0, 167.1 (C=N) ppm. MS (EI): *m*/*z* (%) = 207 (2) [M$^+$], 192 (100), 160 (84), 131 (96), 116 (79). HMRS calcd. for $C_{12}H_{18}NS$: 208.1160; found 208.1154.

Ethyl 2-Ethyl-*N*-methylbenzenecarbimidothioate (27): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 201 mg, 1.23 mmol) in THF (6 mL), *s*BuLi (2.4 mL of a 1.3 M solution in cyclohexane, 3.08 mmol) and methyl iodide (77 μL, 1.23 mmol) and ethyl iodide (99 μL, 1.23 mmol), respectively. Reaction time after addition of base: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 208 mg (yield: 82%) of compound **27** as a colourless oil. R_f = 0.4−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 24:76. ^{1}H NMR [(*E*) isomer]: δ = 1.25 (t, *J* = 7.6 Hz, 3 H, CH_2*Me*), 1.35 (t, *J* = 7.4 Hz, 3 H, SCH_2*Me*), 2.61 (q, *J* = 7.6 Hz, 2 H, CH_2Me), 3.03 (s, 3 H, NMe), 3.07 (q, 2 H, SCH_2Me, *J* = 7.4 Hz), 7.06−7.34 (m, 4 H, Ar-H) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 1.10 (t, *J* = 7.5 Hz, 3 H, SCH_2*Me*), 1.23 (t, *J* = 7.6 Hz, 3 H, CH_2*Me*), 2.41 (q, *J* = 7.5 Hz, 2 H, SCH_2Me), 2.70 (q, *J* = 7.6 Hz, 2 H, CH_2Me, *J* = 7.6 Hz), 3.40 (s, 3 H, NMe), 7.06−7.34 (m, 4 H, Ar-H) ppm. ^{13}C NMR [(*E*) isomer]: δ = 14.5, 15.2 (SCH_2*Me* + CH_2*Me*), 24.5 (S*C*H_2Me), 25.5 (*C*H_2Me), 41.1 (NMe), 126.0, 128.1, 128.9, 129.1, 138.0, 141.5, 167.7 (C=N) ppm. ^{13}C NMR [(*Z*) isomer]: δ = 14.6, 15.4 (SCH_2*Me* + CH_2*Me*), 26.0 (S*C*H_2Me), 26.9 (*C*H_2Me), 40.5 (NMe), 126.3, 127.5, 128.7, 129.5, 136.4, 141.0, 166.7 (C=N) ppm. MS (EI): *m*/*z* (%) = 207 (3) [M$^+$], 177 (100), 146 (82), 131 (58), 116 (52). HMRS calcd. for $C_{12}H_{18}NS$: 208.1160; found 208.1151.

2-(But-3-enyl)-*N*-methylthiobenzamide (28): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 376 mg, 2.28 mmol) in THF (12 mL), *s*BuLi (4.4 mL of a 1.3 M solution in cyclohexane, 5.70 mmol) and allyl iodide (250 μL, 2.73 mmol). Reaction time after addition of base: 1 h, after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 345 mg (yield: 74%) of compound **28**. After crystallization from chloroform/hexane, a white solid was obtained. M.p. 95 °C. R_f = 0.4 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 2.38−2.44 (m, 2 H, CH_2−C=), 2.79−2.83 (m, 2 H, ArCH_2), 3.33 (d, *J* = 4.9 Hz, 3 H, NMe), 4.98−5.06 (m, 2 H, =CH_2), 5.79−5.87 (m, 1 H, −CH=), 7.18−7.32 (m, 4 H, Ar-H), 7.44 (br. s, 1 H, NH) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 32.6, 33.2 (NMe), 35.7, 115.7, 126.5, 127.0, 129.4, 130.2, 137.4, 144.2, 138.4, 202.9 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3045 cm^{-1}, 1570, 1452, 1438, 1374, 1236, 1115 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 205 (15) [M$^+$], 176 (100), 172 (32), 158 (44), 131 (18), 115 (59). $C_{12}H_{15}NS$ (205.32): calcd. C 70.20, H 7.36, N 6.82, S 15.61; found C 70.30, H 7.45, N 7.14, S 15.33.

2-(Diphenylphosphinoylmethyl)-*N*-methylthiobenzamide (29): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 225 mg, 1.38 mmol) in THF (6 mL), *s*BuLi (2.6 mL of a 1.3 M solution in cyclohexane, 3.45 mmol) and chlorodiphenylphosphane (278 μL, 1.59 mmol). Reaction time after addition of base: 1 h; after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 112 mg (yield: 23%) of compound **29**. After crystallization from chloroform/hexane a white solid was obtained. M.p. 244 °C. R_f = 0.1 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 3.30 (d, *J* = 4.6 Hz, 3 H, NMe), 3.65 (d, *J* = 12.0 Hz, 2 H, CH_2), 6.27 (d, *J* = 7.7 Hz, 1 H, Ar-H), 6.98 (d, *J* = 7.5 Hz, 1 H, Ar-H), 7.20−7.76 (m, 12 H, Ar-H), 10.9 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 33.6 (NMe), 35.3 (*J* = 64.0 Hz, CH_2), 124.4 (*J* = 8.6 Hz, Ar-H), 127.7 (*J* = 3.2 Hz, Ar-H), 128.9 (*J* = 2.9 Hz, d, Ar-H), 129.4 (*J* = 12.0 Hz, d, Ar-H), 130.3 (*J* = 4.2 Hz, d, Ar-H), 130.7 (*J* = 2.7 Hz, d, Ar-H), 131.5 (*J* = 9.2 Hz, d, Ar-H), 133.0 (*J* = 2.7 Hz, d, Ar-H), 145.8 (*J* = 5.2 Hz, d, Ar-H), 199.6 (C=S) ppm. ^{31}P NMR: δ = 33.2 ppm. IR (KBr): $\tilde{\nu}$ = 2896 cm^{-1}, 1570, 1462, 1436, 1372($\nu_{P=O}$), 1176 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 365 (4) [M$^+$], 201 (10), 164 (50), 45 (100). $C_{21}H_{20}PNSO$ (365.43): calcd. C 69.02, H 5.52, N 3.83, S 8.48; found C 69.09, H 5.45, N 4.04, S 8.34.

