The Synthesis and Configurational Stability of Enantioenriched α-Thioallyllithium Compounds and the Stereochemical Course of Their Electrophilic Substitution

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Dedicated to Professor Volker Jäger on the occasion of his 60th birthday

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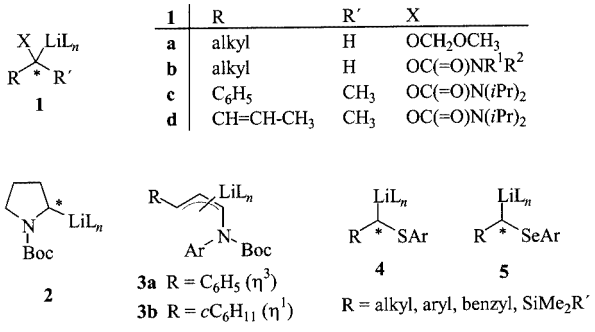
Deprotonation of enantioenriched *S*-allyl *N*-monoalkylmonothiocarbamates furnished the corresponding chiral lithium compounds. The α-thioallyllithium compounds **9** and **25** were found to be configurationally stable in THF solutions at –78 °C. These represent the first configurationally stable α-thio-substituted allyllithium compounds, and they can be utilized in asymmetric synthesis. Alkylations proceeded with stereoinversion or in an *anti*-S_E' process, while addition to carbonyl compounds took place in a *syn*-S_E' process. Hydroxyalkylation products were employed as starting material for Ni^0-catalyzed cross-coupling reactions.

Introduction

Chiral, nonracemic α-heteroatom-substituted alkyllithium compounds are valuable chiral carbanion equivalents,[1] as long as they react in a stereodefined manner. Electrophilic substitution on these d^1-synthons is generally stereospecific. Consequently, configurational stability is desirable for application in asymmetric synthesis, provided that the carbanionic center is the sole source of chiral information (no further chiral centers in the substrate or any chiral ligand). Some configurationally stable α-oxy- and α-amino-substituted organolithium compounds of this type are known. The enantioenriched 1-(alkoxymethoxy)alkyllithium compound **1a** (Scheme 1) was prepared in 1980 and shows configurational stability below −40 °C.[2] Lithium cation chelating *N*,*N*-dialkylcarbamoyloxy groups give configurationally stable α-oxy-substituted alkyllithium compounds **1b**[3,4] and − even more striking − configurationally stable *sec*-benzyl- and *sec*-allyllithium species **1c**[5] and **1d**,[6] respectively (Scheme 1).[7]

The *N*-Boc-α-aminoalkyllithium derivative **2**[8] and the *N*-Boc-α-aminoallyllithium derivatives **3a** and **3b**[9] show similar properties (Scheme 1).[4,10] In sharp contrast, the presence of α-thio[11−14] and α-seleno[13,15] substituents at the carbanionic center of alkyllithium derivatives such as **4** and **5** (Scheme 1) results in rapid enantiomerization even at temperatures as low as −78 °C and below.[16] How should a potentially configurationally stable thioallyllithium compound be designed? This question can be addressed on the basis of the mechanism of the enantiomerization, which has to be suppressed. NMR and reactivity studies with racemic samples of **4** and **5** and other compounds, performed by R. W. Hoffmann et al. and H. J. Reich et al., together with theoretical studies,[17] indicate that the interconversion of the enantiomers here is different from those of other chiral organolithium compounds. The process of enantiomerization from **6** to *ent*-**6** can be divided into three single steps: A) the dissociation of the ion-pair, B) the inversion of the carbanionic center, and C) rotation of the bond between the carbanionic center and the heteroatom (Scheme 2).[7]



Scheme 1. Some chiral organolithium compounds **1**−**5**

For α-thio- and α-seleno-substituted carbanions, step C possesses the highest activation barrier and therefore be-

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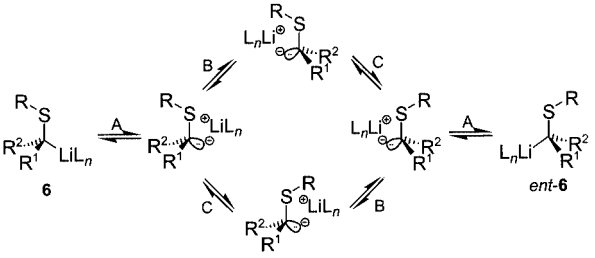
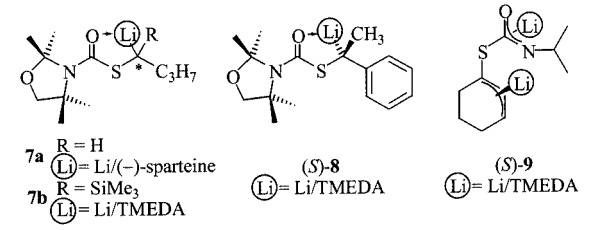


Scheme 2. Mechanism of enantiomerization

comes the rate-determining step for the enantiomerization. Sterically demanding groups in the vicinity of the heteroatom hinder the torsion of the hyperconjugated S−C$^-$ bond and consequently increase the configurational stability; we assume for these investigations that a branched carbanionic center and a bulky protecting group for the sulfhydryl group should result in a configurationally stable organolithium compound. Evidence in support of this assumption is provided by the configurational stability of the enantioenriched α-lithiated thiocarbamate **7b**.[18] The α-branched compound **7b** was prepared by deprotonation of its corresponding thiocarbamate, which was in turn prepared by silylation of the unbranched and configurationally labile (−)-sparteine complex **7a**.[18] The essentially enantiopure α-thio carbanion derivative (*S*)-**8** was synthesized and applied in electrophilic substitutions.[19] Encouraged by these results, we designed and synthesized the enantioenriched α-thio-substituted species **9**, in which the double bond allows for further transformations (Scheme 3).[20]



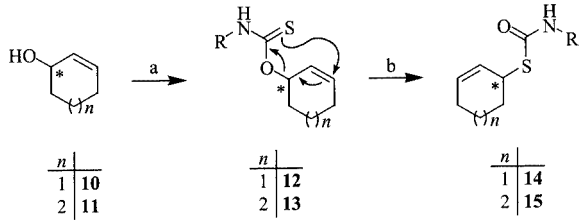
Scheme 3. Lithiated monothiocarbamates

There is still only a small amount known about the stereochemical course of electrophilic substitution reactions of α-thio-substituted lithium compounds. In this investigation some emphasis was therefore put on that point.

Results and Discussion

Preparation of *S*-Allyl *N*-Monoalkylmonothiocarbamates

Because of the unpleasant properties of *sec*-allyl thiols we were in favor of a synthetic approach from *sec*-allyl alcohols, such as **10**, towards the starting thiocarbamates. Addition of sodium alkoxides to isothiocyanates in THF furnished monothiocarbamic acid *O*-esters **12**−**13** in high yields (Scheme 4, Table 1).[21] *N*-Methyl-, *N*-isopropyl-, and *N*-*tert*-butyl-substituted carbamoyl moieties were fused to cyclohex-2-en-1-ol (**10**) or cyclohept-2-en-1-ol (**11**) in this way.[22] The rearrangement of thiocarbamic acid *O*-esters into the corresponding *S*-esters is a well-investigated reaction[21,23] for achiral or racemic substrates.[24] Here the rearrangement of the *O*-esters **12**−**13** into the corresponding *S*-esters **14**−**15** was achieved by heating in a neat state (Scheme 4),[21] with flash column chromatography (FCC) then providing the white crystalline monothiocarbamates. Yields are given in Table 1.



Scheme 4. Synthesis of *S*-allyl *N*-monoalkylmonothiocarbamates; reagents and conditions: (a) i) NaH, THF, 0 °C; ii) R−NCS, THF, 0 °C; iii) H_3O^+; (b) neat, 105−150 °C

We focussed our investigations on cyclic substrates because the reactions of acyclic thiocarbamates in lithiation experiments proved to be more complicated, due to the formation of (*E*)/(*Z*)-isomeric substitution products.

Enantioenriched *sec*-allyl alcohols are accessible by various routes, and in this two-step sequence the enantioenriched alcohols **10** and **11** were employed. For the preparation of enantioenriched *sec*-allyl thiols only two procedures have been published, both involving a route to cyclohex-2-ene-1-thiol.[25,26] Optically active cyclohex-2-en-1-ol (**10**) with an *ee* of up to 96% (*e.r.* = 98:2) was prepared either by kinetic resolution of a racemic cyclohexenol precursor, through lipase-catalyzed enantioselective transesterification[27] [(*R*) form], or by base-mediated rearrangement of cyclohexene oxide with chiral lithium amide bases[28] [(*R*) and (*S*) forms]. (*R*)-Cyclohept-2-en-1-ol (**11**) was prepared by kinetic resolution of *rac*-**11** by Sharpless asymmetric epoxidation.[29] In our hands, epoxidation at −30 °C yielded 42% of enantiopure (*R*)-**11**; Sharpless et al. had reported 80% *ee* (*e.r.* = 90:10) when performing the reaction at −20 °C and applying a slightly lower concentration.[29c]

Thermal rearrangement of enantioenriched *O*-(2-cyclohexenyl) *N*-isopropylthiocarbamate (**12b**) at 105 °C for 3 h produced the optically active *S*-(2-cyclohexenyl) *N*-isopropylthiocarbamate (**14b**) with smooth chirality transfer of 96−97% (Table 1, Entries 3 and 4). The rearrangement of cycloheptenyl *N*-isopropylthiocarbamate (*R*)-**13**, prepared from enantiopure alcohol (*R*)-**11** in 87% yield, at 145 °C for 4.5 h gave the corresponding thiocarbamate (*S*)-**15** in 74% yield with somewhat lower enantiospecificity (91% *ee*, *e.r.* = 95.5:4.5, Table 1, Entry 8). However, the rearrangement of *N*-*tert*-butylthiocarbamate (*S*)-**12c**, prepared from (*S*)-cyclohex-2-en-1-ol [(*S*)-**10**] with 77% *ee* (*e.r.* = 88.5:11.5) and in 91% yield, took place at 110 °C in 3 h with complete conservation of the original enantioenrichment of 77% *ee* (*e.r.* = 88.5:11.5), in 93% yield (Table 1, Entry 6).

The stereochemical course of these rearrangements was elucidated on the basis of an X-ray crystal structure of (+)-

Table 1. Results of carbamoylations and subsequent rearrangements

Entry	Alcohol	R	*O*-Ester	*S*-Ester
1	*rac*-**10**	Me	**12a** 99%	**14a** 80%
2	*rac*-**10**	*i*Pr	**12b** 95%	**14b** 78%
3[a]	(*S*)-**10** 82% *ee*	*i*Pr	(*S*)-**12b** 74% 82% *ee*	(*R*)-**14b** 79% 79% *ee*
4[a]	(*R*)-**10** 96% *ee*	*i*Pr	(*R*)-**12b** 80% 96% *ee*	(*S*)-**14b** 86% 93% *ee*
5	*rac*-**10**	*t*Bu	**12c** 90%	**14c** 91%
6	(*S*)-**10** 77% *ee*	*t*Bu	(*S*)-**12c** 91% 77% *ee*	(*R*)-**14c** 93% 77% *ee*
7	*rac*-**11**	*i*Pr	**13** 68%[b]	**15** 64%[c]
8	(*R*)-**11** > 99% *ee*	*i*Pr	(*R*)-**13** 87% > 99% *ee*	(*S*)-**15** 74% 91% *ee*

[a] Carbamoylation and rearrangement was performed several times on different scales, with enantioenriched cyclohex-2-en-1-ol (**10**) of varying enantiomeric purity; the given figures represent typical values. [b] In addition, 25% of *rac*-**11** was isolated. [c] In addition, 32% of *rac*-**13** was isolated.

14c, which showed the (*R*) configuration (Figure 1). Thiocarbamate (+)-(*R*)-**14c** was furnished by thermal rearrangement of the corresponding *O*-ester (−)-(*S*)-**12c**, the latter compound having been acquired by carbamoylation of alcohol (−)-(*S*)-**10** (vide supra). This is evidence for a suprafacial rearrangement process of the *N*-*tert*-butyl-substituted thiocarbamate (−)-(*S*)-**12c**. Saponification of the thiocarbamate (+)-(*R*)-**14c** with 2.0 M sodium hydroxide solution yielded (+)-cyclohex-2-ene-1-thiol. An analogous reaction sequence starting with alcohol (+)-(*R*)-**10** and proceeding through the thiocarbamates (+)-(*R*)-**12b** and (−)-**14b** finally furnished (−)-(*S*)-cyclohex-2-ene-1-thiol. On the basis of the optical rotation of the isolated thiol, the (*S*) configuration was assigned to the thiocarbamate (−)-**14b**, indicating a suprafacial rearrangement for *N*-isopropyl-substituted thiocarbamate as well.

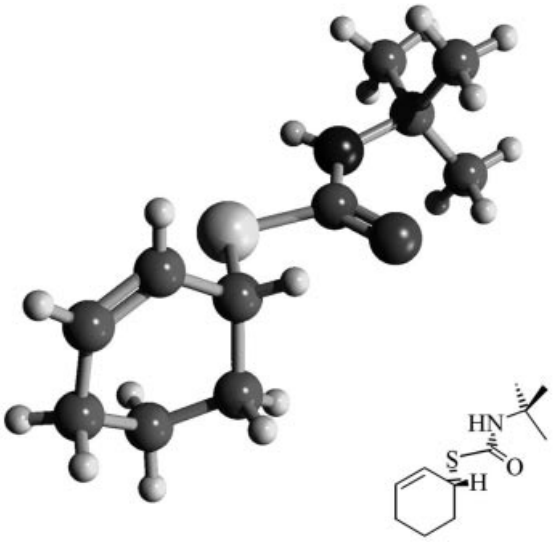


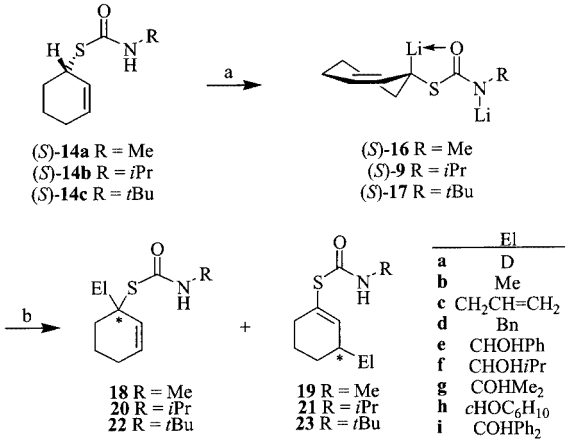
Figure 1. X-ray crystal structure of thiocarbamate (+)-(*R*)-**14c**

The slight loss of enantioenrichment during rearrangement is assumed to be a consequence of partial dissociation and nonenantiospecific recombination of the thiocarbamate during the thermal rearrangement.[30] In general, this carbamoylation/rearrangement sequence should be applicable to any enantioenriched allylic alcohol, providing access to enantioenriched allylic thiocarbamates in a regioselective manner.

Enantioenriched (*S*)-*S*-(2-cyclohexenyl) *N*-methylthiocarbamate [(*S*)-**14a**] was prepared by Pd^0-catalyzed deracemization of the corresponding *O*-ester **12a** by an efficient method reported by Gais, furnishing yellowish (*S*)-**14a** in high yield.[25c] Unfortunately, we were not able to extend this methodology to *N*-isopropyl derivatives without dramatic losses in turnover or enantioselectivity.

Standard Deprotonation Conditions

Optimum deprotonation conditions for thiocarbamate **14b** were established by a series of deuteration experiments at −78 °C in toluene, ether, or THF. A slight excess of *sec*-butyllithium for each of the two acidic protons of *rac*-**14b** in the presence of an equal amount of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) proved to be well suited. Each deprotonation series started with 60 min for lithiation and subsequent quenching of the dilithiated species *rac*-**9** with an excess of MeOD, followed by neutralization with DOAc at −78 °C (Scheme 5).



Scheme 5. Lithiation and subsequent electrophilic substitution [the (*S*) configuration for starting materials having been chosen arbitrarily]; ligands at the lithium centers are omitted for the sake of clarity; reagents and conditions: (a) *s*BuLi/TMEDA, −78 °C, 5−240 min; (b) i) ElX, −78 °C, 15 min to 18 h; ii) HOAc (DOAc for deuterations), −78 °C, 15 min; iii) $NaHCO_3$ (aq), 0 °C

The ratios of the regioisomeric products **20a** and **21a** were determined by ^{1}H NMR and GC, while the D content was ascertained with the aid of calibrated GC-MS. The duration of metallation was successively adjusted. Selected values given in Table 2 indicate that deprotonation in toluene is sluggish and at least 2−4 h are required for almost quantitative lithiation (Table 2, Entries 1 and 2). Deprotonation in diethyl ether occurs more readily and requires 30−60 min, the regioselectivity of deuterations is similar to that observed in toluene (Table 2, Entries 3 and 4). Rapid lithiation was observed in THF solution, slightly more than 5 min being sufficient for quantitative deprotonation, and deuteration in the γ-position being more favored than in toluene or ether (Table 2, Entries 5 and 6). This trend is also reflected in the regioselectivities of the alkylations (vide infra).

Table 2. Results of deuterations of thiocarbamate *rac*-**14b**

Entry[a]	Solvent	Time [min]	Products[b] (D content [%])[c] *rac*-**20a**	:	*rac*-**21a**
1	toluene	120	28 (73.5)	:	72 (95.7)
2	toluene	240	28 (85.0)	:	72 (96.1)
3	Et_2O	30	28 (88.8)	:	72 (98.0)
4	Et_2O	60	34 (93.0)	:	66 (94.5)
5	THF	5	16 (78.3)	:	84 (83.9)
6	THF	30	15 (84.4)	:	85 (98.0)
7[d]	THF	12	(*S*) 11[e] (−)	:	89[f] (−)

[a] 2.5−3.2 equivalents of *s*BuLi/TMEDA were employed. [b] Determined by ^{1}H NMR and GC. [c] Determined by calibrated GC-MS. [d] (*R*)-**14b** with 81% *ee* (*e.r.* = 90.5:9.5) was the starting material; MeOH was used as electrophile. [e] 4% (*S*)-**14b** with 20% *ee* (*e.r.* = 60:40) were isolated. [f] 83% of the double bond regioisomer of carbamate **14b** were isolated.

Reprotonation of enantioenriched allyllithium compound **9** should give quick access to information about configurational stability, by determination of the optical purity of the formed thiocarbamate **14b**. Protonation of the enantiopure benzyllithium compound (*S*)-**8** with methanol, for instance, takes place with complete retention of configuration. However, quenching of the allylic thio carbanion (*R*)-**9** (81% *ee*, *e.r.* = 90.5:9.5) with methanol under conditions used for highly stereospecific alkylations[31] furnished thiocarbamate (*S*)-**14b** with only 25% stereospecificity[32] (20% *ee*, *e.r.* = 60:40), Table 2, Entry 7).

Configurational Stability and Stereochemical Course of Alkylations

The configurational stabilities of the enantioenriched dilithiated species (*R*)- and (*S*)-**9** were investigated by methylation with methyl iodide[33] under different reaction conditions. The α-methylation product **20b** and its γ-regioisomer **21b** (see Scheme 5) were separated by chromatography, and the *ee*s were determined by chiral GC and HPLC, respectively. The configurational stability of allyllithium compound (*R*)-**9** in toluene is quite low; alkylation after 4.5 h of metallation provided almost racemic products (Table 3, Entry 1). Quenching of the lithiated (*S*)-**14b** in toluene after 45 min gave markedly higher enantioenrichment of isolated (*R*)-**20b** and (*R*)-**21b** (Table 3, Entry 2); this is evidence in support of the assumption that low *ee*s are due to racemization rather than lack of stereospecificity of the methylation in toluene. In ether, moderately stereospecificities of 60% and 57% for the formation of carbamates (*S*)-**20b** and (*S*)-**21b** were detected (Table 3, Entry 3), indicating that racemization occurs perceptibly more slowly than in toluene. Prolongation of the reaction time by a factor of three caused a decrease in enantioenrichment (Table 3, Entry 4). Dilithiated species **9** shows the highest configurational stability in THF: methylation took place with the same high stereospecificities[32] after 5, 60, or 270 min of lithiation (Table 3, Entries 5−7).

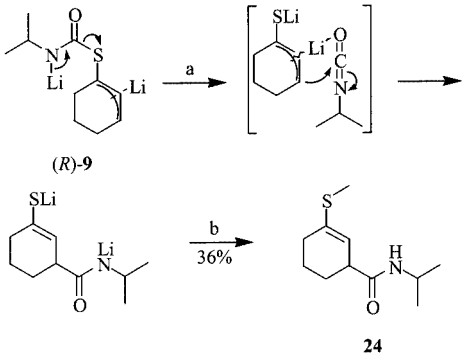
Table 3. Results of methylations of thiocarbamate **14b**

Entry[a]	Solvent	Time [min]	% stereospecificity[b] (% yield)[c] **20b**	**21b**
1	toluene	270	3 (41)	3 (22)
2	toluene	45	66 (8)	52 (4)
3	Et_2O	60	60 (40)	57 (31)
4	Et_2O	180	53 (50)	40 (31)
5[d]	THF	5	96 (21)	77 (43)
6	THF	60	96 (19)	77 (28)
7	THF	270	96 (17)	76 (21)
8[e]	THF	30	94 (21)	72 (45)
9[f]	THF	80	97 (17)	84 (40)
10	THF	40[g]	81 (19)	53 (19)
11	THF	40[h]	<1 (18)	10 (13)
12	THF	40[i]	3[j] (n.d.)	<1[j] (−)

[a] Thiocarbamate (*R*)- or (*S*)-**14b** of 30−75% *ee* was employed as starting materials; 2.4−2.8 equivalents of *s*BuLi/TMEDA were used. [b] Conservation of the original enantioenrichment, determined by GC and HPLC, respectively.[32] [c] Isolated yields. [d] The use of (*S*)-**14b** with 91−93% *ee* gave the same α-stereospecificity. [e] (*S*)-**14b** with 80% *ee* (*e.r.* = 90:10) from Pd^0-catalyzed deracemization was used. [f] Performed at −90 °C. [g] Warmed to −50 °C for 15 min. [h] Warmed to −26 °C for 15 min. [i] Warmed to 0 °C for 15 min. [j] Yield by calibrated GC; 36% of amide **24** were isolated (vide infra).

Use of the enantioenriched thiocarbamate (*S*)-**14b**, synthesized by Pd^0-catalyzed deracemization, achieved comparable stereospecificities and yields (Table 3, Entry 8). A reduction in the reaction temperature to −90 °C improved the stereospecificity of the formation of the γ-product **21b** slightly (Table 3, Entry 9). In comparison to that of α-thiobenzyllithium compound (*S*)-**8**,[19c] the configurational and chemical stability of the dianion (*R*)-**9** at elevated temperatures is quite limited. Warming of a THF solution of (*R*)-**9** to −50 °C for 15 min and subsequent methylation at −78 °C resulted in a significantly lower overall stereospecificity[32] (Table 3, Entry 10). A transitional temperature of −26 °C resulted in almost entire loss of enantioenrichment (Table 3, Entry 11), and warming of (*R*)-**9** to 0 °C for

15 min caused rearrangement to optically inactive carboxamide **24** in 36% yield (Table 3, Entry 12; Scheme 6).



Scheme 6. Rearrangement of (*R*)-**9** on warming; ligands at the lithium centers are omitted for the sake of clarity; reagents and conditions: (a) i) 10 min −78 °C; ii) 15 min 0 °C; iii) 15 min −78 °C; (b) i) MeI, −78 °C, 15 h; ii) HOAc, −78 °C, 15 min; iii) $NaHCO_3$ (aq), 0 °C

Fractional crystallization of a dissolved sample of (*S*)-**21b** with 63% *ee* (*e.r.* = 81.5:18.5) afforded crystals of (*S*)-**21b** with 54% *ee* (*e.r.* = 77:23) to 70% *ee* (*e.r.* = 85:15) suitable for X-ray structure analysis.[34]

The stereochemical course of the methylation with methyl iodide was elucidated by X-ray crystal structure analysis. Dianion (*R*)-**9** gave the carbamates (*S*)-**20b** and (*S*)-**21b** (Figure 2). Methylation with methyl iodide had therefore taken place with stereoinversion of configuration and in an *anti*-S_E' process, respectively.

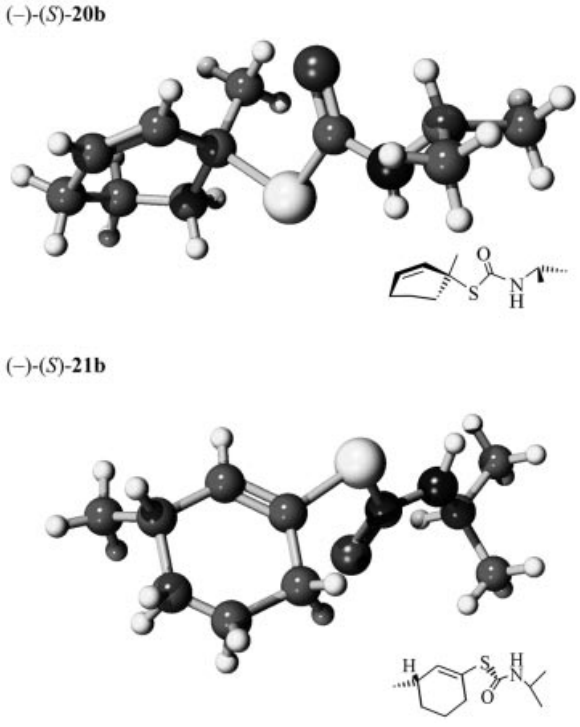
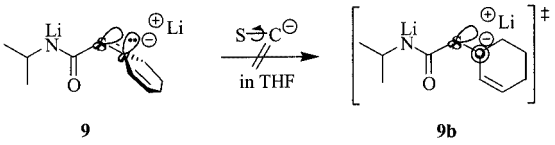


Figure 2. X-ray crystal structures of thiocarbamates (−)-(*S*)-**20b** and (−)-(*S*)-**21b**[20]

The source of the configurational stability of dilithiated species **9** is the branched carbanionic center. Our previous findings with alkyllithium compounds **7a** and **7b**,[18] as well as the observation by Hoffmann et al. that the configurational stabilities of α-thioaryl-substituted alkyllithium compounds are increased by sterically demanding substituents,[11c] support this assumption. The torsion (step C in Scheme 2) of the S−C$^-$ bond, abolishing the hyperconjugation between the n_C orbital and the S−R σ* orbital in the rotamer **9b**, is regarded as the rate-determining step of the racemization (Scheme 7).



Scheme 7. Rate-determining step of racemization of dianion **9**; ligands at the lithium centers are omitted for the sake of clarity

Further increased bulkiness of the carbamoyl moiety should enhance the configurational stability. *N*-*tert*-Butyl-substituted thiocarbamate **14c** was quantitatively lithiated to the dianion **17** under standard conditions, demonstrated by a deuteration experiment in diethyl ether. Remarkably, a change in the regioselectivity, relative to the deuteration of dianion **9** (vide supra), was observed. Here the α-deuteration product **22a** was isolated in 84% yield (> 95% D content), whereas γ-isomer **23a** was formed in only 4% yield (Scheme 5). Unfortunately, methylation of carbanion (*S*)-**17** in order to check the configurational stability could not be achieved.

The methylation of *N*-methyl-substituted *rac*-**14a** under standard conditions worked very well. The formation of the α-methylation product *rac*-**18b** was preferred over that of the γ-product *rac*-**19b** (Scheme 5) in THF even more so than in ether (Table 4, Entries 1 and 2). When thiocarbamate (*S*)-**14a** (isolated from Pd^0-catalyzed deracemization as a yellowish solid that gave satisfactory spectra and elemental analysis) was used, only moderate stereospecificities were obtained (Table 4, Entry 3).[32] A double recrystallization/chromatography sequence yielded white thiocarbamate (*S*)-**14a**, but the subsequent methylation experiment gave higher but still unsatisfactory stereospecificities of 71% and 60%, respectively (Table 4, Entry 4). This indicates that even traces of impurities from the Pd^0-catalyzed deracemization cause perceptible loss of stereospecificity. The addition of hexamethylphosphoric triamide (HMPT) in order to enhance the configurational stability of carbanion (*S*)-**16** by ion-pair separation had only a marginal effect on the stereospecificity (Table 4, Entry 5). The addition of 7 equiv. of lithium chloride to a solution of (*S*)-**16** in THF did not cause loss of stereospecificity (Table 4, Entry 6).[35] The in situ *N*-silylation of thiocarbamate (*S*)-**14a** with F_3CSO_3-$SiMe_3$ (TMSOTf; Table 4, Entry 7)[36] or other silylating reagents caused reduced stereospecificity.

Chemical correlation established the (*R*) absolute configuration for the thiocarbamate (+)-**18b** as follows. A small

Table 4. Results of methylations of thiocarbamate (*S*)-**14a**

Entry[a]	Solvent	Time [min]	% stereospecificity[b] (+)-(*R*)-**18b**	(% yield)[c] (+)-(*R*)-**19b**
1[d]	Et_2O	120	*rac* (50)	*rac* (39)
2[d]	THF	10	*rac* (71)	*rac* (16)
3[e]	THF	10	63 (47)	52 (12)
4	THF	50	71 (74)	60 (8)
5[f]	THF	55	77 (41)	40 (5)
6[g]	THF	50	82 (79)	70 (8)
7[h]	THF	10	28 (63)	n.d. (4)

[a] (*S*)-**14a** of 94% *ee* (*e.r.* = 97:3) was employed as starting material; 2.4−2.5 equivalents of *s*BuLi/TMEDA were used. [b] Conservation of the original enantioenrichment, determined by GC.[32] [c] Isolated yields. [d] *rac*-**14a** was used. [e] Yellowish (*S*)-**14a** of 92% *ee* (*e.r.* = 96:4) from Pd^0-catalyzed deracemization was used. [f] 5.0 equivalents HMPT were used instead of TMEDA. [g] 7 equivalents LiCl were added. [h] 1.1 equivalents TMSOTf were added at 0 °C prior to *s*BuLi at −78 °C.

amount of thiocarbamate (−)-(*S*)-**20b** (from the X-ray structure determination) was saponified with 1 N aqueous sodium hydroxide solution to provide the corresponding (−)-thiol and subjected to analytical GC on a chiral stationary phase (CPGC). A sample of compound (+)-**18b** was treated in the same way, resulting in a reversed order of the major and the minor signal in the CPGC. Thus, the dianionic species (*S*)-**16** is alkylated by methyl iodide with stereoinversion of configuration, as in the case of allyllithium compound **9**. The (*R*) absolute configuration was assigned to thiocarbamate (+)-**19b** by analogy.

The steric demand of the isopropyl group seems to be crucial for the configurational stability of the α-thiocarbamoyl-substituted *sec*-allyllithium compounds. Thus, the thiocarbamate (*S*)-**14b** (96% *ee*, *e.r.* = 98:2) was lithiated and subsequently alkylated with allyl bromide to provide the thiocarbamates (+)-**20c** and (+)-**21c** or alkylated with benzyl bromide to give the thiocarbamates (+)-**20d** and (+)-**21d**, respectively. Alkylation products were separated by column chromatography, and enantiomeric purity was determined by GC or HPLC. The stereospecificities of alkylations are generally high (namely 96%, except for the γ-allylation with 90% stereospecificity, Table 5, Entries 2 and 4).

The absolute configuration of thiocarbamate (+)-**21d** was determined by X-ray structure analysis (Figure 3), confirming the (*S*) configuration and therefore once more the stereoinversion of configuration during the electrophilic alkylation. The absolute configurations of further alkylation products were assigned with the assumption, but without any additional proof, of stereoinversion.

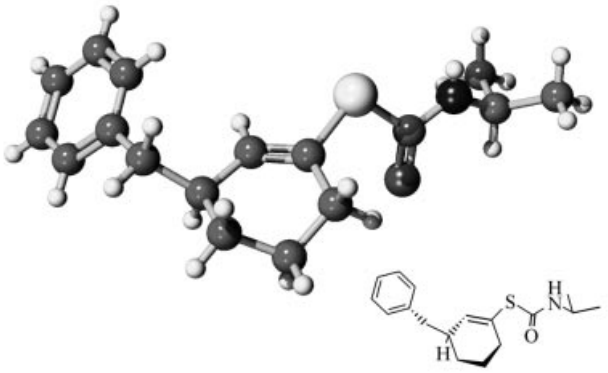


Figure 3. X-ray crystal structure of thiocarbamate (+)-(*S*)-**21d**

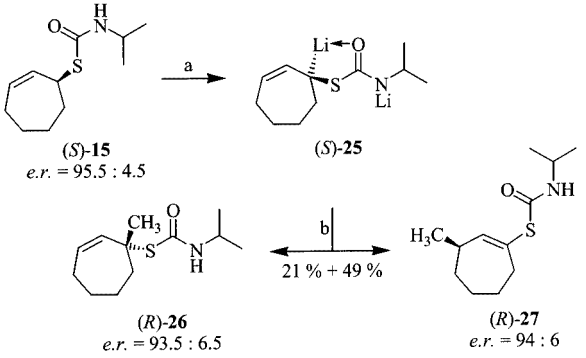
Lithiation was also carried out with the cycloheptenyl thiocarbamate **15**. Deuteration of allyllithium compound **25** under standard conditions in ether afforded a 41:59 mixture of α-/γ-product, with 79% and > 99% D content, respectively. Methylation furnished the α-methylation product **26** and its γ-isomer **27** in high yield (Scheme 8).

The tendency of the regioselectivity of methylation of the *S*-cycloheptenyl dianion **25** shows the same solvent dependence as electrophilic substitutions of lithiated *S*-cyclohexenyl *N*-isopropylthiocarbamate **9**. The γ-attack is more favored in THF solution than in ethereal solution (Table 6, Entries 1 and 2). When thiocarbamate (−)-(*S*)-**15** (91% *ee*, *e.r.* = 95.5:4.5) was subjected to methylation, optically active products were isolated: 21% of the α-methylation product (+)-(*R*)-**26** with 87% *ee* (*e.r.* = 93.5:6.5; 96% stereospecificity) and 49% of the γ-isomer (+)-(*R*)-**27** formed with 88% *ee* (*e.r.* = 94:6; 97% stereospecificity, Table 6, Entry 3).[37]

Table 5. Results of alkylations of thiocarbamate **14b**

Entry[a,b]	Solvent	Time [min]	ElX (equiv.)	Yield[c]	% stereospecificity[d]
1	Et_2O	80	AllylBr (1.5)	32%	*rac*-**20c**
				43%	*rac*-**21c**
2[e]	THF	15	AllylBr (1.6)	18%	96 (+)-(*S*)-**20c**
				38%	90 (+)-(*S*)-**21c**
3	Et_2O	80	BnBr (1.6)	13%	*rac*-**20d**
				46%	*rac*-**21d**
4[e]	THF	15	BnBr (1.6)	7%	96 (+)-(*S*)-**20d**
				59%	96 (+)-(*S*)-**21d**

[a] See Table 3, entries 3 and 6 for related methylations. [b] 2.5 equivalents of *s*BuLi/TMEDA were used. [c] Isolated yields. [d] Conservation of the original enantioenrichment, determined by GC or HPLC.[32] [e] (*S*)-**14b** of 96% *ee* (*e.r.* = 98:2) was employed as starting material.