***N*-Methyl-2-(tributylstannanylmethyl)thiobenzamide (30):** The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 253 mg, 1.55 mmol) in THF (7 mL), *s*BuLi (2.6 mL of a 1.3 M solution in cyclohexane, 3.41 mmol) and tri-*n*-butyltin chloride (515 μL, 1.70 mmol). Reaction time after addition of base: 1 h; after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 428 mg (yield: 61%) of compound **30** as a brown oil. R_f = 0.4 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.77−1.47 [m, 27 H, $(CH_2)_3$*Me* + $(CH_2)_3$Me], 2.43 (s, 2 H, CH_2), 3.30 (d, *J* = 4.9 Hz, 3 H, NMe), 6.96−7.15 (m, 4 H, Ar-H), 7.31 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 10.8 [*C*$H_2$$(CH_2)_2$Me], 14.1 [$(CH_2)_3$*Me*], 17.0 ($CH_2$), 27.8, 29.4 ($CH_2$*C*$H_2$$CH_2$Me), 33.1 (NMe), 123.4, 126.9, 129.2, 140.9, 141.2, 203.2 (C=S) ppm. MS (EI): *m*/*z* (%) = 455 (1) [M$^+$], 399 (2), 383 (2), 115 (100), 100 (72), 58 (52). HMRS calcd. for $C_{21}H_{39}NSSn$: 456.1749; found 456.1742.

Methyl(3-methylisothiochromen-1-ylidene)amine (31): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 315 mg, 1.93 mmol) in THF (15 mL), *s*BuLi (3.3 mL of a 1.3 M solution in cyclohexane, 4.25 mmol) and acetyl chloride (413 μL, 5.79 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 339 mg (yield: 93%) of compound **31**. After crystallization from hexane, orange crystals were obtained. M.p. 103 °C. R_f = 0.5 (petroleum ether/ethyl acetate, 8:2). ^{1}H NMR: δ = 2.49 (s, 3 H, NMe), 4.11 (s, 3 H, Me), 6.70 (s, 1 H), 7.43−7.62 (m, 3 H, Ar-H), 9.03 (d, *J* = 8.4 Hz,

1 H) ppm. ^{13}C NMR: δ = 22.8 (Me), 40.92 (NMe), 113.3, 126.2, 127.8, 132.5, 132.7, 133.0, 133.2, 141.3, 185.8 (C=N) ppm. IR (KBr): $\tilde{\nu}$ = 2918 cm^{-1}, 2360, 1632, 1552, 1482, 1310, 1264, 1142, 826 cm^{-1}. MS (EI): *m*/*z* (%) = 189 (65) [M$^+$], 115 (27), 87 (18), 55 (95), 43 (100). $C_{11}H_{11}NS$ (189.28): calcd. C 69.80, H 5.86, N 7.40, S 16.94; found C 69.41, H 5.91, N 7.08, S 16.62.

2-(2-Hydroxypropyl)-*N*-methylthiobenzamide (32): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 2 g, 12.2 mmol) in THF (50 mL), *s*BuLi (21.8 mL of a 1.3 M solution in cyclohexane, 28.2 mmol) and acetaldehyde (3.5 mL, 61 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 1.782 g (yield: 76%) of compound **32**. After crystallization from hexane, a white solid was obtained. M.p. 85 °C. R_f = 0.1 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.20 (d, *J* = 6.1 Hz, 3 H, Me), 2.49−2.66 (m, 2 H, CH_2), 2.65 (d, *J* = 4.0 Hz, 3 H, NMe), 3.34 (s, 1 H, OH), 3.91− 3.99 (m, 1 H,CH), 7.08−7.47 (m, 4 H, Ar-H), 9.64 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 24.6 (CH_2), 33.3 (NMe), 41.5 (Me), 61.9 (CH), 126.6, 129.5, 129.7, 130.3, 134.2, 144.1, 200.6 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3284 (OH), 3178, 3064, 2970, 1574, 1464, 1372, 1120 ($\nu_{C=S}$), 1042, 762 cm^{-1}. MS (EI): *m*/*z* (%) = 209 (17) [M$^+$], 176 (100), 158 (33), 131 (43), 117 (25). $C_{11}H_{15}NSO$ (209.31): calcd. C 63.12, H 7.22, N 6.69, O 7.64, S 15.32; found C 63.05, H 7.13, N 6.63, O 7.87, S 15.12.

2-(2-Hydroxy-3-methylbutyl)-*N*-methylthiobenzamide (33): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 304 mg, 1.86 mmol) in THF (12 mL), *s*BuLi (3.6 mL of a 1.3 M solution in cyclohexane, 4.66 mmol) and isobutyraldehyde (508 μL, 5.59 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 320 mg (yield: 79%) of compound **33**. After crystallization from ethyl acetate/hexane, white crystals were obtained. M.p. 126 °C. R_f = 0.1 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.01 (d, *J* = 6.9 Hz, 3 H, CH*Me*$_2$), 1.00 (d, *J* = 6.7 Hz, 3 H, CH*Me*$_2$), 1.77−1.88 (m, 1 H, NCH), 2.16 (d, *J* = 4.0 Hz, 1 H, OH), 2.63−2.81 (m, 2 H, C*H*$_2$-Ar), 3.27 (d, *J* = 4.8 Hz, 3 H, NMe), 3.74−3.84 (m, 1 H, C*H*OH), 7.16−7.36 (m, 3 H, Ar-H), 7.65−7.69 (m, 1 H, Ar-H), 9.63 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 17.6, 18.9 (CH*Me*$_2$), 33.5 (NMe), 34.6 (*C*HMe$_2$), 36.2 (CH_2), 79.4 (*C*HOH), 124.7, 129.7, 129.8, 130.2, 134.1, 144.6, 200.9 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3310 ν_{OH}), 3175, 3060, 2975, 1561, 1368, 1134 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 237 (4) [M$^+$], 204 (32), 176 (42), 55 (54), 43 (100). $C_{13}H_{19}NSO$ (237.36): calcd. C 65.78, H 8.07, N 5.90, O 6.74, S 13.51; found C 65.32, H 8.01, N 5.78, O 6.71, S 13.46.

2-(2-Hydroxy-2,4-dimethylpent-2-enyl)-*N*-methylthiobenzamide (34): The general procedure was applied with 2,*N*-dimethylthiobenzamide (**4**, 1.044 g, 6.3 mmol) in THF (30 mL), *s*BuLi (10 mL of a 1.4 M solution in cyclohexane, 14.0 mmol) and distilled mesityl oxide (871 μL, 7.6 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (7:3) afforded 1.014 g (yield: 61%) of compound **34**. After crystallization from ethyl acetate/hexane, white crystals were obtained. M.p. 139 °C. R_f = 0.3 (petroleum ether/ethyl acetate, 7:3). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.45 [s, 3 H, C(OH)*Me*), 1.65 (d, *J* = 0.8 Hz, 3 H, CH=C*Me*$_2$), 1.75 (d, *J* = 1.0 Hz, 3 H, CH=C*Me*$_2$), 2.15 (s, 1 H, OH), 2.82 and 2.94 (AB, *J* = 14.0 Hz, 2 H, ArCH_2), 3.27 (d, *J* = 4.7 Hz, 3 H, NMe), 5.36 (m, 1 H, C*H*=CMe$_2$), 7.15−7.28 (m, 3 H, Ar-H), 7.63−7.66 (m, 3 H, Ar-H), 9.92 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 19.1, 27.9, 31.0 [C(OH)*Me*), 33.5 (NMe), 44.9, 75.0, 126.9, 128.9, 130.3, 131.7, 135.0, 145.2, 131.1, 131.7, 201.1 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3284 (ν_{OH}), 3178, 3056, 2970, 2926, 1552, 1368, 1131 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 263 (12) [M$^+$], 245 (12), 230 (16), 164 (95), 132 (82), 43 (100). $C_{15}H_{21}NSO$ (263.40): calcd. C 68.40, H 8.04, N 5.32, S 12.17; found C 68.30, H 8.11, N 5.58, S 12.10.