Scheme 8. Methylation of thiocarbamate (−)-(*S*)-**15**; ligands at the lithium centers are omitted for the sake of clarity; reagents and conditions: (a) *s*BuLi/TMEDA, −78 °C, 30 min; (b) i) MeI, −78 °C, 15 h; ii) HOAc, −78 °C, 15 min; iii) $NaHCO_3$ (aq), 0 °C

Table 6. Results of methylations of thiocarbamate **15**

Entry[a]	Solvent	Time [min]	% stereospecificity,[b] (+)-(*R*)-**26**	(% yield)[c] (+)-(*R*)-**27**
1	Et_2O	80	*rac* (52)	*rac* (36)
2	THF	60	*rac* (27)	*rac* (61)
3[d]	THF	30	96 (21)	97 (49)

[a] 2.5 equivalents of *s*BuLi/TMEDA were used. [b] Conservation of the original enantioenrichment, determined by GC.[32] [c] Isolated yields. [d] (*S*)-**15** of 91% *ee* (*e.r.* = 95.5:4.5) was employed as starting material.

Hydroxyalkylations

The regioselective addition of benzaldehyde or 2-methylpropanal to the dianion *rac*-**9** furnished diastereomeric mixtures of alcohols *rac*-**21e** (PhCHO) and *rac*-**21f** (*i*PrCHO), respectively, in 55% yield in both cases. The diastereomeric ratios are 55:45 in both cases (Table 7). Thiocarbamate *anti*-*rac*-**21f** and its diastereoisomer *syn*-*rac*-**21f** could be separated by column chromatography. The *anti*/*syn* assignment was made on the basis of an X-ray structure analysis of the adduct *syn*-*rac*-**21f**. This matches with the previous assignment[38] on the basis of the $^3J_{H,H}$ coupling constants of the protons of the two newly formed stereocenters, taking literature references into account.[39]

Table 7. Addition of dianion *rac*-**9** to aldehydes

Entry	ElX	Yield[a]	*d.r.*[b] *syn*-**21** : *anti*-**21**	$^3J_{H,H}$ [Hz] *syn*-**21**	*anti*-**21**
1	PhCHO	55% **21e**	55 : 45	5.0	5.5
2	*i*PrCHO	55% **21f**	55 : 45	3.7	4.9

[a] Isolated yields. [b] Determined by ^{1}H NMR.

Attempts to carry out a diastereoselective addition involving a cyclic six-membered transition state[40] after transmetallation from lithium to titanium or boron were less successful.[41] Allyllithium compound *rac*-**9** added to cyclohex-2-en-1-one predominantly onto the carbonyl group (43% yield of the γ-1,2-adduct) with almost negligible diastereoselectivity (*d.r.* = 53:47). Consequently, we placed the emphasis on the addition of allyllithium compound **9** to symmetric ketones.[42] Adducts of acetone (**21g**), cyclohexanone (**21h**), and benzophenone (**21i**) were isolated as white solids by column chromatography in good yields (see Scheme 5; Table 8, Entries 1, 2, 5−7).

The addition of acetone and cyclohexanone to the enantioenriched dianion **9** furnished adducts **21g** and **21h**, with high stereospecificities of 97 and 94%, respectively (Table 8, Entries 2 and 6).[43] When benzophenone was employed as electrophile, substantial loss of enantioenrichment occurred; the addition might proceed via a radical pair formed by single-electron transfer (SET),[44] causing partial racemization (Table 8, Entry 8). The same observation has been made during addition of thiobenzyllithium compound (*S*)-**8** to benzophenone.[19c]

Crystals suitable for X-ray structure analysis grown from enantioenriched adduct (−)-(*R*)-**21g** turned out to be racemic. The obtained crystal structure, depicted in Figure 4, shows hydrogen bonding between the NH protons and the oxygen atoms of the introduced hydroxy groups.[45] These interactions might give rise to higher crystallizability of the racemate.

The *N*-methyl-substituted thiocarbamate **14a** was hydroxyalkylated with acetone in the same manner as the *N*-isopropylthiocarbamate **14b**, furnishing not only the γ-adduct **19g** in high yield (87−90%), but, in addition, a small amount of the α-product **18g** when the reaction was run in ether (Scheme 5; Table 8, Entries 3 and 4). Employment of (*S*)-**14a** (95% *ee*, *e.r.* = 97.5:2.5) as starting material yielded thiocarbamate (+)-(*S*)-**19g** in 87% yield and with 66% stereospecificity (63% *ee*, *e.r.* = 81.5:18.5). This represents the same order of magnitude as found for methylations of dianion (*S*)-**16** (vide supra).

Attempts to determine the absolute configuration of hydroxyalkylation products through derivatization or correlation with known compounds by independent synthesis failed. Derivatization of thiocarbamate (+)-**19g** by Ni^0-catalyzed cross-coupling with methylmagnesium bromide[46,47] furnished isoterpineol (+)-**28**[48] in 91% yield under optimized conditions (Scheme 9). Isoterpineol (−)-**28** was formed from thiocarbamate (−)-**21g** under the same conditions in 74% yield. NOE experiments on the homoallylic alcohol **28** found that no isomerization of the double bond had occurred during the cross-coupling reaction.

The absolute configuration of hydroxyalkylation products is based on ab initio calculations by Grimme. It has recently been shown[49] that reliable theoretical predictions for the optical rotations of large chiral molecules can be obtained by time-dependent density functional response theory (TDDFT). By comparison of the theoretical calculated and the experimentally measured $[\alpha]_D$ values, it is also easily possible to assign absolute configurations to noncrystallizable compounds. According to our computations,[50] the bulky 1-hydroxy-1-methylethyl substituent of **28** prefers the pseudoequatorial position (population > 98% at room temp.), and so this conformer of the six-membered ring is considered here exclusively. However, by rotation around

Table 8. Addition of thioallyllithium compounds to ketones

Entry[a]	Starting compd.	Solvent	Time [min]	ElX (equiv.)	Adduct[b]	Specificity[d]
1	*rac*-**14b**	Et_2O	45	acetone (25)	*rac*-**21g** 64%	–
2[c]	(*R*)-**14b**	THF	15	acetone (1.5)	(−)-(*R*)-**21g** 47%	97%
3	*rac*-**14a**	Et_2O	60	acetone (5.0)	*rac*-**18g** 6%, *rac*-**19g** 90%	–
4[e]	(*S*)-**14a**	THF	15	acetone (5.9)	(+)-(*S*)-**19g** 87%	66%
5	*rac*-**14b**	Et_2O	50	cyclohexanone (5)	*rac*-**21h** 70%	–
6[f]	(*S*)-**14b**	THF	8	cyclohexanone (5)	(+)-(*S*)-**21h** 80%	94%
7	*rac*-**14b**	Et_2O	45	benzophenone (5)	*rac*-**21i** 69%	–
8[f]	(*S*)-**14b**	THF	15	benzophenone (5)	(+)-(*S*)-**21i** 74%	24%

[a] 2.1−2.5 equivalents of *s*BuLi/TMEDA were used. [b] Isolated yields. [c] (*R*)-**14b** of 75% *ee* (*e.r.* = 87.5:12.5) was used. [d] Conservation of the original enantioenrichment, determined by GC or MPLC. [e] (*S*)-**14a** of 95% *ee* (*e.r.* = 97.5:2.5) was used. [f] (*S*)-**14b** of 96% *ee* (*e.r.* = 98:2) was used.

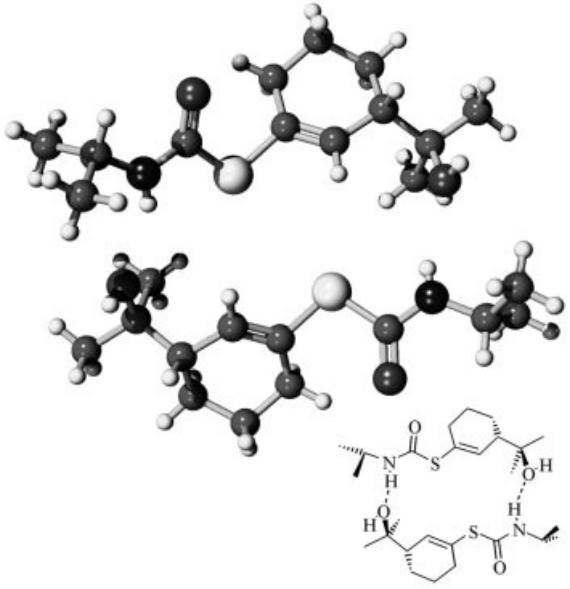
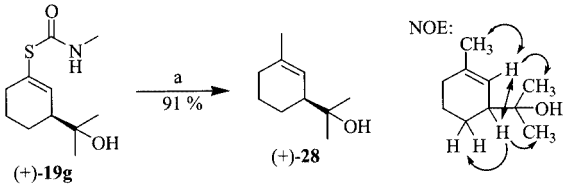


Figure 4. X-ray crystal structure of thiocarbamate *rac*-**21g**



Scheme 9. Ni^0-catalyzed cross-coupling; reagents and conditions: (a) i) 15 mol % $Ni(dppe)Cl_2$, MeMgBr, toluene, 90 °C, 18 h; ii) HCl (aq)

the C-1′−C-1 bond three possible conformers possessing relative minima in energy could be formed. In the lowest-energy conformation **28a**, the dihedral angle θ between the oxygen atom and 1′-H is about −60° (Figure 5).

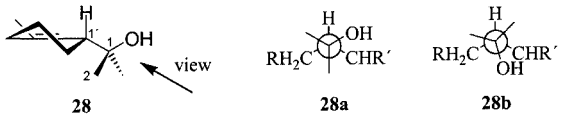


Figure 5. Conformers of isoterpineol **28**

Only 1.1 kJ/mol higher in energy is the conformer **28b**, with θ ≈ −120°. The third conformer, with θ = +50°, is 4.3 kJ/mol higher in energy and so is not considered further. The computations were performed for both **28a** and **28b**, and the theoretical $[\alpha]_D$ values were weighted by the corresponding Boltzmann populations at room temperature. Only these averaged values are reported here for comparison with the experimental data.[58] At the sodium D line frequency we obtained a theoretical result of $[\alpha]_D$(theor.) = +76 for the (*S*) enantiomer and so may assign the absolute configuration as (*S*) = (+). Keeping in mind that optical rotation can be heavily influenced by solvation (the calculations refer to the gas phase), the agreement with the experimentally ascertained $[\alpha]_D$(exp.) = −38 seems reasonable for the other enantiomer. Inspection of the data at the other wavelengths 546 nm {[α](theor.) = +92, [α](exp.) = −46}, 436 nm {[α](theor.) = +164, [α](exp.) = −92}, and 365 nm {[α](theor.) = +277, [α](exp.) = −146} clearly show that the overestimation is systematic and that the frequency dependence of [α] is described very well by theory. In summary, we can conclude that thiocarbamate (+)-**19g**, the source of isoterpineol (+)-(*S*)-**28**, possesses the (*S*) configuration, and the (*R*) configuration was assigned to thiocarbamate (−)-**21g**, the source of isoterpineol (−)-(*R*)-**28**. It is concluded that the hydroxyalkylation of the dianionic species (*R*)-**9** and (*S*)-**16** with acetone takes place suprafacially through a *syn*-S_E' process; the absolute configurations of (+)-(*S*)-**21h** and (+)-(*S*)-**21i** were assigned in analogy, without further proof.

Conclusion

Optically active *S*-(2-alkenyl) *N*-monoalkylmonothiocarbamates **14a**−**c** and **15** as precursors for allyllithium compounds have been synthesized starting from enantioenriched *sec*-allylic alcohols, by a carbamoylation/enantiospecific rearrangement methodology, giving access to both enantiomers. The rate of deprotonation, the configurational stability of allyllithium compound **9**, and the regioselectivity of electrophilic substitutions of all investigated lithiated allylthiocarbamates show marked solvent dependence. Alkylations of configurationally stable allyllithium com-

pounds **9** and **25** − each possessing an *N*-isopropyl-substituted carbamoyl group − proceed with high stereospecificity and stereoinversion of configuration in both the α- and the γ-positions.

Hydroxyalkylations of enantioenriched thioallyllithium **9** take place exclusively in the γ-position with high stereospecificity in a suprafacial fashion, indicating a *syn*-S_E' process. Ni^0-catalyzed cross-coupling of acetone adducts (+)-**19g** and (−)-**21g** with MeMgBr yielded optically active isoterpineol **28**, setting the stage for determination of absolute configuration by DFT calculations of optical properties at the aug-SV(p)/BH-LYP level.

Experimental Section

General Remarks: All solvents were dried and purified prior to use: toluene and Et_2O were distilled from sodium benzophenone ketyl, and THF was distilled from potassium benzophenone ketyl. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was distilled from powdered CaH_2 and stored under Ar in the dark. Aldehydes were distilled prior to use. Solutions of *sec*-butyllithium were purchased (ca. 1.3 M in cyclohexane/hexane, 92:8), filtered through a pad of Celite under argon in order to remove any precipitate, and stored in a freezer (−30 °C); only a slight yellow hue is acceptable. The content of *s*BuLi was determined by titration.[59,60] All other commercially available reagents were used as received. All reactions were performed under Ar in flame-dried glassware. Flash column chromatography (FCC) was performed on Merck 60 silica gel, 0.040−0.063 mm, and monitored by thin layer chromatography (TLC) on Merck 60 F_{254} silica gel; PE: light petroleum ether, b.p. 36−46 °C; EE: ethyl acetate. NMR: Bruker ARX 300, AM 360 (NOE experiments), or AMX 400 (routine 2D spectra) and Varian Unity Plus 600 (2D spectra, NOE experiments); spectra from solutions in $CDCl_3$ (δ_C = 77.0 ppm) are calibrated relative to residual content of $CHCl_3$ (δ_H = 7.24 ppm) or $SiMe_4$ (δ_H = 0.00 ppm), spectra from solutions in other deuterated solvents are calibrated to $SiMe_4$ (δ_H = 0.00 ppm; δ_C = 0.00 ppm). Some resonance signals for thiocarbamic acid *O*-esters are doubled due to (*E*)/(*Z*)-amide isomers; the related signals are consequently given in groups, separated by a slash. IR: Nicolet 5 DXC. MS: Finnigan MAT 8200 (EI); Finnigan MAT 8230 (GC-MS); Varian Saturn II (GC-MS); Micromass Quattro LC (ESI). Optical rotations: Perkin−Elmer 341 polarimeter. Melting points: Gallenkamp MFB 595 (uncorrected values). Elemental analyses: Elementar Analysensysteme Vario EL III. GC: Hewlett−Packard 5890, 25 m × 0.2 mm HP 1, 107 kPa pre-column pressure N_2, 1 min at 50 °C/10 °C × min^{-1}/15 min at 290 °C; Agilent 6890, 30 m × 0.32 mm HP 5, 1.5 mL × min^{-1} H_2, start at 50 °C/10 °C × min^{-1}/30 min at 300 °C; Hewlett−Packard 6890, 25 m × 0.2 mm HP 1701, 100 kPa pre-column pressure N_2, 1 min at 50 °C/10 °C × min^{-1}/20 min at 270 °C; Hewlett−Packard 6890, cyclodextrins from Supelco (30 m × 0.32 mm) or Macherey−Nagel (25 m × 0.2 mm), 100 kPa pre-column pressure N_2, isothermal runs. HPLC: A) Knauer WellChrom Maxi-Star K-1000 pump with A0285 mixing unit and A0293 spectral photometer at 220 nm; B) Waters 600E Multisolvent Delivery System and 996 photodiode array detector.

Carbamoylation of Allylic Alcohols. General Procedure A: Sodium hydride (60% in mineral oil, approx. 1.2 equiv.) was washed free of mineral oil with two small portions of THF. The sodium hydride was suspended in THF at 0 °C in a flask sealed with a rubber septum. A solution of the allylic alcohol in THF was added dropwise to the stirred suspension by syringe. A solution of the isothiocyanate in THF was added dropwise after 1 h of stirring, and after an additional 1 h of stirring, the reaction mixture was carefully hydrolyzed, still at 0 °C, with sat. $NaHCO_3$ solution. The phases were separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The obtained crude thiocarbamic acid *O*-esters were subjected to FCC, yielding pure thiocarbamates **12a−c** and **13**, respectively.

***rac*-*O*-Cyclohex-2-enyl *N*-Methylmonothiocarbamate (*rac*-12a):** Sodium hydride (144 mg, 5.98 mmol, 1.19 equiv.), suspended in THF (3 mL), *rac*-cyclohex-2-en-1-ol (*rac*-**10**, 488 mg, 4.97 mmol), dissolved in THF (1 mL), and methyl isothiocyanate (384 mg, 5.25 mmol, 1.06 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (180 mL SiO_2; EE/cyclohexane, 1:4) yielded *rac*-**12a** (842 mg, 4.92 mmol, 99%) as a low-melting white solid (solid at −20 °C, colorless liquid at room temp.). R_f = 0.52 (EE/cyclohexane, 1:4). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.54−2.14 (m, 6 H, $4CH_2/5CH_2/6CH_2$); 2.81/3.04 (each d, ^3J = 4.9/5.2 Hz, 3 H, N−CH_3); 5.71−5.84, 5.88−5.98 (each m, 2 H + 1 H, 1CH/2CH/3CH); 6.31/6.85 (each br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 24.8, 28.2 ($4CH_2/5CH_2/6CH_2$); 29.4/31.5 (N−CH_3); 73.7/75.5 (1CH); 125.3/125.6 (3CH); 132.6/132.9 (2CH); 189.7/190.6 (C=S) ppm. IR (film): $\tilde{\nu}$ = 3270 s [ν(N−H)], 3033 m, 2940 s, 2868 m, 2835 w, 1657 m, 1525 s [ν(C=S)], 1446 m, 1361 m, 1209 s [δ(N−H)], 1144 s, 1045 s, 1005 s, 718 m, 663 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 171 (68) [M^+]; 143 (6) [retro Diels−Alder {M − C_2H_4}$^+$]; 112 (30) [{M − MeNCO}$^+$]; 99 (35); 92 (45) [HS(COH)NHMe$^+$]; 81 (100) [{M − S(CO)NHMe}$^+$]; 57 (87) [$MeNCO^+$]. $C_8H_{13}NOS$ (171.26): calcd. C 56.11 H 7.65 N 8.18; found C 55.97 H 7.42 N 8.33.

***rac*-*O*-Cyclohex-2-enyl *N*-Isopropylmonothiocarbamate (*rac*-12b):** Sodium hydride (0.760 g, 19.0 mmol; 1.27 equiv.), suspended in THF (8 mL), *rac*-cyclohex-2-en-1-ol (*rac*-**10**, 1.47 g, 15.0 mmol), dissolved in THF (3 mL), and isopropyl isothiocyanate (1.61 g, 16.1 mmol, 1.07 equiv.), dissolved in THF (3 mL), were treated according to General Procedure A. Purification by FCC (250 mL SiO_2; gradient Et_2O/PE, 1:5 → 1:3) yielded *rac*-**12b** (2.83 g, 14.2 mmol, 95%) as a low-melting white solid (solid at − 25 °C, colorless liquid at room temp.). R_f = 0.37 (Et_2O/PE, 1:5); R_f = 0.48 (Et_2O/PE, 1:3). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12/1.19 [each d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.56−1.73, 1.75−2.14 (each m, 2 H + 4 H, $4CH_2/5CH_2/6CH_2$); 3.95/4.34 (each ψ-oct, 1 H, *i*PrCH); 5.72−5.84 (m, 2 H, 1CH/2CH); 5.89−5.99 (m, 1 H, 3CH); 6.01/6.60 (each br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8 ($5CH_2$); 21.8/22.2 [*i*Pr(CH_3)$_2$]; 24.8 ($4CH_2$); 28.2 ($6CH_2$); 45.2/46.8 (*i*PrCH); 73.1/75.2 (1CH); 125.2/125.7 (2CH); 132.5/132.8 (3CH); 188.3 (C=S) ppm. IR (film): $\tilde{\nu}$ = 3250 s [ν(N−H)], 3039 m, 2973 s, 2940 s, 2868 m, 2835 w, 1650 m, 1519 s [ν(C=S)], 1460 s, 1400 s, 1341 m, 1315 m, 1216 s [δ(N−H)], 1147 s, 1131 s, 1045 m, 1006 m, 986 m, 120 w, 729 w cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 199 (87) [M^+]; 120 (74) [HS(COH)NH-*i*Pr$^+$]; 97 (13) [SCNH-*i*Pr$^+$]; 81 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 79 (58) [{M − S(CO)NH-*i*Pr − H_2}$^+$]; 58 (32) [NH-*i*Pr$^+$]; 53 (20) [retro-Diels−Alder {M − S(CO)NH-*i*Pr − C_2H_4}$^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.33 kV, 31 V], ES^+): *m*/*z* (%) = 222 (100) [M + Na^+] → {222 (80); 142 (100) [HO(CS)NH-*i*Pr + Na^+]; 81 (2) [{M − S(CO)NH-*i*Pr}$^+$]; 79 (3) [{M − S(CO)NH-*i*Pr − H_2}$^+$]; 23 (75) [Na^+]}; 200 (25) [M + H^+] → {200 (2); 120 (85) [HO(CS)NH-*i*Pr + H^+]; 81 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 79 (20) [{M − S(CO)NH-*i*Pr − H_2}$^+$]}. $C_{10}H_{17}NOS$ (199.31): calcd. C 60.26, H 8.60, N 7.03; found C 60.38, H 8.83, N 7.36.

Thiocarbamate (−)-(*S*)-12b: Sodium hydride (96 mg, 2.4 mmol, 1.25 equiv.), suspended in THF (1 mL), (−)-(*S*)-cyclohex-2-en-1-ol [(*S*)-**10**] (188 mg, 1.92 mmol, 82% *ee*, *e.r.* = 91:9), dissolved in THF (1 mL), and isopropyl isothiocyanate (204 mg, 2.02 mmol, 1.05 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (91 mL SiO_2; gradient Et_2O/PE, 1:10 → 1:3) yielded (−)-(*S*)-**12b** (282 mg, 1.41 mmol, 74%) as a viscous, colorless liquid and a few % of the corresponding *S*-ester **14b** (8 mg, 0.04 mmol, 2%). $[\alpha]_D^{20} = -149$ [*c* = 1.13, $CHCl_3$, at 91% *ee* (*e.r.* = 95.5:4.5)].

Thiocarbamate (+)-(*R*)-12b: Sodium hydride (125 mg, 3.13 mmol, 1.20 equiv.), suspended in THF (2 mL), (+)-(*R*)-cyclohex-2-en-1-ol [(*R*)-**10**, 255 mg, 2.60 mmol, 96% *ee*, *e.r.* = 98:2], dissolved in THF (1 mL), and isopropyl isothiocyanate (276 mg, 2.73 mmol, 1.05 equiv.), dissolved in THF (1 mL), were allowed to react according to General Procedure A. Purification by FCC (110 mL SiO_2; Et_2O/PE, 1:5) yielded (+)-(*R*)-**12b** (415 mg, 2.08 mmol, 80%) as a viscous, colorless liquid; a further 4% of rearranged thiocarbamate (*S*)-**14b** was isolated. $[\alpha]_D^{20} = +156$ [*c* = 1.13, $CHCl_3$, at 95% *ee* (*e.r.* = 97.5:2.5)].

***rac*-*O*-Cyclohex-2-enyl *N*-*tert*-Butylmonothiocarbamate (*rac*-12c):** Sodium hydride (240 mg, 6.00 mmol, 1.20 equiv.), suspended in THF (3 mL), *rac*-cyclohex-2-en-1-ol (*rac*-**10**, 491 mg, 5.00 mmol), dissolved in THF (1 mL), and *tert*-butyl isothiocyanate (625 mg, 5.43 mmol, 1.09 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (160 mL SiO_2; Et_2O/PE, 1:5) yielded *rac*-**12c** (955 mg, 4.48 mmol, 90%) as colorless crystals. M.p. 102 °C (Et_2O/PE). R_f = 0.38 (Et_2O/PE, 1:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 [s, 9 H, *t*Bu(CH_3)$_3$]; 1.60−1.74, 1.84−2.15 (each m, 2 H + 4 H, 4CH_2/5CH_2/6CH_2); 7.77−5.87 (m, 2 H, 1CH/2CH); 5.95 (dt, $^3J_{2,3}$ = 9.3 Hz; $^3J_{3,4}$ = 3.5 Hz, 1 H, 3CH); 6.68 (br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.0 (5CH_2); 24.8 (4CH_2); 28.2 (6CH_2); 29.1 [*t*Bu(CH_3)$_3$]; 54.4 (*t*BuC); 75.9 (1CH); 125.1 (2CH); 132.9 (3CH); 189.6 (C=S) ppm. IR (KBr): ṽ = 3241 s [ν(N−H)], 3033 s, 2993 s, 2983 s, 2970 s, 2948 s, 2933 s, 2917 s, 2869 s, 2834 m, 1652 m, 1538 s [ν(C=S)], 1418 s, 1390 s, 1364 s, 1260 s, 1203 s [δ(N−H)], 1169 s, 1055 s, 1021 s, 978 s, 934 m, 900 m, 734 m, 699 m, 654 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 213 (71) [M$^+$]; 134 (25) [HO(CSH)NH-*t*Bu$^+$]; 114 (39); 97 (22) [SCNH-*t*Bu$^+$]; 81 (100) [{M − S(CO)NH-*t*Bu}$^+$]; 79 (44) [{M − S(CO)NH-*t*Bu − H_2}$^+$]; 57 (37) [*t*Bu$^+$]; 53 (7) [retro Diels−Alder {M − S(CO)NH-*t*Bu − C_2H_4}$^+$]. $C_{11}H_{19}NOS$ (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 61.92, H 8.85, N 6.56.

Thiocarbamate (−)-(*S*)-12c: Sodium hydride (390 mg, 9.75 mmol, 1.38 equiv.), suspended in THF (4 mL), (−)-(*S*)-cyclohex-2-en-1-ol [(*S*)-**10**, 695 mg, 7.08 mmol, 77% *ee*, *e.r.* = 88.5:11.5], dissolved in THF (1.5 mL), and *tert*-butyl isothiocyanate (864 mg, 7.50 mmol, 1.06 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (150 mL SiO_2; gradient Et_2O/PE, 1:10 → 1:5) yielded (−)-(*S*)-**12c** (1.37 g, 6.42 mmol, 91%) as colorless crystals. M.p. 96 °C (Et_2O/PE). $[\alpha]_D^{20} = -126$ (*c* = 1.22, $CHCl_3$, at 77% *ee* (*e.r.* = 88.5:11.5)].

***rac*-*O*-Cyclohept-2-enyl *N*-Isopropylmonothiocarbamate (*rac*-13):** Sodium hydride (41 mg, 1.1 mmol, 1.2 equiv.), suspended in THF (1 mL), *rac*-cyclohept-2-en-1-ol (*rac*-**11**,[61] 100 mg, 0.892 mmol), dissolved in THF (1 mL), and isopropyl isothiocyanate (95 mg, 0.94 mmol, 1.05 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (35 mL SiO_2; Et_2O/PE, 1:5) yielded *rac*-**13** [130 mg, 0.61 mmol, 68% (91% based on conversion)] as a viscous, colorless liquid; a further 25% of unchanged alcohol *rac*-**11** was isolated. R_f = 0.59 (Et_2O/PE, 1:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11/1.17 (each d, ^3J = 6.5 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.27−1.47, 1.56−1.75, 1.76−2.01, 2.02−2.22 (each m, 1 H + 3 H + 2 H + 2 H, 4CH_2/5CH_2/6CH_2/7CH_2); 3.95/4.34 (each ψ-oct, 1 H, *i*PrCH); 5.59−5.84, 5.86−5.96 (each m, 2 H + 1 H, 1CH/2CH/3CH); 6.06/6.79 (each br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.9/22.3 [*i*Pr(CH_3)$_2$]; 25.9/26.0, 26.5, 28.4, 32.6/32.7 (4CH_2/5CH_2/6CH_2/7CH_2); 45.2/46.8 (*i*PrCH); 79.5/81.4 (1CH); 131.0/131.7 (2CH); 132.7/133.4 (3CH); 188.0 (C=S) ppm. IR (film): ṽ = 3401 w, 3256 s [ν(N−H)], 3033 w, 2973 s, 2934 s, 2855 s, 1657 w, 1512 s [ν(C=S)], 1460 s, 1400 s, 1371 m, 1341 m, 1308 m, 1223 s [δ(N−H)], 1170 m, 1151 s, 1131 s, 1032 s, 953 w cm^{-1}. $C_{11}H_{19}HOS$ (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 62.13, H 9.17, N 6.49.

Thiocarbamate (−)-(*R*)-13: Sodium hydride (73 mg, 1.8 mmol, 1.2 equiv.), suspended in THF (1 mL), (*R*)-cyclohept-2-en-1-ol [(*R*)-**11**,[62] 170 mg, 1.52 mmol, > 99.6% *ee*, *e.r.* > 99.8:0.2],[63] dissolved in THF (1 mL), and isopropyl isothiocyanate (162 mg, 1.60 mmol, 1.05 equiv.), dissolved in THF (1 mL), were treated according to General Procedure A. Purification by FCC (35 mL SiO_2; Et_2O/PE 1:5) yielded (−)-(*R*)-**12b** (283 mg, 1.33 mmol, 87%) as a viscous, colorless liquid. $[\alpha]_D^{20} = -0.25$ [*c* = 1.19, $CHCl_3$, at > 99.6% *ee* (*e.r.* > 99.8:0.2)]. $[\alpha]_{578}^{20} = -0.34$; $[\alpha]_{546}^{20} = -0.59$; $[\alpha]_{436}^{20} = -3.4$; $[\alpha]_{365}^{20} = -9.7$.

***rac*-*S*-Cyclohex-2-enyl *N*-Methylmonothiocarbamate (*rac*-14a):** The *O*-ester *rac*-**12a** (2.90 g, 16.9 mmol) was heated to 150 °C over 1 h in a flask with a long neck. After 5 h, the flask was allowed to cool to room temp. and the crude thiocarbamate *rac*-**14a** was purified by FCC (210 mL SiO_2; gradient Et_2O/PE 1:10 → 1:5) to give *rac*-**14a** (2.33 g, 13.6 mmol, 80%) as colorless crystals; a further 12% of cyclohex-2-ene-1-thiol and 2% of starting material (*rac*-**12a**) were isolated. M.p. 61 °C (Et_2O/PE). R_f = 0.31 (Et_2O/PE, 1:1). t_r (HP 1) = 12.5 min; t_r (HP 1701) = 17.5 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55−1.72, 1.73−1.84, 1.92−2.05 (each m, 2 H + 1 H + 3 H, 4CH_2/5CH_2/6CH_2); 2.80/2.81 (each d, ^3J = 4.9 Hz, 3 H, N−CH_3); 4.10−4.18 (m, 1 H, 1CH); 5.49 (br. s, 1 H, NH); 5.61−5.68 (dddt, $^3J_{1,2}$ = 4.1, $^3J_{2,3}$ = 10.0, $^4J_{2,6CH}$ = 0.5 Hz, $^4J_{2,4}$ = 2.0, 1 H, 2CH); 5.72−5.79 (dtd, $^4J_{1,3}$ = 1.5, $^3J_{3,4}$ = 3.6 Hz, 1 H, 3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7 (5CH_2); 24.8 (4CH_2); 27.7 (N−CH_3); 30.2 (6CH_2); 40.7 (1CH); 126.8 (2CH); 130.4 (3CH); 167.8 (C=O) ppm. IR (KBr): ṽ = 3283 s [ν(N−H)], 3032 m, 2940 m, 2927 m, 2900 m, 2854 w, 2822 w, 1644 s [ν(C=O)], 1532 s [δ(N−H)], 1406 m, 1242 s, 1230 s, 1203 m, 1038 w, 874 w, 827 m, 755 m, 630 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 171 (37) [M$^+$]; 138 (1); 114 (6) [{M − MeNCO}$^+$]; 92 (46) [HS(COH)NHMe$^+$]; 81 (100) [{M − S(CO)NHMe}$^+$]; 79 (43) [{M − S(CO)NHMe − H_2}$^+$]; 58 (22) [CONHMe$^+$]; 53 (16) [retro Diels−Alder {M − S(CO)NHMe − C_2H_4}$^+$]. $C_8H_{13}NOS$ (171.26): calcd. C 56.11, H 7.65, N 8.18; found C 56.03, H 7.71, N 8.18.