2-(1-Hydroxycyclopent-2-enylmethyl)-*N*-methylthiobenzamide (35), *N*-Methyl-2-(3-oxocyclopentylmethyl)thiobenzamide (36) and *N*-{4,5-dihydrospiro[cyclopent-2-ene-1,3′-isothiochromen]-1′(4′H)-ylidene}-*N*-methylamine (37): Treatment of 2,*N*-dimethylthiobenzamide (**4**, 338 mg, 2.04 mmol) with *s*BuLi (3.5 mL of a 1.3 M solution in cyclohexane, 4.5 mmol) and 2-cyclopentenone (172 μL, 2.04 mmol) in THF (6 mL) was carried out according to the general procedure. Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. This produced a crude mixture of compounds **35**, **36** and **37**. Purification by silica gel chromatography with petroleum ether/ethyl acetate (7:3) afforded 121 mg of **35** as white crystals (yield: 16%), 171 mg of **36** as white crystals (yield: 34%) and 40 mg of **37** as brown crystals (yield: 8%).

Compound 35: R_f = 0.2 (petroleum ether/ethyl acetate, 7:3). M.p. 103 °C. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.90−2.01 (m, 1 H, C*H*$_2$−CH=), 2.11 (s, 1 H, OH), 2.16−2.26 (m, 1 H, C*H*$_2$−CH=), 2.43−2.55 [m, 2 H, C(OH)−C*H*$_2$], 2.86 and 3.05 (AB, *J* = 14.1 Hz, C*H*$_2$-Ar), 3.29 (d, *J* = 4.8 Hz, 3 H, NMe), 5.83−5.87 (m, 1 H, CH=CH), 6.00−6.04 (m, 1 H, CH=CH), 7.17−7.33 (m, 3 H, Ar-H), 7.68−7.71 (m, 1 H, Ar-H), 9.96 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 31.2, 33.4 (NMe), 40.1, 42.9, 87.2, 127.0, 129.2, 130.6, 131.2, 145.0, 135.2, 135.9, 200.9 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3290 (ν_{OH}), 3204, 2978, 2932, 1586, 1464, 1370, 1142 ($\nu_{C=S}$), 1068, 1040 cm^{-1}. MS (EI): *m*/*z* (%) = 247 (6) [M$^+$], 229 (45), 214 (21), 196 (91), 165 (82), 131 (70), 116 (100), 83 (86). $C_{14}H_{17}NSO$ (247.36): calcd. C 67.98, H 6.93, S 12.96; found C 67.83, H 6.99, S 12.99.

Compound 36: R_f = 0.1 (petroleum ether/ethyl acetate, 7:3). M.p. 134 °C. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.59−1.68 (m, 1 H, C*H*$_2$−CH$_2$−C=O), 1.79−1.91 (m, 1 H, C*H*$_2$−CH$_2$−C=O), 2.01−2.31 (2 m, 4 H, CH$_2$−C=O), 2.53−2.58 (m, 1 H, C*H*−CH$_2$−Ar−H), 2.83−2.87 (m, 2 H, C*H*$_2$-Ar), 3.30 (d, *J* = 4.9 Hz, 3 H, NMe), 7.17−7.32 (m, 4 H, Ar-H), 7.66 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 29.7 (*C*H$_2$−CH$_2$−C=O), 33.4 (NMe), 38.5, 38.6, 38.8, 45.5 (C*H*$_2$-Ar), 126.9, 127.1, 129.4, 130.4, 136.2, 144.3, 202.5 (C=O), 219.9 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3168 cm^{-1}, 3052, 2970, 1738 ($\nu_{C=O}$), 1556, 1362, 1142 ($\nu_{C=S}$), 1038 cm^{-1}. MS (EI): *m*/*z* (%) = 247 (18) [M$^+$], 215 (10), 190 (38), 176 (100), 165 (41), 143 (42), 117 (42), 83 (45). $C_{14}H_{17}NSO$ (247.36): calcd. C 67.98, H 6.93, N 6.93; found C 68.02, H 6.95, N 6.95.

Compound 37: R_f = 0.7 (petroleum ether/ethyl acetate, 7:3). M.p. 114 °C. ^{1}H NMR: δ = 1.98−2.11 (m, 2 H, CH_2), 2.30−2.60 (m, 2 H, CH_2), 3.09 and 3.33 (AB, *J* = 14.7 Hz, C*H*$_2$-Ar), 3.34 (s, 3 H, NMe), 5.65−5.69 (m, 1 H, CH=CH), 5.88−5.92 (m, 1 H, CH=CH), 7.12−7.15 (m, 1 H, Ar-H), 7.30−7.34 (m, 2 H, Ar-H), 7.98−8.01 (m, 1 H, Ar-H) ppm. ^{13}C NMR: δ = 31.6, 39.0, 40.5 (NMe), 44.8, 60.9, 126.6, 127.7, 130.0, 130.5, 133.5, 134.0, 135.0, 136.9, 161.1 (*C*=NMe) ppm. IR (KBr): $\tilde{\nu}$ = 2922 cm^{-1}, 2360, 1584, 1450, 1386, 1010, 930, 764, 746 cm^{-1}. MS (EI): *m*/*z* (%) = 229 (65) [M$^+$], 196 (82), 165 (25), 116 (100), 89 (38). HRMS calcd. for $C_{14}H_{15}NS$: 229.0925; found 229.0929.