***rac*-*S*-Cyclohex-2-enyl *N*-Isopropylmonothiocarbamate (*rac*-14b):** The *O*-ester *rac*-**12b** (2.30 g, 11.5 mmol) was heated to 105 °C over 1 h. After 3 h, the flask was allowed slowly to come to room temp. and the obtained solid was subjected to FCC (210 mL SiO_2; gradient Et_2O/PE, 1:5 → 1:3), yielding *rac*-**14b** (1.80 g, 9.03 mmol, 78%) as colorless crystals. M.p. 96 °C (Et_2O/PE). R_f = 0.36 (Et_2O/PE, 1:3). t_r (HP 5) = 13.2 min; t_r (HP 1701) = 17.9 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 [d, ^3J = 6.3 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.55−1.72, 1.73−1.84, 1.93−2.04 (each m, 2 H + 1 H + 3 H, 4CH_2/5CH_2/6CH_2); 3.99 (ψ-oct, 1 H, *i*PrCH); 4.09−4.15 (m, 1 H, 1CH); 5.24 (br. s, 1 H, NH); 5.64 (dddt, $^3J_{1,2}$ = 4.0, $^3J_{2,3}$ = 10.0, $^4J_{2,4}$ = 2.1, $^4J_{2,6CH}$ = 0.7 Hz, 1 H, 2CH); 5.75 (dtd, $^4J_{1,3}$ = 1.5, $^3J_{3,4}$ = 3.5 Hz, 1 H, 3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

19.7 ($5CH_2$); 24.7 ($4CH_2$); 22.7 [iPr(CH_3)$_2$]; 30.2 ($6CH_2$); 40.7 (1CH); 43.5 (iPrCH); 126.9 (2CH); 130.3 (3CH); 166.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3274 s [ν(N−H)], 3030 m, 2968 s, 2937 s, 2924 s, 2871 w, 2858 w, 1642 s [ν(C=O)], 1626 s, 1535 s [δ(N−H)], 1455 m, 1385 w, 1368 m, 1231 s, 1223 s, 1204 s, 867 m, 815 s, 751 m, 724 m, 638 m cm^{-1}. MS (EI [70 eV]): m/z (%) = 199 (86) [M$^+$]; 166 (1); 120 (55) [HS(COH)NH-iPr$^+$]; 114 (21) [{M − CONH-iPr}$^+$]; 113 (12) [{M − iPrNCO}$^+$]; 86 (15) [CONH-iPr$^+$]; 81 (100) [{M − S(CO)NH-iPr}$^+$]; 79 (73) [{M − S(CO)NH-iPr − H_2}$^+$]; 58 (9) [CONH-iPr$^+$]; 53 (16) [retro Diels−Alder {M − S(CO)NH-iPr − C_2H_4}$^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.33 kV, 31 V], ES$^+$): m/z (%) = 222 (100) [M + Na$^+$] → {222 (15); 142 (40) [HO(CS)NH-iPr + Na$^+$]; 81 (3) [{M − S(CO)NH-iPr}$^+$]; 79 (1) [{M − S(CO)NH-iPr − H_2}$^+$]; 23 (100) [Na$^+$]}; 200 (15) [M + H$^+$] → {200 (2); 120 (90) [HO(CS)NH-iPr + H$^+$]; 81 (100) [{M − S(CO)NH-iPr}$^+$]; 79 (20) [{M − S(CO)NH-iPr − H_2}$^+$]}. $C_{10}H_{17}NOS$ (199.32): calcd. C 60.26, H 8.60, N 7.03; found C 60.40, H 8.66, N 7.07.

Thiocarbamate (*R*)-14b: The thiocarbamate (*S*)-**12b** (280 mg, 1.40 mmol, 82% *ee*, *e.r.* = 91:9) was heated to 105 °C for 5 h. Purification of the crude product by FCC gave (*R*)-**14b** (222 mg, 1.11 mmol, 79%) as colorless crystals.[64] 79% *ee* (*e.r.* = 89.5:10.5); 96% stereospecificity. M.p. 92 °C (Et_2O/PE).

Thiocarbamate (−)-(*S*)-14b: The thiocarbamate (*R*)-**12b** (153 mg, 0.77 mmol, 96% *ee*, *e.r.* = 98:2) was heated to 105 °C for 5 h in a flask with a long neck. Purification of the crude product by FCC afforded (*S*)-**14b** (132 mg, 0.66 mmol, 86%) as colorless crystals. 93% *ee* (*e.r.* = 96.5:3.5); 97% stereospecificity. M.p. 91 °C (Et_2O/PE). t_r (DEX β-120, 120 °C) = 199/202 min. $[\alpha]_D^{20}$ = −216 (c = 1.06, $CHCl_3$, at 96% *ee* (*e.r.* = 98:2); synthesized starting from enantioenriched cyclohex-2-en-1-thiol).[25c]

***rac*-*S*-Cyclohex-2-enyl *N*-*tert*-Butylmonothiocarbamate (*rac*-14c):** The *O*-ester *rac*-**12c** (700 mg, 3.28 mmol) was heated to 110 °C for 3 h in a flask with a long neck. FCC of the crude thiocarbamate (140 mL SiO_2; gradient Et_2O/PE, 1:20 → 1:3) gave *rac*-**14c** (637 mg, 2.99 mmol, 91%) as colorless crystals. M.p. 111 °C (Et_2O/PE). R_f = 0.52 (Et_2O/PE, 1:5). t_r (HP 1) = 13.4 min; t_r (HP 1701) = 17.6 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 [s, 9 H, tBu(CH_3)$_3$]; 1.57−1.73, 1.74−1.85, 1.94−2.06 (each m, 2 H + 1 H + 3 H, $4CH_2$/$5CH_2$/$6CH_2$); 4.03−4.10 (m, 1 H, 1CH); 5.09 (s, 1 H, NH); 5.65 (ddtd, $^3J_{1,2}$ = 4.0, $^3J_{2,3}$ = 10.0, $^4J_{2,4}$ = 2.0, $^4J_{2,6CH}$ = 0.7 Hz, 1 H, 2CH); 5.77 (dtd, $^4J_{1,3}$ = 1.5, $^3J_{3,4}$ = 3.6 Hz, 1 H, 3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8 ($5CH_2$); 24.7 ($4CH_2$); 29.0 [tBu(CH_3)$_3$]; 29.6 ($6CH_2$); 40.9 (1CH); 53.1 (tBuC); 126.9 (2CH); 130.3 (3 CH); 165.2 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3288 s [ν(N−H)], 3029 s, 2965 s, 2936 s, 2919 s, 2854 s, 2831 s, 2717 w, 1649 s [ν(C=O)], 1524 s [δ(N−H)], 1454 s, 1394 m, 1363 s, 1250 s, 1217 s, 1037 m, 997 m, 859 s, 760 s, 746 s, 724 m, 620 s cm^{-1}. MS (EI [70 eV]): m/z (%) = 213 (16) [M$^+$]; 134 (2) [HO(CSH)NH-tBu$^+$]; 114 (13); 97 (1) [SCNH-tBu$^+$]; 81 (100) [{M − S(CO)NH-tBu}$^+$]; 79 (36) [{M − S(CO)NH-tBu − H_2}$^+$]; 57 (58) [tBu$^+$]. $C_{11}H_{19}NOS$ (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 61.76, H 8.94, N 6.42.

Thiocarbamate (+)-(*R*)-14c: In a flask with a long neck, the *O*-ester (*S*)-**12c** (253 mg, 1.19 mmol, 77% *ee*, *e.r.* = 88.5:11.5) was brought to 110 °C over 1.5 h and then allowed to cool to room temp. over 3 h. The crude product was purified by FCC (35 mL SiO_2; gradient Et_2O/PE, 1:20 → 1:3) to afford (+)-(*R*)-**14c** (235 mg, 1.10 mmol, 93%) as colorless crystals. 77% *ee* (*e.r.* = 88.5:11.5); 100% stereospecificity. M.p. 105 °C ($CHCl_3$). t_r (DEX β-6-TBDM, 120 °C) = 121/126 min. $[\alpha]_D^{20}$ = +149 [c = 2.00, $CHCl_3$, at 77% *ee* (*e.r.* = 88.5:11.5)].

***rac*-*S*-Cyclohept-2-enyl *N*-Isopropylmonothiocarbamate (*rac*-15):** The *O*-ester *rac*-**13** (120 mg, 0.562 mmol) was heated to 110 °C over 1.5 h. After 1 h, the flask was allowed to cool to room temp. over 1 h, and the obtained solid was subjected to FCC (35 mL SiO_2; Et_2O/PE, 1:5), giving *rac*-**15** (77 mg, 0.36 mmol, 64%, 94% based on conversion) as colorless crystals; further starting material *rac*-**13** (38 mg, 0.18 mmol, 32%) was also isolated.[65] M.p. 65 °C (Et_2O/PE). R_f = 0.48 (Et_2O/PE, 1:3). t_r (HP 1701) = 19.1 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 [d, ^3J = 6.6 Hz, 6 H, iPr(CH_3)$_2$]; 1.44−1.66, 1.67−1.86, 1.87−1.94, 2.07−2.16 (each m, each 2 H, $4CH_2$/$5CH_2$/$6CH_2$/$7CH_2$); 3.91−4.02 (m, 1 H, iPrCH); 4.26−4.32 (m, 1 H, 1CH); 5.20 (br. s, 1 H, NH); 5.73−5.77 (m, 2 H, 2CH/3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8 [iPr(CH_3)$_2$]; 27.0, 27.2, 28.3, 33.5 ($4CH_2$/$5CH_2$/$6CH_2$/$7CH_2$); 43.6 (iPrCH); 44.8 (1CH); 132.1 (2CH); 133.4 (3CH); 166.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3322 s [ν(N−H)], 3019 m, 2973 s, 2920 s, 2875 m, 2852 m, 1646 s [ν(C=O)], 1519 s [δ(N−H)], 1454 m, 1389 w, 1366 m, 1321 w, 1221 s, 1203 s, 1168 s, 1130 m, 1069 w, 1051 w, 956 m, 876 s, 817 s, 789 s, 691 m, 650 w, 610 s cm^{-1}. MS (EI [70 eV]): m/z (%) = 213 (20) [M$^+$]; 180 (1); 128 (11) [{M − iPrNCO}$^+$]; 120 (48) [HS(COH)NH-iPr$^+$]; 95 (100) [{M − SCONH-iPr}$^+$]; 94 (45) [{M − HSCONH-iPr}$^+$]; 79 (32); 67 (40) [{M − SCONH-iPr − H_2}$^+$]. $C_{11}H_{19}NOS$ (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 61.90, H 9.22, N 6.48.

Thiocarbamate (−)-(*S*)-15: Thiocarbamate (−)-(*R*)-**13** (270 mg, 1.27 mmol, > 99.6% *ee*, *e.r.* > 99.8:0.2) was brought to 145 °C over 30 min and, after 4.5 h, allowed to cool to room temp. over an additional 30 min. The formed solid was subjected to FCC (95 mL SiO_2; Et_2O/PE, 1:5), yielding thiocarbamate (−)-(*S*)-**15** (200 mg, 0.937 mmol, 74%) as colorless crystals. 91% *ee* (*e.r.* = 95.5:4.5); 91% stereospecificity. M.p. 71 °C (Et_2O/PE). t_r (DEX β-120, 135 °C) = 149/151 min. $[\alpha]_D^{20}$ = −217 [c = 1.04, $CHCl_3$, at 91% *ee* (*e.r.* = 95.5:4.5)].

Deuterations. General Method B: Lithiation and subsequent deuteration of thiocarbamate **14b** was performed under varying conditions. Detailed procedure for an experiment with preparative separation and characterization of the resulting products **20a** and **21a**: A solution of thiocarbamate *rac*-**14b** (32 mg, 0.16 mmol) and TMEDA (42 mg, 0.36 mmol, 2.2 equiv.) in toluene (1 mL) in a flask with a magnetic stirrer bar and a rubber septum was cooled to −78 °C in a dry ice/acetone bath. sBuLi (0.29 mL, 1.23 M solution, 0.36 mmol, 2.2 equiv.) was added dropwise, the flask was sealed with Parafilm®, and stirring at −78 °C was continued for additional 14.5 h. MeOD (30 μL, 0.72 mmol, 4.5 equiv.) was then added by syringe, and 10 min later the reaction mixture was neutralized with DOAc (0.36 mL, 1.0 M solution in Et_2O, 0.36 mmol, 2.2 equiv.). The flask was removed from the cooling bath, and when the reaction mixture had warmed to approx. 0 °C, sat. $NaHCO_3$ solution (2 mL) was added. The combined organic layers of extraction with Et_2O (3 × 10 mL) were washed with brine (1 mL), dried with $MgSO_4$, and filtered, and the solvents were removed in vacuo. A ^{1}H NMR spectrum of the crude product was recorded, and approx. 1 mg was subjected to GC-MS analysis. FCC (31 mL SiO_2; gradient Et_2O/PE, 1:20 → 1:5) provided the thiocarbamate *rac*-**20a** (12 mg, 0.60 mmol, 37%) and its regioisomer *rac*-**21a** (13 mg, 0.65 mmol, 40%), both isolated as colorless crystals (formed in a ratio of 48:52 by reference to GC).

***rac*-*S*-(1-Deuteriocyclohex-2-enyl) *N*-Isopropylmonothiocarbamate (*rac*-20a):** M.p. 89 °C (Et_2O/PE). R_f = 0.33 (Et_2O/PE, 1:3). t_r (HP 1) = 13.3 min; t_r (HP 1701) = 17.9 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 [d, ^3J = 6.7 Hz, 6 H, iPr(CH_3)$_2$]; 1.62−1.73, 1.78−1.86, 1.96−2.07 (each m, 2 H + 1 H + 3 H, $4CH_2$/$5CH_2$/

6CH_2); 4.04 (br. s, 1 H, *i*PrCH); 5.06 (br. s, 1 H, NH); 5.67 (dt, $^3J_{2,3}$ = 9.9, $^4J_{2,4}$ = 2.0 Hz, 1 H, 2CH); 5.81 (dt, $^3J_{3,4}$ = 3.6 Hz, 1 H, 3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7 (5CH_2); 24.8 (4CH_2); 22.9 [*i*Pr(CH_3)$_2$]; 30.1 (6CH_2); 40.8 (*i*PrCH); 43.6 (t, $^1J_{1CD}$ = 12 Hz, 1CD); 126.8 (2CH); 130.6 (3CH) ppm. IR (KBr): $\tilde{\nu}$ = 3276 s [ν(N−H)], 3030 m, 2968 s, 2924 s, 2870 w, 2855 w, 1642 s [ν(C=O)], 1626 s, 1533 s [δ(N−H)], 1455 m, 1385 w, 1367 m, 1230 s, 1222 s, 1204 s, 867 s, 815 s, 751 m, 724 m, 638 m cm^{-1}. GC-MS (EI [80 eV]): *m*/*z* (%) = 200 (32) [M$^+$]; 120 (20) [HS(COH)NH-*i*Pr$^+$]; 115 (11) [{M − *i*PrNCO}$^+$]; 86 (6) [CONH-*i*Pr$^+$]; 82 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 80 (39) [{M − S(CO)NH-*i*Pr − H_2}$^+$]; 70 (13); 58 (9) [CONH-*i*Pr$^+$]; 54 (10) [retro-Diels−Alder {M − S(CO)NH-*i*Pr − C_2H_4}$^+$]; 43 (33) [*i*Pr$^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.31 kV, 33 V], ES$^+$): *m*/*z* (%) = 223 (100) [M + Na$^+$]; 201 (22) [M + H$^+$]. HR-MS (EI [70 eV]): $C_{10}H_{16}$DNOS (200.31): calcd. 200.10936; found 200.11979.

***rac*-*S*-(3-Deuteriocyclohex-1-enyl) *N*-Isopropylmonothiocarbamate (*rac*-21a):** M.p. 102 °C (Et_2O/PE). R_f = 0.25 (Et_2O/PE, 1:3). t_r (HP 1) = 13.4 min; t_r (HP 1701) = 18.4 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 [d, ^3J = 6.7 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.53−1.63, 1.65−1.76 (each m, 2 H + 2 H, 4CH_2/5CH_2); 2.09−2.20 (m, 1 H, 3 CHD); 2.26−2.34 (m, 2 H, 6CH_2); 3.99 (ψ-oct, 1 H, *i*PrCH); 5.22 (br. s, 1 H, NH); 6.19−6.21 (m, 1 H, 2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1, 23.6 (4CH_2/5CH_2); 22.8 [*i*Pr(CH_3)$_2$]; 26.7 (t, $^1J_{3CD}$ = 19 Hz, 3CHD); 32.2 (6CH_2); 43.6 (*i*PrCH); 128.7 (1C); 139.7 (2CH); 165.6 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3284 s [ν(N−H)], 3022 m, 2968 s, 2957 s, 2942 s, 2925 s, 2882 s, 1647 s [ν(C=O)], 1622 s, 1524 s [δ(N−H)], 1448 m, 1386 w, 1365 w, 1317 m, 1220 s, 870 m, 812 s, 702 w, 613 m cm^{-1}. GC-MS (EI [80 eV]): *m*/*z* (%) = 200 (4) [M$^+$]; 115 (92) [{M − *i*PrNCO}$^+$]; 86 (8) [CONH-*i*Pr$^+$]; 82 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 70 (35); 58 (5) [CONH-*i*Pr$^+$]; 54 (8) [retro Diels−Alder {M − S(CO)NH-*i*Pr − C_2H_4}$^+$]; 43 (37) [*i*Pr$^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.31 kV, 33 V], ES$^+$): *m*/*z* (%) = 239 (52) [M + K$^+$]; 223 (50) [M + Na$^+$]; 201 (100) [M + H$^+$]. HR-MS (EI [70 eV]): $C_{10}H_{16}$DNOS (200.31): calcd. 200.10936; found 200.11521.

Alkylations. General Procedure C: Alkylations were performed under standard deprotonation conditions (General Procedure B); the ratio of *s*BuLi and electrophile − the alkyl halide − was crucial here for optimum yields. The optimum molar amount of employed electrophile is given by the total molar amount of *s*BuLi minus the molar amount of thiocarbamate (the molar amount of thiocarbamate must not be multiplied by the number of the acidic protons − it has to be substracted one time). If lower amounts were used, conversions were lower, if higher amounts were used, additional *N*-alkylation occurred, resulting in reduced yields of the more readily purified and crystallizable *N*-monoalkylthiocarbamates. Representative procedure: Thiocarbamate (*S*)-**14b** (200 mg, 1.00 mmol, 96% *ee*, *e.r.* = 98:2) and TMEDA (291 mg, 2.51 mmol, 2.51 equiv.) were dissolved in THF (5.0 mL) in a flask equipped with a rubber septum. The flask was cooled to −78 °C in a dry ice/acetone bath, and *s*BuLi (1.32 mL, 1.32 M solution, 2.51 mmol, 2.51 equiv.) was added dropwise over a period of 5 min through a precooled needle. The yellow reaction mixture was stirred for an additional 10 min, and benzyl bromide (1.55 mL, 1.0 M solution in THF, 1.55 mmol, 1.55 equiv.) was added dropwise over a period of 3 min through a precooled needle. The flask was sealed with Parafilm® and, after the mixture had stirred for an additional 15.5 h, HOAc/Et_2O (2.51 mL, 1.0 M solution in Et_2O, 2.51 mmol, 2.50 equiv.) was added. The reaction mixture was allowed to warm to approx. 0 °C, and saturated $NaHCO_3$ solution (5 mL) was added. The phases were separated, and the aqueous layer was extracted with EE (3 × 15 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo to afford a yellowish oil, which was subjected to FCC (110 mL SiO_2; gradient Et_2O/PE, 1:50 → 1:15). Thiocarbamates (+)-(*S*)-**20d** (19 mg, 66 μmol, 7%) and (+)-(*S*)-**21d** (172 mg, 0.594 mmol, 59%) were isolated, both as colorless crystals, and each formed with 92% *ee* (*e.r.* = 96:4), 96% stereospecificity.

***S*-(1-Methylcyclohex-2-enyl) *N*-Isopropylmonothiocarbamate (20b):** Methylations followed General Procedure C; yields and stereospecificities are given in Table 3. M.p. 103 °C (Et_2O/PE for *rac*-**20b**); m.p. 103 °C [EE/cyclohexane for (*R*)-**20b** at 87% *ee* (*e.r.* = 93.5:6.5)]. R_f = 0.54 (Et_2O/PE, 1:3). t_r (HP 1) = 13.3 min; t_r (HP 1701) = 17.6 min; t_r (DEX β-120, 115 °C) = 221/226 min; t_r (DEX α-120, 107 °C) = 243/249 min. (*R*)-**20b**: $[\alpha]_D^{20}$ = +159 [*c* = 0.62, $CHCl_3$, at 87% *ee* (*e.r.* = 93.5:6.5)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 [d, ^3J = 6.4 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.60, 1.60−1.68 (s + m, 3 H + 2 H, 1-CH_3 + 5CH_2); 1.76−1.87, 1.91−2.07, 2.26−2.32 (each m, 1 H + 2 H + 1 H, 4CH_2/6CH_2); 3.98 (ψ-oct, 1 H, *i*PrCH); 5.17 (br. s, 1 H, NH); 5.70−5.76 (m, 2 H, 2CH/3CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4 (5CH_2); 22.8/22.9 [*i*Pr(CH_3)$_2$]; 24.7 (4CH_2); 29.0 (1-CH_3); 35.8 (6CH_2); 43.1 (*i*PrCH); 50.5 (1C); 128.6, 132.5 (2CH/3CH); 165.8 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3289 s (ν N−H), 3019 m, 2973 s, 2927 s, 2880 w, 2855 w, 1644 s [ν(C=O)], 1525 s [δ(N−H)], 1453 m, 1368 m, 1223 s, 1170 m, 1131 m, 1091 w, 874 m, 815 s, 736 m, 630 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 213 (34) [M$^+$]; 155 (1) [{M − *i*PrNH}$^+$]; 120 (24) [HS(COH)NH-*i*Pr$^+$]; 95 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 79 (19) [{M − HS(CO)NH-*i*Pr − CH_3}$^+$]; 77 (9) [Ph$^+$]; 67 (6) [retro Diels−Alder {M − S(CO)NH-*i*Pr − C_2H_4}$^+$]. $C_{11}H_{19}$NOS (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 61.97, H 9.19, N 6.49.

***S*-(3-Methylcyclohex-1-enyl) *N*-Isopropylmonothiocarbamate (21b):** Methylations followed General Procedure C; yields and stereospecificities are given in Table 3. M.p. 79 °C (Et_2O/PE for *rac*-**21b**); m.p. 79 °C [EE/cyclohexane for (*R*)-**21b** at 71% *ee* (*e.r.* = 85.5:14.5)]. R_f = 0.42 (Et_2O/PE, 1:3). t_r (HP 1701) = 18.6 min; t_r (DEX β-120, 115 °C) = 221/226 min. (*R*)-**21b**: $[\alpha]_D^{20}$ = +5.6 [*c* = 0.97, $CHCl_3$, at 71% *ee* (*e.r.* = 85.5:14.5)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (d, ^3J = 7.2 Hz, 3 H, 3-CH_3); 1.14, 1.13−1.18 (d + m, ^3J = 6.4 Hz, 6 H + 1 H, *i*Pr(CH_3)$_2$ + C*H*H′); 1.57−1.68, 1.73−1.84, 2.19−2.39 (each m, 1 H + 2 H + 3 H, 3CH/4CH_2/5CH_2/6CH_2); 3.99 (ψ-oct, 1 H, *i*PrCH); 5.24 (br. s, 1 H, NH); 6.06−6.08 (m, 1 H, 2CH). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.84 (d, ^3J = 6.4 Hz, 3 H, *i*PrCH_3); 0.85 (d, ^3J = 6.4 Hz, 3 H, *i*PrCH_3′); 0.94 (d, ^3J = 7.1 Hz, 3 H, 3-CH_3); 1.03−1.18, 1.56−1.80, 2.13−2.27, 2.49−2.71 (each m, 1 H + 3 H + 1 H + 2 H, 3CH/4CH_2/5CH_2/6CH_2); 4.01 (ψ-oct, 1 H, *i*PrCH); 4.79 (br. s, 1 H, NH); 6.23−6.26 (m, 1 H, 2CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (3-CH_3); 22.5 (4CH_2); 22.8 [*i*Pr(CH_3)$_2$]; 29.9, 32.1 (5CH_2/6CH_2); 32.3 (3CH); 43.6 (*i*PrCH); 127.7 (1C); 145.5 (2CH); 165.5 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3302 s [ν(N−H)], 3026 m, 2968 s, 2958 s, 2942 s, 2927 s, 2868 m, 2848 m, 1657 s [ν(C=O)], 1622 s, 1528 s [δ(N−H)], 1453 m, 1367 w, 1315 m, 1222 s, 1131 m, 867 m, 815 m, 696 w, 611 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 213 (2) [M$^+$]; 170 (0.5) [{M − *i*Pr}$^+$]; 155 (1) [{M − *i*PrNH}$^+$]; 128 (39) [McLafferty {M − *i*PrNCO}$^+$]; 113 (18) [{M − *i*PrNCO − Me}$^+$]; 95 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 85 (7) [{M − *i*PrNCO − *n*-Pr}$^+$]; 79 (10) [{M − S(CO)NH-*i*Pr − CH_4}$^+$]; 77 (6) [Ph$^+$]; 67 (7) [retro Diels−Alder {M − S(CO)NH-*i*Pr − C_2H_4}$^+$]. $C_{11}H_{19}$NOS (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 62.09, H 9.01, N 6.42.

Warming Experiments: Dilithiated species (*R*)-**9** was prepared from thiocarbamate (*R*)-**14b** by General Procedure B. The flask with spe-

cies (*R*)-**9** was kept − after the injection of *s*BuLi was completed − for 10 min in the dry ice/acetone bath, and it was then set in a cooling bath of indicated temperature (−50 °C or −26 °C or 0 °C) for 15 min while stirring was continued. The flask was quickly transferred back into the dry ice/acetone cooling bath and after an additional 15 min of stirring the MeI solution was added. Further operative steps followed General Procedure C.

***N*-Isopropyl-3-(methylsulfanyl)cyclohex-2-enecarboxamide (24):** R_f = 0.47 (EE). t_r (HP 1701) = 20.5 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH$_3$); 1.12 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH$_3$′); 1.56−1.91, 2.11−2.18 (each m, 4 H + 2 H, 4CH$_2$/5CH$_2$/6CH$_2$); 2.22 (s, 3 H, *S*−CH$_3$); 2.93−3.00 (m, 1 H, 1CH); 4.04 (dsept, ^3J = 8.1 Hz, 1H *i*PrCH); 5.27−5.30 (m, 1 H, 2CH); 5.41 (br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (*S*−CH$_3$); 21.2 (5CH$_2$); 22.7, 22.8 [*i*Pr(CH$_3$)$_2$/*i*Pr(CH$_3$′)$_2$]; 26.4, 29.6 (4CH$_2$/6CH$_2$); 41.3, 44.2 (*i*PrCH/1CH); 114.9 (2CH); 139.2 (3C); 173.3 (C=O) ppm. IR (KBr): ṽ = 3303 s [ν(N−H)], 3059 w, 2972 s, 2939 s, 2916 s, 2877 m, 1637 s [ν(C=O)], 1541 s [δ(N−H)], 1469 w, 1450 m, 1428 m, 1380 w, 1365 w, 1334 w, 1301 w, 1225 s, 1172 w, 1127 w, 1041 m, 908 m, 803 m, 667 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 213 (17) [M$^+$]; 199 (7) [{M − MeS}$^+$]; 155 (1) [{M − *i*PrNH}$^+$]; 127 (100) [{M − CONH-*i*Pr}$^+$]; 113 (23); 79 (78) [{M − H(CO)NH-*i*Pr − SCH$_3$}$^+$]; 77 (27) [Ph$^+$]. $C_{11}H_{19}NOS$ (213.34): calcd. C 61.93, H 8.98, N 6.57; found C 61.67, H 8.93, N 6.39.

Methylations of thiocarbamate **14a** were performed according to General Procedure C. Yields and stereospecificities are given in Table 4. In one case (Table 4, Entry 5), TMEDA was replaced by 5.0 equiv. HMPT. Dry lithium chloride (7.1 equiv.) was dissolved in THF at room temp. with the aid of an ultrasonic bath (Table 4, Entry 6). In situ *N*-silylation (Table 4, Entry 7) was performed by dropwise addition of 1.1 equiv. of a 1.0 M solution of TMSOTf in THF to the solution of thiocarbamate (*S*)-**14a** and TMEDA in THF at 0 °C. The reaction mixture was stirred for 30 min at room temp., cooled to −78 °C in a dry ice/acetone bath, and subsequently treated with 2.51 equiv. of *s*BuLi and 1.51 equiv. of MeI/THF according to General Procedure C.

***S*-(1-Methylcyclohex-2-enyl) *N*-Methylmonothiocarbamate (18b):** Yields and stereospecificities are given in Table 4. M.p. 57 °C (EE/cyclohexane for *rac*-**18b**); m.p. 64−65 °C [EE/cyclohexane for (+)-(*R*)-**18b** at 67% *ee* (*e.r.* = 83.5:16.5)]. R_f = 0.43 (EE/cyclohexane, 1:2). t_r (HP 1) = 12.5 min; t_r (HP 1701) = 17.2 min; t_r (DEX β-120, 120 °C) = 198/202 min. (*R*)-**18b**: $[\alpha]_D^{20}$ = +117 [*c* = 1.08, $CHCl_3$, at 58% *ee* (*e.r.* = 79:21)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58, 1.58−1.66 (s + m, 3 H + 2 H, 1-CH$_3$ + 5CH$_2$); 1.75−1.86, 1.89−2.06, 2.25−2.33 (each m, 1 H + 2 H + 1 H, 4CH$_2$/6CH$_2$); 2.77 (d, ^3J = 4.8 Hz, 3 H, N−CH$_3$); 5.36 (br. s, 1 H, NH); 5.69−5.72 (m, 2 H, 2CH/3CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3 (5CH$_2$); 24.7 (4CH$_2$); 27.2 (N−CH$_3$); 29.1 (1-CH$_3$); 35.6 (6CH$_2$); 50.5 (1C); 128.6 (3CH); 132.2 (2CH); 167.6 (C=O) ppm. IR (KBr): ṽ = 3305 s [ν(N−H)], 3021 m, 2958 s, 2932 s, 2863 m, 2832 m, 1642 s [ν(C=O)], 1526 s [δ(N−H)], 1443 w, 1410 m, 1362 w, 1225 s, 1169 m, 1086 w, 1004 w, 869 w, 825 m, 788 m, 729 m, 619 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 185 (9) [M$^+$]; 95 (100) [{M − S(CO)NH-Me}$^+$]; 79 (29) [{M − HS(CO)NHMe − CH$_3$}$^+$]; 77 (23) [Ph$^+$]; 67 (6) [retro Diels−Alder {M − S(CO)NHMe − C$_2$H$_4$}$^+$]; 57 (44) [MeNCO$^+$]. $C_9H_{15}NOS$ (185.29): calcd. C 58.34, H 8.16, N 7.56; found C 58.51, H 8.03, N 7.44.

***S*-(3-Methylcyclohex-1-enyl) *N*-Methylmonothiocarbamate (19b):** Yields and stereospecificities are given in Table 4. M.p. 87 °C (EE/cyclohexane for *rac*-**19b**); m.p. 77−78 °C [EE/cyclohexane for (+)-(*R*)-**19b** at 57% *ee* (*e.r.* = 78.5:21.5)]. R_f = 0.34 (EE/cyclohexane, 1:2). t_r (HP 1) = 13.2 min; t_r (HP 1701) = 18.3 min; t_r (DEX β-225, 155 °C) = 48/51 min. (*R*)-**19b**: $[\alpha]_D^{20}$ = +3.0 [*c* = 0.51, $CHCl_3$, at 57% *ee* (*e.r.* = 78.5:21.5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (d, ^3J = 7.1 Hz, 3 H, 3-CH$_3$); 1.10−1.23, 1.55−1.69, 1.71−1.85, 2.18−2.40 (each m, 1 H + 1 H + 2 H + 3 H, 3CH/4CH$_2$/5CH$_2$/6CH$_2$); 2.83 (d, ^3J = 4.9 Hz, 3 H, N−CH$_3$); 5.43 (br. s, 1 H, NH); 6.05−6.08 (m, 1 H, 2CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (3-CH$_3$); 22.4 (4CH$_2$); 27.8 (N−CH$_3$); 29.9, 32.1 (5CH$_2$/6CH$_2$); 32.3 (3CH); 127.4 (1C); 145.5 (2CH) ppm. IR (KBr): ṽ = 3308 s [ν(N−H)], 3024 w, 2955 s, 2929 s, 2914 m, 2871 m, 2860 m, 2848 m, 1656 s [ν(C=O)], 1517 s [δ(N−H)], 1452 w, 1411 m, 1319 w, 1225 s, 1160 m, 1124 m, 1006 m, 969 w, 872 w, 812 m, 631 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 185 (4) [M$^+$]; 95 (100) [{M − S(CO)NHMe}$^+$]; 79 (21) [{M − HS(CO)NHMe − CH$_3$}$^+$]; 77 (12) [Ph$^+$]; 67 (26) [retro-Diels−Alder {M − S(CO)NHMe − C$_2$H$_4$}$^+$]; 57 (7) [MeNCO$^+$]. $C_9H_{15}NOS$ (185.29): calcd. C 58.34, H 8.16, N 7.56; found C 58.59, H 8.38, N 7.55.

***S*-[1-(Prop-2-enyl)cyclohex-2-enyl] *N*-Isopropylmonothiocarbamate (20c):** Allylations followed General Procedure C; yields and stereospecificities are given in Table 5. M.p. 59 °C (EE/cyclohexane for *rac*-**20c**); m.p. 56 °C [EE/cyclohexane for (+)-(*S*)-**20c** at 92% *ee* (*e.r.* = 96:4)]. R_f = 0.43 (Et$_2$O/PE, 1:3); R_f = 0.16 (EE/cyclohexane, 1:10). t_r (HP 1) = 15.2 min; t_r (HP 1701) = 19.5 min; t_r (DEX β-6-TBDM, 122 °C) = 174/178 min. (*S*)-**20c**: $[\alpha]_D^{20}$ = +133 [*c* = 0.90, $CHCl_3$, at 92% *ee* (*e.r.* = 96:4)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH$_3$)$_2$]; 1.58−1.77, 1.79−1.92, 1.94−2.09, 2.13−2.22 (each m, 2 H + 1 H + 2 H + 1 H, 4CH$_2$/5CH$_2$/6CH$_2$); 2.67−2.82 (m, 2 H, 1CH$_2$); 3.97 (ψ-oct, 1 H, *i*PrCH); 5.02−5.04, 5.06−5.10 (each m, 1 H + 1 H, 3′CH$_2$); 5.13 (br. s, 1 H, NH); 5.72−5.91 (m, 3 H, 2′CH/2CH/3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.0 (5CH$_2$); 22.7/22.8 [*i*Pr(CH$_3$)$_2$]; 24.7 (4CH$_2$); 33.1 (6CH$_2$); 43.1 (*i*PrCH); 44.6 (1′CH$_2$); 53.4 (1C); 117.7 (3′CH$_2$); 129.6 (3CH); 130.5 (2CH); 134.3 (2′CH); 165.9 (C=O) ppm. IR (KBr): ṽ = 3292 s [ν(N−H)], 3073 w, 3021 m, 2974 s, 2932 s, 2876 w, 2835 w, 1642 s [ν(C=O)], 1520 s [δ(N−H)], 1444 m, 1367 m, 1216 s, 1164 m, 1129 w, 1059 w, 949 m, 912 m, 871 m, 814 s, 739 m, 627 m cm^{-1}. GC-MS (EI [70 eV]): *m*/*z* (%) = 239 (8) [M$^+$]; 198 (2) [{M − allyl}$^+$]; 154 (5) [{M − *i*PrNCO}$^+$]; 121 (71) [{M − S(CO)NH-*i*Pr}$^+$]; 120 (72) [HS(COH)NH-*i*Pr$^+$ + McLafferty {M − HOCSNH-*i*Pr}$^+$]; 113 (44); 105 (27); 92 (30) [McLafferty {M − HOCSNH-*i*Pr − C$_2$H$_3$}$^+$]; 93 (35) [McLafferty {M − HOCSNH-*i*Pr − C$_2$H$_4$}$^+$]; 91 (54) [McLafferty {M − HOCSNH-*i*Pr − C$_2$H$_5$}$^+$]; 79 (100) {M − HSCONH-*i*Pr − allyl}$^+$]; 77 (39) [Ph$^+$]; 70 (67); 67 (38); 41 (34). $C_{13}H_{21}NOS$ (239.38): calcd. C 65.23, H 8.84, N 5.85; found C 65.20, H 8.62, N 5.72.