2-(2-Hydroxypropyl)-*N*-isopropylthiobenzamide (38): The general procedure was applied with *N*-isopropyl-2-methylthiobenzamide (**5**, 172 mg, 0.89 mmol) in THF (6 mL), *s*BuLi (1.7 mL of a 1.3 M solu-

tion in cyclohexane, 2.22 mmol) and acetaldehyde (502 μL, 8.91 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (6:4) afforded 194 mg (yield: 88%) of compound **38**. After crystallization from chloroform/hexane, a white solid was obtained. M.p. 140 °C. R_f = 0.4 (petroleum ether/ethyl acetate, 6:4). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.28 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.33 (d, *J* = 6.1 Hz, 3 H, C(OH)*Me*), 1.37 (d, *J* = 6.5 Hz, 3 H, NCH*Me*$_2$), 2.38 (d, *J* = 3.1 Hz, 1 H, OH), 2.67−2.79 (m, 2 H, C*H*$_2$-Ar), 4.08−4.17 [m, 1 H, C*H*(OH)], 4.72−4.80 (m, 1 H, NC*H*Me), 7.13−7.33 (m, 3 H, Ar-H), 7.57−7.61 (m, 1 H, Ar-H), 9.27 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 21.6, 21.7 (CH*Me*$_2$), 24.7, 41.2, 48.5 (*C*HMe$_2$), 70.5, 126.8, 129.6, 129.8, 129.9, 133.6, 144.7, 198.3 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3316 (ν_{OH}), 3184, 3032, 2968, 1566, 1458, 1420, 1122 ($\nu_{C=S}$), 1102 cm^{-1}. MS (EI): *m*/*z* (%) = 237 (9) [M$^+$], 204 (77), 117 (20), 58 (38), 43 (100). $C_{13}H_{19}NSO$ (237.36): calcd. C 65.78, H 8.07, N 5.90, S 13.51; found C 66.06, H 7.96, N 6.04, S 13.32.

2-(2-Hydroxy-3-methylbutyl)-*N*-isopropylthiobenzamide (39): The general procedure was applied with *N*-isopropyl-2-methylthiobenzamide (**5**, 171 mg, 0.87 mmol) in THF (6 mL), *s*BuLi (1.7 mL of a 1.3 M solution in cyclohexane, 2.22 mmol) and isobutyraldehyde (130 μL, 1.33 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 223 mg (yield: 80%) of compound **39**. After crystallization from chloroform/hexane, a yellow solid was obtained. M.p. 116 °C. R_f = 0.2 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.02 [d, *J* = 6.6 Hz, 6 H, CH(OH)CH*Me*$_2$], 1.29 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.38 (d, *J* = 6.6 Hz, 3 H, NCH*Me*$_2$), 1.74−1.85 [m, 1 H, CH(OH)C*H*Me$_2$], 2.24 (d, *J* = 3.9 Hz, 1 H, OH), 2.67−2.81 (m, 2 H, C*H*$_2$-Ar) 3.67−3.72 [m, 1 H, C*H*(OH)], 4.70−4.78 (m, 1 H, NC*H*Me$_2$), 7.13−7.33 (m, 3 H, Ar-H), 7.60−7.64 (m, 1 H, Ar-H), 9.31 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 18.2, 19.1, 21.4, 21.7 (NCH*Me*$_2$), 35.0, 36.5, 48.5, 80.1, 126.6, 129.6, 129.8, 130.0, 134.2, 144.8, 198.4 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3321 (ν_{OH}), 3162, 2912, 1543, 1447, 1379, 1161 ($\nu_{C=S}$), 990 cm^{-1}. MS (EI): *m*/*z* (%) = 265 (5) [M$^+$], 232 (10), 204 (23), 135 (17), 118(20), 58 (50), 43 (100). $C_{15}H_{23}NSO$ (265.42): calcd. C 67.88, H 8.73, N 5.28, S 12.08; found C 67.50, H 8.73, N 5.68, S 11.75.

2-(2-Hydroxypropyl)-*N*-phenylthiobenzamide (40): The general procedure was applied with 2-methyl-*N*-phenylthiobenzamide (**6**, 330 mg, 1.45 mmol) in THF (8 mL), *s*BuLi (2.8 mL of a 1.3 M solution in cyclohexane, 3.63 mmol) and acetaldehyde (502 μL, 8.91 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 300 mg (yield: 77%) of compound **40**. After crystallization from chloroform/hexane, a yellow solid was obtained. M.p. 117 °C. R_f = 0.16 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.40 (d, *J* = 6.2 Hz, 3 H, CH-*Me*), 2.21 (d, *J* = 3.6 Hz, 1 H, OH), 2.80−2.98 (m, 2 H, C*H*$_2$-Ar), 4.22−4.30 (m, 1 H, C*H*OH), 7.19−7.46 (m, 6 H, Ar-H), 7.72−7.75 (m, 1 H, Ar-H), 7.97−8.01 (m, 2 H, Ar-H), 10.93 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 24.8 (CH$_2$), 42.4 (Me), 71.0 (CH), 123.2, 126.9, 127.0, 129.2, 129.9, 130.6, 133.0, 139.8, 146.0, 199.0 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3298 (ν_{OH}), 3174, 3128, 3014, 2958, 2924, 1552, 1392, 1116 ($\nu_{C=S}$), 990 cm^{-1}. MS (EI): *m*/*z* (%) = 271 (2) [M$^+$], 238 (59), 222 (49), 117 (39), 71 (100). $C_{16}H_{17}NSO$ (271.38): calcd. C 70.82, H 6.31, N 5.16, S 11.81; found C 70.73, H 6.33, N 5.46, S 11.52.

2-(2-Hydroxy-3-methylbutyl)-*N*-phenylthiobenzamide (41): The general procedure was applied with 2-methyl-*N*-phenylthiobenzamide (**6**, 227 mg, 1.1 mmol) in THF (6 mL), *s*BuLi (1.9 mL of a 1.3 M solution in cyclohexane, 2.5 mmol) and isobutyraldehyde (148 μL, 1.5 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 223 mg (yield: 68%) of compound **41**. After crystallization from chloroform/hexane, a yellow solid was obtained. M.p. 116 °C. R_f = 0.2 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.97 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_2$), 0.99 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_2$), 1.77−1.90 (m, 1 H, C*H*Me$_2$), 2.19 (br. s, 1 H, OH), 2.77−3.02 (m, 2 H, C*H*$_2$-Ar), 3.82−3.87 [m, 1 H, C*H*(OH)], 7.19−7.45 (m, 6 H, Ar-H), 7.74−7.78 (m, 1 H, Ar-H), 7.97−8.01 (m, 2 H, Ar-H), 11.00 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 18.1, 19.0, 34.8, 36.5, 80.3, 123.2, 126.9, 129.2, 129.7, 129.9, 130.7, 133.7, 139.9, 146.0, 199.0 (C=S) ppm. MS (EI): *m*/*z* (%) = 299 (4) [M$^+$], 266 (98), 222 (68), 145 (64), 93 (100), 77 (66). $C_{18}H_{21}NSO$ (299.43): calcd. C 71.20, H 7.07, N 4.68, S 10.71; found C 71.22, H 6.93, N 4.60, S 10.50.

***N*-Methyl-2-(1-methylbut-3-enyl)thiobenzamide (42):** The general procedure was applied with 2-ethyl-*N*-methylthiobenzamide (**7**, 236 mg, 1.32 mmol) in THF (10 mL), *s*BuLi (2.4 mL of a 1.3 M solution in cyclohexane, 3.1 mmol) and allyl iodide (133 μL, 1.45 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (9:1) afforded 139 mg (yield: 48%) of compound **42**. After crystallization from diethyl ether, a white solid was obtained. M.p. 121 °C. R_f = 0.3 (petroleum ether/ethyl acetate, 9:1). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.26 (d, *J* = 6.9 Hz, 3 H, CH*Me*), 2.28−2.45 (2 m, 2 H, CH$_2$), 3.04−3.13 (m, 1 H, CHMe), 3.30 (d, *J* = 4.9 Hz, 3 H, NMe), 4.95−5.01 (m, 2 H, CH=C*H*$_2$), 5.63−5.74 (m, 1 H, C*H*=CH$_2$), 7.16−7.36 (m, 4 H, Ar-H), 7.46 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 22.8 (CH*Me*), 33.1 (NMe), 35.8, 42.9, 116.8, 126.3, 126.9, 129.6, 142.4, 143.9, 137.7, 203.0 (C=S) ppm. MS (EI): *m*/*z* (%) = 219 (5) [M$^+$], 204 (3), 186 (100), 144 (67), 115 (36), 77 (39). $C_{13}H_{17}NS$ (219.35): calcd. C 71.19, H 7.81, N 6.39, S 14.62; found C 71.54, H 7.78, N 6.60, S 14.22.

***N*-Methyl-2-(1-trimethylsilylethyl)thiobenzamide (43):** The general procedure was applied with 2-ethyl-*N*-methylthiobenzamide (**7**, 100 mg, 0.56 mmol) in THF (5 mL), *s*BuLi (945 μL of a 1.3 M solution in cyclohexane, 1.23 mmol) and trimethylsilyl chloride (140 μL, 1.1 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (7:3) afforded 41 mg (yield: 30%) of compound **43**. After crystallization from hexane, a white solid was obtained. M.p. 96 °C. R_f = 0.4 (petroleum ether/ethyl acetate, 7:3). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.00 (s, 9 H, SiMe$_3$), 1.38 (d, *J* = 7.4 Hz, 2 H, CH*Me*), 2.61 (q, *J* = 7.4 Hz, 1 H, C*H*Me), 3.29 (d, *J* = 4.9 Hz, 3 H, NMe), 7.06−7.32 (m, 4 H, Ar), 7.51 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 0.0 (SiMe$_3$), 19.6 (CH*Me*), 27.6 (*C*HMe), 35.4 (NMe), 126.8, 129.0, 130.2, 131.4, 145.2, 145.7, 205.6 (C=S) ppm. MS (EI): *m*/*z* (%) = 251 (19) [M$^+$], 236 (22), 178 (100), 146 (33).

2-(2-Hydroxy-1-methylpropyl)-*N*-methylthiobenzamide (44): The general procedure was applied with 2-ethyl-*N*-methylthiobenzamide (**7**, 469 mg, 2.62 mmol) in THF (20 mL), *s*BuLi (5.1 mL of a 1.3 M solution in cyclohexane, 6.55 mmol) and acetaldehyde (230 μL, 3.93 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. The crude product contained two diastereoisomers (*dr* = 57:43). Purification by silica gel chromatography with petroleum ether/ethyl acetate (7:3) afforded 415 mg (yield: 71%) of compound **44** as a white solid.

Major Diastereoisomer: White solid. M.p. 122 °C. R_f = 0.4 (petroleum ether/ethyl acetate, 7:3). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.18 (d, *J* = 6.9 Hz, 3 H, CH*Me*), 1.33 (d, *J* = 6.0 Hz, 3 H, CH(OH)*Me*), 2.16 (d, *J* = 3.2 Hz, 1 H, OH), 2.84−2.91 (m, *J* = 6.9 Hz, 1 H, C*H*Me), 3.28 (d, *J* = 4.8 Hz, 3 H, NMe), 3.80−3.87 (m, *J* = 6.0 Hz, 1 H, C*H*OH), 7.17−7.56 (m, 4 H, Ar-H), 9.28 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 19.3 (CH*Me*), 22.6, 33.3 (NMe), 42.9, 74.9, 126.0, 126.7, 129.3, 130.0, 139.9, 144.4, 201.5 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3334 (ν_{OH}), 3214, 3068, 2966, 1560, 1456, 1366, 1252, 1142 ($\nu_{C=S}$), 752 cm^{-1}. MS (EI): *m*/*z* (%) = 223 (10) [M$^+$], 190 (100), 178 (44), 146 (99)131 (55), 77 (38). $C_{12}H_{17}NSO$ (223.34): calcd. C 64.54, H 7.67, N 6.27, S 12.75; found C 64.32, H 8.12, N 5.92, S 12.53.

Minor Diastereoisomer: White solid. R_f = 0.2 (petroleum ether/ethyl acetate, 7:3). M.p. 113 °C. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 1.17 (d, *J* = 6.4 Hz, 3 H, CH*Me*), 1.24 [d, *J* = 6.1 Hz, 3 H, CH(OH)*Me*], 1.87 (s, 1 H, OH), 3.20−3.29 (m, *J* = 6.4 Hz, 1 H, C*H*Me), 3.28 (d, *J* = 4.8 Hz, 3 H, NMe), 4.00−4.05 (m, *J* = 6.1 Hz, 1 H, C*H*OH), 7.17−7.56 (m, 4 H, Ar-H), 9.28 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 18.0 (CH*Me*), 20.0, 33.4 (NMe), 40.9, 72.4, 126.7, 128.1, 128.6, 129.1, 138.0, 144.8, 202.1 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3276 (ν_{OH}), 3054, 2966, 1544, 1436, 1360, 1256, 1144 ($\nu_{C=S}$), 764 cm^{-1}. MS (EI): *m*/*z* (%) = 223 (2) [M$^+$], 190 (100), 172 (33), 144 (11), 131 (22), 77 (19). $C_{12}H_{17}NSO$ (223.34): calcd. C 64.54, H 7.67, N 6.27, found C 64.15, H 7.64, N 6.68.

2-(2-Hydroxy-1,3-dimethylbutyl)-*N*-methylthiobenzamide (45): The general procedure was applied with 2-ethyl-*N*-methylthiobenzamide (**7**, 207 mg, 1.15 mmol) in THF (10 mL), *s*BuLi (2.1 mL of a 1.4 M solution in cyclohexane, 2.89 mmol) and isobutyraldehyde (341 μL, 3.46 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. The crude product contained two diastereoisomers (*dr* = 50:50). Purification by silica gel chromatography with petroleum ether/ethyl acetate (6:4) afforded 221 mg (yield: 73%) of compound **45** as a white solid.