***S*-[3-(Prop-2-enyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (21c):** Allylations followed General Procedure C; yields and stereospecificities are given in Table 5. M.p. 65 °C (EE/cyclohexane for *rac*-**21c**); m.p. 66 °C [EE/cyclohexane for (+)-(*S*)-**21c** at 86% *ee* (*e.r.* = 93:7)]. R_f = 0.28 (Et$_2$O/PE, 1:3); R_f = 0.10 (EE/cyclohexane, 1:10). t_r (HP 1) = 16.1 min; t_r (HP 1701) = 20.7 min; t_r (DEX β-225, 150 °C) = 110/118 min. (*S*)-**21c**: $[\alpha]_D^{20}$ = +2.95 [*c* = 0.95, $CHCl_3$, at 86% *ee* (*e.r.* = 93:7)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH$_3$)$_2$]; 1.18−1.28, 1.56−1.86, 2.03−2.12, 2.18−2.37 (each m, 1 H + 3 H + 2 H + 3 H, 3CH/4CH$_2$/5CH$_2$/6CH$_2$/1′CH$_2$); 3.98 (ψ-oct, 1 H, *i*PrCH); 4.98−5.00, 5.01−5.05 (each m, 1 H + 1 H, 3′CH$_2$); 5.26 (br. s, 1 H, NH); 5.67−5.83 (m, 1 H, 2′CH); 6.09−6.12 (m, 1 H, 2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.4 (5CH$_2$); 22.7 [*i*Pr(CH$_3$)$_2$]; 27.5, 32.3 (4CH$_2$/6CH$_2$); 37.2 (3CH); 39.8 (1′CH$_2$); 43.6 (*i*PrCH); 116.5

(3′CH_2); 126.6 (1C); 136.2 (2′CH); 143.3 (2CH); 165.4 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3288 s [ν(N−H)], 3079 m, 3024 m, 2978 s, 2967 s, 2928 s, 2862 m, 2847 m, 1648 s [ν(C=O)], 1620 s, 1523 s [δ(N−H)], 1467 m, 1437 s, 1386 m, 1365 m, 1317 m, 1218 s, 1125 m, 994 m, 913 s, 869 s, 812 s, 699 w, 611 m cm^{-1}. GC-MS (EI [70 eV]): *m*/*z* (%) = 239 (1) [M^+]; 198 (2) [{M − allyl}$^+$]; 154 (12) [{M − *i*PrNCO}$^+$]; 121 (9) [{M − S(CO)NH-*i*Pr}$^+$]; 113 (100) [McLafferty {M − *i*PrNCO − allyl}$^+$]; 79 (51) [{M − S(CO)NH-*i*Pr − propene}$^+$]; 77 (12) [Ph^+]; 70 (56); 42 (22); 41 (21). $C_{13}H_{21}NOS$ (239.38): calcd. C 65.23, H 8.84, N 5.85; found C 65.25, H 8.97, N 5.82.

***S*-(1-Benzylcyclohex-2-enyl) *N*-Isopropylmonothiocarbamate (20d):** Benzylations were carried out by General Procedure C; yields and stereospecificities are given in Table 5. M.p. 106 °C (EE/cyclohexane for *rac*-**20d**); m.p. 99 °C [Et_2O/PE for (+)-(*S*)-**20d** at 92% *ee* (*e.r.* = 96:4)]. R_f = 0.37 (Et_2O/PE, 1:3); R_f = 0.66 (EE/cyclohexane, 1:3). t_r (HP 1) = 20.0 min; t_r (ChiraGrohm 1 (2 × 60 mm), *i*PrOH/*n*hexane, 1:200, 0.10 mL/min) = 9/11 min. (*S*)-**20d**: $[\alpha]_D^{20}$ = +81 [*c* = 0.43, $CHCl_3$, at 92% *ee* (*e.r.* = 96:4)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH_3); 1.18 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH_3′); 1.54−1.67, 1.73−2.08, 2.16−2.24 (each m, 1 H + 4 H + 1 H, 4CH_2/5CH_2/6CH_2); 3.34 (s, 2 H, 1′CH_2); 4.04 (ψ-oct, ^3J = 6.5 Hz, 1 H, *i*PrCH); 5.16 (br. d, 1 H, NH); 5.78 (dψ-t, $^3J_{2,3}$ = 10.0, $^3J_{3,4}$ = 3 Hz, 1 H, 3CH); 5.86 (dm, 1 H, 2CH); 7.16−7.31 (m, 5 H, PhCH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.0 (5CH_2); 22.8, 22.9 (*i*PrCH_3/*i*PrCH_3′); 24.7 (4CH_2); 33.1 (6CH_2); 43.2 (*i*PrCH); 45.9 (1′CH_2); 54.6 (1C); 126.4 (*p*PhCH); 127.6 (*m*PhCH); 129.7 (3 CH); 130.6 (2CH); 131.1 (*o*PhCH); 137.5 (PhC) ppm. IR (KBr): $\tilde{\nu}$ = 3315 s [ν(N−H)], 3028 m, 2971 s, 2932 s, 2874 w, 2860 w, 1641 s [ν(C=O)], 1623 m, 1516 s [δ(N−H)], 1455 m, 1366 w, 1214 s, 1162 m, 1126 w, 919 w, 899 w, 876 m, 813 s, 765 m, 730 m, 707 s, 630 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 289 (16) [M^+]; 204 (4) [{M − *i*PrNCO}$^+$]; 198 (12) [{M − Bn}$^+$]; 171 (68) [{M − S(CO)NH-*i*Pr}$^+$]; 170 (46) [{M − HS(CO)NH-*i*Pr}$^+$]; 155 (6); 141 (9); 129 (21); 113 (86) [{M − *i*PrNCO − Bn}$^+$]; 91 (100) [$C_7H_7^+$ (tropylium)]; 79 (37) [{M − HS(CO)NH-*i*Pr − Bn}$^+$]; 77 (13) [Ph^+]; 70 (15). HR-MS (EI [70 eV]): $C_{17}H_{23}NOS$ (289.44): calcd. 289.15002; found 289.14911.

***S*-(3-Benzylcyclohex-1-enyl) *N*-Isopropylmonothiocarbamate (21d):** Benzylations were carried out by General Procedure C; yields and stereospecificities are given in Table 5. M.p. 93 °C (EE/cyclohexane for *rac*-**21d**); m.p. 105 °C [Et_2O/PE for (+)-(*S*)-**21d** at 92% *ee* (*e.r.* = 96:4)]. R_f = 0.24 (Et_2O/PE, 1:3); R_f = 0.57 (EE/cyclohexane, 1:3). t_r (HP 1) = 21.0 min; t_r (ChiraGrohm 4 (2 × 60 mm), *i*PrOH/*n*hexane, 1:200, 0.10 mL/min) = 14/19 min. (*S*)-**21d**: $[\alpha]_D^{20}$ = +22.1 [*c* = 1.08, $CHCl_3$, at 92% *ee* (*e.r.* = 96:4)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 [d, ^3J = 6.6 Hz, 6 H, *i*Pr$(CH_3)_2$]; 1.19−1.32, 1.55−1.89, 2.24−2.38, 2.50−2.72 (each m, 1 H + 3 H + 2 H + 3 H, 3CH/4CH_2/5CH_2/6CH_2/1′CH_2); 4.01 (ψ-oct, ^3J = 6.5 Hz, 1 H, *i*PrCH); 5.23 (br. d, 1 H, NH); 7.09−7.23 (m, 1 H, 2CH); 7.16−7.31 (m, 3 H, *o*PhCH/*p*PhCH); 7.28 (ψ-t, 2 H, *m*PhCH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.4 (5CH_2); 22.7 [*i*Pr$(CH_3)_2$]; 27.7, 32.4 (4CH_2/6CH_2); 39.3 (3CH); 41.9 (1′CH_2); 43.6 (*i*PrCH); 126.0 (*p*PhCH); 128.3 (*m*PhCH); 128.7 (1C); 129.1 (*o*PhCH); 140.0 (PhC); 143.0 (2CH); 165.4 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3289 s [ν(N−H)], 3023 m, 2973 s, 2933 s, 2908 s, 2860 m, 2848 m, 1657 s [ν(C=O)], 1624 s, 1600 m, 1524 s [δ(N−H)], 1500 s, 1453 m, 1445 m, 1367 m, 1315 m, 1216 s, 1172 m, 1156 m, 1134 m, 874 s, 814 s, 742 s, 696 s, 624 s cm^{-1}. GC-MS (EI [70 eV]): *m*/*z* (%) = 289 (0.5) [M^+]; 204 (10) [{M − *i*PrNCO}$^+$]; 198 (3) [{M − Bn}$^+$]; 171 (2) [{M − S(CO)NH-*i*Pr}$^+$]; 130 (26); 113 (100) [{M − *i*PrNCO − Bn}$^+$]; 91 (43) [$C_7H_7^+$ (tropylium)]; 79 (49) [{M − S(CO)NH-*i*Pr − $PhCH_3$}$^+$]; 70 (66); 42 (27). $C_{17}H_{23}NOS$ (289.44): calcd. C 70.55, H 8.01, N 4.84; found C 70.63, H 8.10, N 4.75.

Thiocarbamate *rac*-**15** was methylated on a 100-mg scale (0.47 mmol) according to General Procedure C; yields are given in Table 6. Performance of the reaction with (*S*)-**15** (100 mg, 0.47 mmol, 91% *ee*, *e.r.* = 95.5:4.5) in THF furnished (+)-(*R*)-**26** (22 mg, 97 μmol, 21%) with 87% *ee* (*e.r.* = 93.5:6.5; 96% stereospecificity) and thiocarbamate (+)-(*R*)-**27** (52 mg, 0.23 mmol, 49%) with 88% *ee* (*e.r.* = 94:6; 97% stereospecificity) both as colorless crystals.

***S*-(1-Methylcyclohept-2-enyl) *N*-Isopropylmonothiocarbamate (26):** M.p. 95 °C (Et_2O/PE for *rac*-**26**); m.p. 96 °C [EE/cyclohexane for (+)-(*R*)-**26** at 87% *ee* (*e.r.* = 93.5:6.5)]. R_f = 0.36 (Et_2O/PE, 1:3). t_r (HP 1701) = 18.9 min; t_r (DEX γ-225, 93 °C) = 888/894 min. (*R*)-**26**: $[\alpha]_D^{20}$ = +170 [*c* = 1.22, $CHCl_3$, at 87% *ee* (*e.r.* = 93.5:6.5)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 [d, ^3J = 6.6 Hz, 6 H, *i*Pr$(CH_3)_2$]; 1.66 (s, 3 H, 1-CH_3); 1.38−1.50, 1.67−1.81, 1.82−1.94, 2.07−2.17, 2.20−2.30, 2.32−2.40 (each m, 1 H + 3 H + 1 H + 1 H + 1 H + 1 H, 4CH_2/5CH_2/6CH_2/7CH_2); 3.99 (ψ-oct, 1 H, *i*PrCH); 5.12 (br. s, 1 H, NH); 5.62 (d, ^3J = 11.6 Hz, 1 H, 2CH); 5.73 (ddd, $^3J_{3,4CH}$ = 6.8, $^3J_{3,4CH'}$ = 5.1 Hz, 1 H, 3CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9 [*i*Pr$(CH_3)_2$]; 26.0, 27.4, 27.9 (5CH_2/6CH_2/7CH_2); 30.8 (1-CH_3); 38.8 (4CH_2); 43.1 (*i*PrCH); 55.8 (1C); 132.5 (2CH); 137.0 (3CH) ppm. IR (KBr): $\tilde{\nu}$ = 3297 s [ν(N−H)], 3014 w, 2968 s, 2927 s, 2874 m, 2856 m, 1644 s [ν(C=O)], 1522 s [δ(N−H)], 1453 m, 1385 w, 1367 w, 1316 w, 1212 s, 1167 m, 1227 w, 1102 w, 951 w, 871 m, 814 s, 778 w, 706 w, 688 w, 610 m cm^{-1}. GC-MS (EI [70 eV]): *m*/*z* (%) = 227 (3) [M^+]; 142 (5) [{M − *i*PrNCO}$^+$]; 120 (11) [HS(COH)NH-*i*Pr$^+$]; 109 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 92 (12); 79 (10); 67 (46). $C_{12}H_{21}NOS$ (227.37): calcd. C 63.39, H 9.31, N 6.16; found C 63.44, H 9.35, N 5.97.

***S*-(3-Methylcyclohept-1-enyl) *N*-Isopropylmonothiocarbamate (27):** M.p. 85 °C (Et_2O/PE for *rac*-**27**); m.p. 81 °C [EE/cyclohexane for (+)-(*R*)-**27** at 88% *ee* (*e.r.* = 94:6)]. R_f = 0.25 (Et_2O/PE, 1:3). t_r (HP 1701) = 19.9 min; t_r (DEX β-225, 135 °C) = 170/177 min. (*R*)-**27**: $[\alpha]_D^{20}$ = +15.5 [*c* = 0.97, $CHCl_3$, at 88% *ee* (*e.r.* = 94:6)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (d, ^3J = 7.1 Hz, 3 H, 3-CH_3); 1.14 [d, ^3J = 6.5 Hz, 6 H, *i*Pr$(CH_3)_2$]; 1.25−1.38, 1.44−1.64, 1.68−1.77, 1.87−1.96, 2.37−2.49, 2.55−2.64 (each m, 1 H + 3 H + 1 H + 1 H + 2 H + 1 H, 3CH/4CH_2/5CH_2/6CH_2/7CH_2); 4.01 (br. s, 1 H, *i*PrCH); 5.22 (br. s, 1 H, NH); 6.03−6.06 (m, 1 H, 2CH) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 22.7, 22.8 [3-CH_3/*i*Pr$(CH_3)_2$]; 26.4, 30.3, 35.0 (4CH_2/5CH_2/6CH_2); 35.4 (3CH); 37.7 (7CH_2); 43.6 (*i*PrCH); 131.8 (1C); 149.9 (2CH) ppm. IR (KBr): $\tilde{\nu}$ = 3305 s [ν(N−H)], 2976 m, 2957 m, 2920 s, 2874 w, 2848 m, 1652 s [ν(C=O)], 1620 w, 1516 s [δ(N−H)], 1455 m, 1383 w, 1361 w, 1337 w, 1331 w, 1208 s, 1167 m, 1150 w, 1135 w, 966 w, 869 m, 809 s, 704 w, 622 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 227 (6) [M^+]; 142 (63) [McLafferty {M − *i*PrNCO}$^+$]; 127 (14) [McLafferty {M − *i*PrNCO − CH_3}$^+$]; 109 (100) [{M − S(CO)NH-*i*Pr}$^+$]; 92 (18); 79 (26); 67 (49); 57 (56); 55 (44). $C_{12}H_{21}NOS$ (227.37): calcd. C 63.39, H 9.31, N 6.16; found C 63.17, H 9.10, N 6.01.

Hydroxyalkylations. General Procedure D: Addition to aldehydes and ketones basically followed General Procedure C, but an excess of carbonyl compound (1.5−25 equiv.) was employed as electrophile.

***rac*-*S*-[3-(1-Hydroxybenzyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (*rac*-21e):** Addition to 1.5 equiv. of benzaldehyde for 19 h at −78 °C by General Procedure D produced a viscous oil, which was subjected to FCC (SiO_2, gradient Et_2O/PE). Separation of diastereomeric adducts *syn*-*rac*-**21e** and *anti*-*rac*-**21e** by simple

FCC was insufficient, the isolated mixture of diastereomers showed *d.r.* = 55:45 (1.23:1; *syn*/*anti*). HPLC provided a sample of almost diastereomerically pure *syn*-*rac*-**21e**.