First Diastereoisomer: White solid. R_f = 0.3 (petroleum ether/ethyl acetate, 6:4). M.p. 150 °C. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.89 (d, *J* = 6.6 Hz, 3 H, CH*Me*$_2$), 0.90 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_2$), 1.27 (d, *J* = 6.9 Hz, 3 H, CH*Me*), 1.43 (d, *J* = 5.3 Hz, 1 H, OH), 1.54−1.66 (m, *J* = 6.6, 6.8 Hz, 1 H, C*H*Me$_2$), 3.30 (d, *J* = 4.9 Hz, 3 H, NMe), 3.33−3.49 (m, 2 H, C*H*OH + C*H*Me), 7.16−7.36 (m, 4 H, Ar-H), 7.50 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 15.6, 18.3 (CH*Me*$_2$), 20.3 (CH*Me*), 31.2 (*C*HMe$_2$), 33.3 (NMe), 38.1 (*C*HMe), 80.9 (*C*H-OH), 126.6, 127.2, 128.2, 129.4, 141.2, 144.1, 202.9 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3462 (ν_{OH}), 3170, 3030, 2958, 1540, 1438, 1386, 1364, 1248 ($\nu_{C=S}$), 1060, 1046, 1014 cm^{-1}. MS (EI): *m*/*z* (%) = 251 (1) [M$^+$], 233 (11), 218 (26), 190 (100), 146 (42), 77 (16). $C_{14}H_{21}NSO$ (251.39): calcd. C 66.89, H 8.42, N 5.57, O 6.36, S 12.75; found C 66.83, H 8.56, N 5.51, O 6.66, S 12.45.

Second Diastereoisomer: White solid. R_f = 0.6 (petroleum ether/ethyl acetate, 6:4). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.88 (d, *J* = 6.8 Hz, 3 H, CH*Me*$_2$), 1.01 (d, *J* = 6.9 Hz, 3 H, CH*Me*$_2$), 1.13 (d, *J* = 6.8 Hz, 3 H, CH*Me*), 1.98−2.10 (m, 1 H, C*H*Me$_2$), 2.14 (br. s, 1 H, OH), 3.02−3.15 (m, 1 H, C*H*Me), 3.54−3.60 (m, 1 H, C*H*OH), 3.24 (d, *J* = 4.8 Hz, 3 H, NMe), 7.15−7.60 (m, 4 H, Ar-H), 9.54 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 13.7, 18.7 (CH*Me*$_2$), 20.9 (CH*Me*), 29.4 (*C*HMe$_2$), 33.5 (NMe), 37.9 (*C*HMe), 82.5 (*C*HOH), 126.0, 126.5, 129.6, 130.0, 140.2, 144.2, 201.2 (C=S) ppm. MS (EI): *m*/*z* (%) = 251 (2) [M$^+$], 233 (6), 218 (18), 190 (100), 146 (97), 77 (32).

2-[1-(1-Hydroxycyclopent-2-enyl)ethyl]-*N*-methylthiobenzamide (46): The general procedure was applied with 2-ethyl-*N*-methylthiobenzamide (**7**, 316 mg, 1.76 mmol) in THF (12 mL), *s*BuLi (3.4 mL of a 1.3 M solution in cyclohexane, 4.4 mmol) and 2-cyclopentenone (200 μL, 2.29 mmol). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. The crude product contained two diastereoisomers (*dr* = 81:19). Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 211 mg (yield: 46%) of compound **46** as a white solid. After crystallization from chloroform/pentane, the major diastereoisomer was obtained pure as a white solid. M.p. 147 °C. R_f = 0.4 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ =1.21 (d, *J* = 7.1 Hz, 3 H, Me), 1.66−1.72 (m, 1 H, C*H*$_2$−CH=CH), 2.00 (s, 1 H, OH), 2.40−2.45 (m, 1 H, C*H*$_2$−CH=CH), 2.54−2.61 (m, 2 H, C*H*$_2$−CHOH), 3.31 (d, *J* = 4.8 Hz, 3 H, NMe), 3.36 (q, *J* = 7.1 Hz, 1 H, C*H*Me), 5.63−5.65 (m, 1 H, CH$_2$−C*H*=CH), 6.04−6.06 (m, 1 H, CHOH−C*H*=), 7.23−7.58 (m, 4 H, Ar-H), 9.84 (br. s, 1 H, NH) ppm. ^{13}C NMR: δ = 17.8 (CH*Me*), 31.8, 33.3 (N*Me*), 39.3, 43.3, 90.9, 126.8, 127.1, 129.4, 130.0, 132.4, 137.2, 138.1, 144.9, 145.0, 201.6 (C=S) ppm. MS (EI): *m*/*z* (%) = 261 (6) [M$^+$], 229 (45), 214 (21), 196 (91), 165 (82), 131(70), 116 (100), 83 (86).

General Procedure for the Double Deprotonation of Thionaphthamides 13, 15 and 16 and Treatment with Electrophiles (Compounds 47−52): A solution of thioamides **13**, **15** or **16** (1 equiv.) in THF was cooled to −78 °C. A solution of *sec*-butyllithium in cyclohexane (2−5 equiv.) was then added dropwise. The reaction mixture was stirred at −78 °C for 1−2 h. The appropriate electrophile (1−7 equiv.) was added dropwise, and the resulting mixture was stirred at −78 °C for 30 min to 1 h. 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 the residue was purified by silica gel chromatography with petroleum ether/ethyl acetate as eluent.

Methyl 2-Ethyl-*N*-methyl-1-naphthalenecarbimidothioate (47): The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 300 mg, 1.39 mmol), *s*BuLi (2.68 mL of a 1.3 M solution in cyclohexane, 3.43 mmol), methyl iodide (173 μL, 2.78 mmol) and THF (15 mL). Reaction time after addition of base: 1 h; after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 294 mg (yield: 87%) of compound **47** as a colourless oil. R_f = 0.5−0.6 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 24:76. ^{1}H NMR [(*E*) isomer]: δ = 1.26 (t, *J* = 7.5 Hz, 3 H, CH$_2$*Me*), 2.49 (s, 3 H, SMe), 2.72 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$Me), 2.97 (s, 3 H, NMe), 7.38−7.84 (m, 6 H, Ar) ppm. ^{1}H NMR [(*Z*) isomer]: δ = 1.29 (t, *J* = 7.5 Hz, 3 H, CH$_2$Me), 1.74 (s, 3 H, SMe), 2.75 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$Me), 3.51 (s, 3 H, NMe), 7.38−7.84 (m, 6 H, Ar) ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 13.1, 14.1 (SMe), 15.0, 15.1 (CH$_2$*Me*), 26.2, 26.3 (*C*H$_2$Me), 40.1, 40.6 (NMe), 124.3, 124.7, 125.3, 125.4, 126.5, 126.6, 126.7, 126.8, 127.9, 128.0, 128.8, 129.2, 129.5, 130.9, 131.7, 132.5, 138.5, 166.0, 167.2 (C=N) ppm. MS (EI): *m*/*z* (%) = 244 (74) [M + H]$^+$, 196 (100), 182 (19), 105 (4). HRMS calcd. for $C_{15}H_{18}NS$: 244.1161; found 244.1160.

***N*-Methyl-2-(1-trimethylsilylmethyl)-1-thionaphthamide (48):** The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 962 mg, 4.47 mmol), *s*BuLi (8.7 mL of a 1.3 M solution in cyclohexane, 11.1 mmol), trimethylsilyl chloride (1.5 mL, 11.1 mmol) and THF (25 mL). Reaction time after addition of base: 1 h; after addition of electrophile: 30 min. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) af-

forded 1.171 g (yield: 91%) of compound **48**. After crystallization from hexane, a white solid was obtained. M.p. 122 °C. (*Z*)/(*E*) ratio = 100:0. ^{1}H NMR: δ = 0.08 (s, 9 H, $SiMe_3$), 2.17 and 2.41 (AB, *J* = 13.7 Hz, 2 H, CH_2-Ar), 3.06 (d, *J* = 4.9 Hz, 3 H, NMe), 7.10−7.71 (m, 7 H, Ar + NH) ppm. ^{13}C NMR: δ = 0.7, 1.3, 1.5 ($SiMe_3$), 25.0 (CH_2), 33.3 (NMe), 125.2, 125.4, 127.3, 128.4, 128.6, 128.7, 130.6, 131.6, 134.6, 138.1, 202.8 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3280 cm^{-1}, 3044, 1520, 1270, 1142 ($\nu_{C=S}$), 846, 822 cm^{-1}. MS (EI): *m*/*z* (%) = 287 (29) [M$^+$], 272 (17), 214 (100), 182 (17), 73 (30). $C_{16}H_{21}NSSi$ (287.50): calcd. C 66.85, H 7.36, N 4.87, Si 9.85, S 11.15; found C 66.63, H 7.21, N 4.81, Si 10.10, S 11.11.

2-(2-Hydroxypropyl)-*N*-methyl-1-thionaphthamide (49): The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 1.503 g, 6.98 mmol), *s*BuLi (12.3 mL of a 1.3 M solution in cyclohexane, 16.0 mmol), distilled acetaldehyde (1.18 mL, 20.9 mmol) and THF (50 mL). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (7:3) afforded 1.461 g (yield: 81%) of compound **49**. After crystallization from diethyl ether, a white solid was obtained. M.p. 143 °C. R_f = 0.3 and 0.4 (petroleum ether/ethyl acetate, 7:3). (*Z*)/(*E*) ratio = 64:36. ^{1}H NMR [(*Z*) isomer]: δ = 1.11 (d, *J* = 6.1 Hz, 3 H, CH*Me*), 2.42−2.89 (m, 2 H, CH_2−Ar−H), 3.06 (d, *J* = 4.6 Hz, 3 H, NMe), 3.83−3.90 (m, 1 H, CH), 7.06−7.96 (m, 6 H, Ar-H), 7.51 (br. s, 1 H, NH) ppm. ^{1}H NMR [(*E*) isomer]: δ = 1.02 (d, *J* = 6.1 Hz, 3 H, CH-Me), 2.42−2.89 (m, 2 H, CH_2−Ar−H), 3.13 (d, *J* = 4.6 Hz, 3 H, NMe), 3.83−3.90 (m, 1 H, CH), 7.06−7.96 (m, 6 H, Ar-H), 8.22 (br. s, 1 H, NH) ppm. ^{13}C NMR [(*Z*) isomer]: δ = 24.3, 32.4 (NMe), 41.9, 68.8, 125.7, 126.6, 127.7, 127.9, 128.4, 128.7, 130.0, 131.4, 132.2, 140.4, 199.9 (C=S) ppm. ^{13}C NMR [(*E*) isomer]: δ = 24.0, 32.7 (NMe), 42.3, 68.6, 124.9, 125.8, 126.9, 127.8, 128.3, 128.6, 130.0, 130.7, 132.1, 140.1, 199.9, 201.1 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3300 (ν_{OH}), 3210, 2986, 1558, 1506, 1454, 1374, 1114 ($\nu_{C=S}$), 1084, 1046. cm^{-1}. MS (EI): *m*/*z* (%) = 259 (17) [M$^+$], 226 (100), 214 (34), 181 (15), 166 (16), 152 (7). $C_{15}H_{17}NSO$ (259.37): calcd. C 69.46, H 6.61, N 5.40, O 6.17, S 12.36; found C 69.12, H 6.51, N 5.34, O 6.44, S 12.08.

2-(2-Hydroxy-3-methylbutyl)-*N*-methyl-1-thionaphthamide (50): The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 304 mg, 1.41 mmol), *s*BuLi (3.3 mL of a 1.3 M solution in cyclohexane, 4.24 mmol), isobutyraldehyde (386 μL, 4.24 mmol) and THF (12 mL). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (6:4) afforded 288 mg (yield: 71%) of compound **50**. After crystallization from ethyl acetate/hexane, white crystals were obtained. M.p. 148 °C. R_f = 0.4−0.5 (petroleum ether/ethyl acetate, 6:4). (*Z*)/(*E*) ratio = 67:33. ^{1}H NMR [(*Z*) isomer]: δ = 1.00 (2d, *J* = 7.2 Hz, 6 H, CMe_2), 1.64 (d, *J* = 3.7 Hz, 1 H, OH), 1.71−1.91 (m, 1 H, C*H*Me$_2$), 2.72−2.93 (m, 2 H, CH_2-Ar), 3.37 (d, *J* = 4.9 Hz, 3 H, NMe), 3.76−3.85 (m, 1 H, C*H*OH), 7.12−8.20 (m, 6 H, Ar-H), 9.22 (br. s, 1 H, NH) ppm. ^{1}H NMR [(*E*) isomer]: δ = 1.01 (d, *J* = 7.7 Hz, 6 H, CMe_2), 1.53 (d, *J* = 3.7 Hz, 1 H, OH), 1.71−1.91 (m, 1 H, C*H*Me$_2$), 2.72−2.93 (m, 2 H, CH_2-Ar), 3.39 (d, *J* = 4.9 Hz, 3 H, NMe), 3.55−3.65 (m, 1 H, C*H*OH), 7.12−8.20 (m, 6 H, Ar-H) ppm. ^{13}C NMR [(*Z*) isomer]: δ = 17.7, 18.9, 33.0 (NMe), 34.7, 36.9, 78.2, 126.1, 126.2, 127.0, 127.1, 128.1, 129.3, 130.7, 131.2, 132.7, 141.1, 200.3 (C=S) ppm. ^{13}C NMR [(*E*) isomer]: δ = 17.4, 18.3, 33.3 (NMe), 34.9, 37.6, 78.1, 125.1, 126.2, 127.4, 127.9, 128.4, 129.2, 130.0, 132.5, 133.0, 140.5, 202.1 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3320 (ν_{OH}), 3192, 3054, 2958, 2922, 1554, 1366, 1140 ($\nu_{C=S}$), 1020, 810 cm^{-1}. MS (EI): *m*/*z* (%) = 287 (16) [M$^+$], 254 (86), 226 (100), 215 (67), 185 (49), 74 (44). $C_{17}H_{21}NSO$ (287.42): calcd. C 71.04, H 7.36, N 4.87, O 5.57, S 11.15; found C 70.43, H 7.48, N 4.66, O 5.89, S 11.06.

2-(1-Hydroxycyclopent-2-enylmethyl)-*N*-methyl-1-thionaphthamide (51): The general procedure was applied with 2,*N*-dimethyl-1-thionaphthamide (**13**, 166 mg, 0.77 mmol), *s*BuLi (1.4 mL of a 1.3 M solution in cyclohexane, 1.9 mmol), 2-cyclopentenone (80 μL, 0.93 mmol) and THF (10 mL). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (8:2) afforded 136 mg (yield: 60%) of compound **51**. After crystallization from ethyl acetate/hexane, a white solid was obtained. M.p. 130 °C. R_f = 0.1 (petroleum ether/ethyl acetate, 8:2). (*Z*)/(*E*) ratio = 64:36. ^{1}H NMR [(*Z*) + (*E*) isomers]: δ = 1.74−2.22 (2 m, 2 H, CH_2−CH=), 2.23 (s, 1 H, OH), 2.34−2.25 [m, 2 H, C(OH)−CH_2], 2.95−3.24 (m, 2 H, CH_2−Ar), 3.43 (d, *J* = 4.8 Hz, 3 H, NMe), 5.72−6.03 [2 m, 2 H, CH(OH)−C*H*= and CH_2−C*H*=], 7.32−8.12 (m, 6 H, Ar-H), 8.52 [br. s, 1 H, NH, (*E*)], 9.21 [br. s, 1 H, NH, (*Z*)] ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 31.1, 31.4, 32.9, 33.0 (NMe), 39.7, 40.7, 43.3, 43.7, 86.4, 86.8, 126.0, 126.1, 126.2, 126.4, 127.0, 127.1, 128.0, 128.1, 128.4, 128.5, 128.6, 128.7, 129.7, 130.8, 132.8, 134.9, 135.9, 141.6, 200.5, 201.4 (C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3280 (ν_{OH}), 3158, 3054, 2956, 2930, 1540, 1358, 1146 ($\nu_{C=S}$), 754 cm^{-1}. MS (EI): *m*/*z* (%) = 297 (6) [M$^+$], 237 (15), 194 (59), 152 (44), 110 (59), 85 (100). $C_{18}H_{19}NSO$ (297.42): calcd. C 72.69, H 6.44, N 4.71, S 10.78; found C 72.28, H 6.52, N 4.96, S 10.81.

2-(2-Hydroxy-3-methylbutyl)-*N*-phenyl-1-thionaphthamide (52): The general procedure was applied with 2-methyl-*N*-phenyl-1-thionaphthamide (**15**, 233 mg, 0.84 mmol), *s*BuLi (1.5 mL of a 1.3 M solution in cyclohexane, 2.1 mmol), isobutyraldehyde (250 μL, 2.52 mmol) and THF (10 mL). Reaction time after addition of base: 2 h; after addition of electrophile: 1 h. Purification by silica gel chromatography with petroleum ether/ethyl acetate (9:1) afforded 191 mg (yield: 65%) of compound **52**. After crystallization from toluene, yellow crystals were obtained. M.p. 145 °C. R_f = 0.1−0.2 (petroleum ether/ethyl acetate, 9:1). (*Z*)/(*E*) ratio = 71:29. ^{1}H NMR [(*Z*) + (*E*) isomers]: δ = 0.96−1.01 (3 d, *J* = 7.6 Hz, 6 H, CH−Me_2), 1.74−1.86 (m, 1 H, C*H*−Me$_2$), 1.94 (br. s, 1 H, OH), 2.89−3.01 (m, 2 H, CH_2−Ar−H), 3.77−3.81 (m, 1 H, CHOH), 6.98−8.29 (m, 11 H, Ar-H), 9.23 [br. s, 1 H, NH, (*E*)], 10.42 [br. s, 1 H, NH, (*Z*)] ppm. ^{13}C NMR [(*Z*) + (*E*) isomers]: δ = 17.6, 17.8, 17.9, 18.6, 34.3, 34.6, 36.8, 37.1, 77.5, 78.5, 122.8, 123.0, 125.6, 125.9, 126.7, 126.8, 126.9, 127.2, 127.3, 127.8, 127.9, 128.0, 128.9, 129.1, 130.3, 130.4, 132.4, 139.2, 141.7, 197.8, 199.4

Table 6. Crystal data and refinement for compound **13**

Empirical formula	$C_{13}H_{13}NS$
Formula mass	215.32
Crystal system	monoclinic
Space group	$P12_1/c1$
a [Å]	9.566 (13)
b [Å]	10.031 (4)
c [Å]	12.854 (3)
β [°]	100.58
V [Å^3]	1212.6 (6)
Z	4
T [K]	293
$\rho_{calcd.}$ [g cm^{-3}]	2.359
μ(Mo-K_α) [mm^{-3}]	0.7107
R	0.041
wR	0.043

(C=S) ppm. IR (KBr): $\tilde{\nu}$ = 3472 (ν_{OH}), 3312, 3248, 3054, 2956, 1598, 1556, 1496, 1380, 1130 ($\nu_{C=S}$) cm^{-1}. MS (EI): *m*/*z* (%) = 349 (8) [M^+], 316 (100), 288 (37), 276 (31), 223 (27), 43 (53).

X-ray Crystal Data for 13: See Table 6. CCDC-180819 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

This collaborative project was generously supported by the programme "Réseau Interrégional de Chimie Organique Fine (RINCOF)" of the "Contrat de Plan Interrégional du Grand Bassin Parisien", to which we are grateful. Discussions and suggestions from our partners at Rouen (IRCOF) Profs. Guy Quéguiner, Nelly Plé and Alain Turck are gratefully acknowledged.

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Received March 8, 2002
[O02131]