Adduct *syn*-21e: R_f = 0.25 (Et_2O/PE, 1:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.16 [d, ^3J = 6.5 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.43−1.62, 1.80−1.89, 2.22−2.29, 2.67−2.75 (each m, 3 H + 1 H + 2 H + 1 H, 3CH/4CH_2/5CH_2/6CH_2); 2.65 (br. s, 1 H, OH); 4.03 (ψ-oct, 1 H, *i*PrCH); 4.78 (d, $^3J_{3,1'}$ = 5.0 Hz, 1 H, 1′CH); 5.43 (br. s, 1 H, NH); 6.07 (s, 1 H, 2CH); 7.24−7.30, 7.34−7.38 (each m, 1 H + 4 H, PhCH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 22.3 (4CH_2/5CH_2); 22.7/22.8 [*i*Pr(CH_3)$_2$]; 32.7 (6CH_2); 43.9 (*i*PrCH); 45.2 (3CH); 76.2 (1′CH); 126.2 (PhCH); 127.4 (*p*PhCH); 128.2 (PhCH); 131.0 (1C); 141.6 (2CH); 142.3 (PhC); 165.4 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3494 s [ν(O−H)], 3316 s [ν(N−H)], 3062 w, 3030 w, 2972 s, 2933 s, 2867 m, 1653 s [ν(C=O)], 1525 s [δ(N−H)], 1497 s, 1453 s, 1388 w, 1369 w, 1319 w, 1207 s, 1168 m, 1190 w, 1068 m, 1047 m, 1027 m, 1005 m, 871 m, 811 m, 763 m, 702 s cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 287 (0.5) [{M − H_2O}$^+$]; 244 (0.5) [{M − H_2O − *i*Pr}$^+$]; 220 (3) [McLafferty {M − *i*PrNCO}$^+$]; 199 (80) [McLafferty {M − Ph−CHO}$^+$]; 120 (24) [HS(COH)NH-*i*Pr$^+$]; 114 (49); 113 (100); 107 (55) [Ph−CHOH$^+$]; 81 (47) [McLafferty {M − Ph−CHO − S(CO)NH-*i*Pr}$^+$]; 79 (84) [{M − BnOH − S(CO)NH-*i*Pr}$^+$]; 77 (35) [Ph$^+$]; 60 (22). HR-MS (ESI [MeOH/$CHCl_3$], ES$^+$): $C_{17}H_{23}NO_2S$ (305.44): [M + H$^+$] calcd. 306.1528; found 306.1527; [M + Na$^+$] calcd. 328.1347; found 328.1379.

Adduct *anti*-21e:[66] R_f = 0.23 (Et_2O/PE, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17/1.18 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.42−1.70, 1.82−1.93, 2.17−2.35, 2.60−2.77 (each m, 3 H + 1 H + 2 H + 2 H, OH/3CH/4CH_2/5CH_2/6CH_2); 4.03 (ψ-oct, 1 H, *i*PrCH); 4.59 (d, ^3J = 5.5 Hz, 1 H, 1′CH); 5.49 (br. s, 1 H, NH); 6.28 (d, ^3J = 2.0 Hz, 1 H, 2CH); 7.23−7.39 (m, 5 H, PhCH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6 (4CH_2); 22.7 [*i*Pr(CH_3)$_2$]; 25.4 (5CH_2); 32.6 (6CH_2); 43.8 (*i*PrCH); 45.0 (3CH); 77.1 (1′CH); 126.0 (PhCH); 127.3 (*p*PhCH); 128.3 (PhCH); 130.8 (1C); 139.7 (2CH); 143.3 (PhC); 165.5 (C=O).

***rac*-*S*-[3-(1-Hydroxy-2-methylpropyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (*rac*-21f):** Addition to 1.5 equiv. of 2-methylpropanal for 14 h at −78 °C according to General Procedure D produced a viscous syrup. Diastereomeric adducts *syn*-*rac*-**21f** and *anti*-*rac*-**21f** were separated by FCC (SiO_2, gradient Et_2O/PE) yielding crystallizing, resin-like compounds. ^1H NMR on the crude product established *d.r.* = 55:45 (1.20:1; *syn*/*anti*), in good agreement with the ratio of 54:46 (1.16:1; *syn*/*anti*) of the isolated adducts. Crystals of the adduct *syn*-*rac*-**21f** suitable for X-ray structure analysis were grown by diffusion of PE into a solution of *syn*-*rac*-**21f** in Et_2O.

Adduct *syn*-21f: M.p. 123 °C (Et_2O/PE). R_f = 0.33 (Et_2O/PE, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, ^3J = 6.7 Hz, 3 H, 3′CH_3); 0.99 (d, ^3J = 6.6 Hz, 3 H, 2′-CH_3); 1.12/1.13 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.44−1.92, 2.16−2.32 (each m, 5 H + 3 H, OH/4CH_2/5CH_2/6CH_2/2′CH); 2.49−2.58 (m, 1 H, 3CH); 3.25 (dψ-t, $^3J_{1',2'}$ = 8.3, $^3J_{1',3}$ = 3.7 Hz, 1 H, 1′CH); 4.00 (ψ-oct, 1 H, *i*PrCH); 5.48 (br. s, 1 H, NH); 6.00−6.03 (m, 1 H, 2CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9 (3′CH_3); 19.1 (2′-CH_3); 20.3, 22.5 (4CH_2/5CH_2); 22.7 [*i*Pr(CH_3)$_2$]; 30.4 (2′CH); 32.7 (6CH_2); 40.7 (3CH); 43.8 (*i*PrCH); 79.3 (1′C); 130.3 (1C); 143.3 (2CH); 165.5 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3436 s [ν(O−H)], 3244 s [ν(N−H)], 3035 w, 2973 s, 2955 s, 2939 s, 1930 s, 2871 m, 1653 s [ν(C=O)], 1534 s [δ(N−H)], 1467 m, 1455 m, 1443 m, 1391 m, 1366 m, 1323 w, 1217 s, 1168 m, 1130 m, 1072 m, 1004 m, 984 m, 891 m, 813 m, 642 w, 533 w cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 271 (1) [M$^+$]; 228 (3) [{M − *i*Pr}$^+$]; 199 (71) [McLafferty {M − *i*Pr-CHO}$^+$]; 413 (8); 120 (33) [HS(COH)NH-*i*Pr$^+$]; 114 (94); 113 (81); 81 (100) [McLafferty {M − *i*Pr−CHO − S(CO)NH-*i*Pr }$^+$]; 79 (59) [{M − *i*Pr−CH_2OH − S(CO)NH-*i*Pr}$^+$]; 77 (12) [Ph$^+$]; 55 (26). MS (ESI {MeOH/$CHCl_3$}, [1.33 kV, 42 V], ES$^+$): *m*/*z* (%) = 294 (100) [M + Na$^+$]; 272 (20) [M + H$^+$]. HR-MS (ESI [MeOH/$CHCl_3$], ES$^+$): $C_{14}H_{25}NO_2S$ (271.42): [M + H$^+$] calcd. 272.1684; found 272.1661; [M + Na$^+$] calcd. 294.1504; found 294.1494.

Adduct *anti*-21f: R_f = 0.26 (Et_2O/PE, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.82 (d, ^3J = 8.8 Hz, 3 H, 3′CH_3); 0.94 (d, ^3J = 8.7 Hz, 3 H, 2′-CH_3); 1.12/1.13 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.41−1.94, 2.22−2.29 (each m, 6 H + 2 H, OH/4CH_2/5CH_2/6CH_2/2′CH); 2.44−2.55 (m, 1 H, 3 CH); 3.13 (dψ-t, $^3J_{1',2'}$ = 6.7, $^3J_{1',3}$ = 4.9 Hz, 1 H, 1′CH); 4.00 (ψ-oct, 1 H, *i*PrCH); 5.58 (br. s, 1 H, NH); 6.27 (d, ^3J = 1.9 Hz, 1 H, 2CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6 (3′CH_3); 19.6 (2′-CH_3); 22.7 [*i*Pr(CH_3)$_2$]; 22.8, 25.7 (4CH_2/5CH_2); 31.0 (2′CH); 32.6 (6CH_2); 40.3 (3CH); 43.7 (*i*PrCH); 80.1 (1′C); 130.7 (1C); 140.3 (2CH); 165.6 (C=O). $C_{14}H_{25}NO_2S$ (271.42): calcd. C 61.95, H 9.28, N 5.16; found C 61.85, H 9.34, N 5.08.

***S*-[3-(1-Hydroxy-1-methylethyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (21g):** Hydroxyalkylations were carried out according to General Procedure D; yields and stereospecificities are given in Table 8. M.p. 86 °C (EE/cyclohexane for *rac*-**21g**); (−)-(*R*)-**21g** was isolated as a resin-like compound. R_f = 0.17 (Et_2O/PE, 2:1); R_f = 0.30 (EE/cyclohexane, 1:1). t_r (HP 1) = 17.7 min; t_r (DEX β-225, 160 °C) = 156/161 min. (*R*)-**21g**: $[\alpha]_D^{20}$ = −16.0 [*c* = 0.775, $CHCl_3$, at 73% *ee* (*e.r.* = 86.5:13.5)]. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.16 (s, 3 H, 1′-CH_3); 1.22 (s, 3 H, 2′CH_3); 1.26−1.39, 1.50−1.65, 1.75−1.93, 2.20−2.34 (each m, 1 H + 1 H + 3 H + 3 H, OH/3CH/4CH_2/5CH_2/6CH_2); 3.98 (ψ-oct, 1 H, *i*PrCH); 5.46 (br. d, 1 H, NH); 6.30 (br. s, 1 H, 2CH). ^1H NMR (300 MHz, C_6D_6); δ = 0.84 (d, ^3J = 6.5 Hz, 3 H, *i*PrCH_3); 0.85 (d, ^3J = 6.5 Hz, 3 H, *i*PrCH_3′); 1.13 (s, 3 H, 1′-CH_3); 1.14 (s, 3 H, 2′CH_3); 1.42 (br. s, 1 H, OH); 1.24−1.37, 1.51−1.68, 1.75−1.85, 2.14−2.22, 2.40−2.59 (each m, 1 H + 2 H + 1 H + 1 H + 2 H, 3CH/4CH_2/5CH_2/6CH_2); 4.01 (ψ-oct, 1 H, *i*PrCH); 4.91 (br. s, 1 H, NH); 6.60−6.63 (m, 1 H, 2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8 [*i*Pr(CH_3)$_2$]; 23.1, 23.3 (4CH_2/5CH_2); 26.5 (1′-CH_3); 28.4 (2′CH_3); 32.3 (6CH_2); 43.7 (*i*PrCH); 48.7 (3CH); 72.8 (1′C); 130.4 (1C); 140.6 (2CH); 165.6 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3404 s [ν(O−H)], 3257 s [ν(N−H)], 3040 w, 2972 s, 2948 s, 2935 s, 2877 w, 2855 m, 1646 s [ν(C=O)], 1620 m, 1532 s [δ(N−H)], 1456 m, 1379 m, 1368 m, 1268 w, 1215 s, 1135 m, 932 w, 906 m, 874 m, 812 m, 640 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 242 (2) [{M − CH_3}$^+$]; 211 (1) [{M − *i*Pr}$^+$]; 199 (59) [McLafferty {M − acetone}$^+$]; 172 (2) [{M − *i*PrNCO}$^+$]; 171 (2) [{M − CONH-*i*Pr}$^+$]; 157 (7) [{M − *i*PrNCO − CH_3}$^+$]; 139 (5) [{M − S(CO)NH-*i*Pr}$^+$]; 120 (36) [HS(COH)NH-*i*Pr$^+$]; 114 (53); 81 (95) [McLafferty {M − acetone − S(CO)NH-*i*Pr}$^+$]; 79 (41) [{M − $CH_3CHOHCH_3$ − S(CO)NH-*i*Pr }$^+$]; 59 (100) [$CH_3COHCH_3^+$]. MS (ESI {MeOH/$CHCl_3$}, ES$^+$): *m*/*z* (%) = 537 (30) [{2 × M + Na}$^+$]; 280 (100) [M + Na$^+$]; 258 (12) [M + H$^+$]. $C_{13}H_{23}NO_2S$ (257.39): calcd. C 60.66, H 9.01, N 5.44; found C 60.81, H 8.93, N 5.34.

Acetone Adducts of Thiocarbamate 14a: Hydroxyalkylations were carried out according to General Procedure D; yields and stereospecificities are given in Table 8.

***S*-[1-(1-Hydroxy-1-methylethyl)cyclohex-2-enyl] *N*-Methylmonothiocarbamate (18g):** M.p. 146 °C (Et_2O/PE for *rac*-**18g**). R_f = 0.25 (EE/cyclohexane, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 (s,

3 H, 1′-CH_3); 1.37 (s, 3 H, 2′CH_3); 1.63−1.80, 1.83−2.21 (each m, 2 H + 5 H, OH/4CH_2/5CH_2/6CH_2); 2.81 (d, ^3J = 4.9 Hz, 3 H, N−CH_3); 5.89 (br. s, 1 H, NH); 5.64 (dd, $^3J_{2,3}$ = 10.1, $^4J_{2,4}$ = 2.0 Hz, 1 H, 2CH); 5.82−5.88 (dm, 1 H, 3CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.1 (1′-CH_3/2′CH_3); 24.8, 26.3 (4CH_2/5CH_2); 27.7 (N−CH_3); 29.2 (6CH_2); 65.3 (1C); 76.6 (1′C); 126.7 (2CH); 131.1 (3CH); 167.2 (C=O) ppm. IR (KBr): ṽ = 3352 s [ν(O−H)], 3291 s [ν(N−H)], 2979 s, 2958 m, 2940 s, 2861 w, 2856 w, 1629 s [ν(C=O)], 1504 s [δ(N−H)], 1462 m, 1437 m, 1409 m, 1382 w, 1366 w, 1218 s, 1164 m, 1064 m, 1064 w, 1006 w, 963 m, 920 w, 890 m, 825 m, 791 m, 735 w, 679 m, 592 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 229 (2) [M$^+$]; 211 (6) [{M − H_2O}$^+$]; 171 (73) [McLafferty {M − acetone}$^+$]; 154 (12); 139 (28) [{M − SCONHMe}$^+$]; 114 (26); 113 (28); 92 (94) [HS(HO)CNHMe$^+$]; 81 (100) [McLafferty {M − acetone − S(CO)NHMe}$^+$]; 79 (57) [{M − $CH_3CHOHCH_3$ − S(CO)NHMe}$^+$]; 59 (63) [$CH_3COHCH_3^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.31 kV, 34 V], ES$^+$): *m*/*z* (%) = 252 (100) [M + Na$^+$]; 230 (12) [M + H$^+$] → {230 (105); 212 (100) [{M − H_2O} + Na$^+$]; 155 (20); 139 (20); 92 (18) [HS(HO)CNHMe$^+$]}. HR-MS (ESI [MeOH/$CHCl_3$], ES$^+$): $C_{11}H_{19}NO_2S$ (229.34) [{2 × M} + H$^+$]: calcd. 459.2351; found 459.2316; [{2 × M} + Na$^+$]: calcd. 481.2171; found 481.2155 (both Coulomb dimers).

***S*-[3-(1-Hydroxy-1-methylethyl)cyclohex-1-enyl] *N*-Methylmonothiocarbamate (19g):** Isolated as a resin-like compound. R_f = 0.17 (EE/cyclohexane, 1:1). t_r (DEX β-225, 170 °C) = 100/107 min. (*S*)-**19g**: $[\alpha]_D^{20}$ = +9.2 [*c* = 1.0, $CHCl_3$, at 63% *ee* (*e.r.* = 81.5:18.5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (s, 3 H, 1′-CH_3); 1.25 (s, 3 H, 2′CH_3); 1.27−1.41, 1.52−1.68, 1.77−1.95, 2.22−2.36 (each m, 1 H + 2 H + 2 H + 3 H, OH/3CH/4CH_2/5CH_2/6CH_2); 2.82 (d, ^3J = 4.9 Hz, 3 H, N−CH_3); 5.62 (br. s, 1 H, NH); 6.32 (br. s, 1 H, 2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.1, 23.3 (4CH_2/5CH_2); 26.5 (1′-CH_3); 27.9 (N−CH_3); 28.4 (2′CH_3); 32.4 (6CH_2); 48.6 (3CH); 72.8 (1′C); 130.3 (1C); 140.7 (2CH); 167.2 (C=O) ppm. IR (KBr): ṽ = 3423 s [ν(O−H)], 3278 s [ν(N−H)], 2981 s, 2975 s, 3952 s, 2947 s, 2861 w, 1655 s [ν(C=O)], 1534 s [δ(N−H)], 1452 m, 1407 m, 1379 m, 1223 s, 1178 w, 1153 w, 1128 m, 1006 w, 932 w, 906 m, 847 w, 815 m, 624 m cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 229 (0.2) [M$^+$]; 214 (1) [{M − CH_3}$^+$]; 171 (46) [McLafferty {M − acetone}$^+$]; 157 (5) [{M − MeNCO − CH_3}$^+$]; 113 (23); 92 (61) [HS(HO)CNHMe$^+$]; 81 (83) [McLafferty {M − acetone − S(CO)NHMe}$^+$]; 79 (37) [{M − $CH_3CHOHCH_3$ − S(CO)NHMe}$^+$]; 59 (100) [$CH_3COHCH_3^+$]. MS (ESI {MeOH/$CHCl_3$}, [1.32 kV, 29 V], ES$^+$): *m*/*z* (%) = 268 (12) [M + K$^+$]; 252 (100) [M + Na$^+$]; 230 (22) [M + H$^+$] → {230 (35); 212 (100) [{M − H_2O} + Na$^+$]; 155 (28); 139 (95)}. $C_{11}H_{19}NO_2S$ (229.34): calcd. C 57.61, H 8.35, N 6.11; found C 57.69, H 8.23, N 6.55. HR-MS (ESI [MeOH/$CHCl_3$], ES$^+$): [M + NH_4^+]: calcd. 247.1480; found 247.1522; [M + Na$^+$]: calcd. 252.1034; found 252.1072.

***S*-[3-(1-Hydroxycyclohexyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (21h):** Hydroxyalkylations were carried out according to General Procedure D; yields and stereospecificities are given in Table 8. M.p. 153 °C (Et_2O/PE for *rac*-**21h**); m.p. 141 °C [Et_2O/PE for (+)-(*S*)-**21h** at 90% *ee* (*e.r.* = 95:5)]. R_f = 0.12 (Et_2O/PE, 1:1). t_r [ZWE-805 (4 × 250 mm), H_2O/THF/*n*-hexane, 1:1000:4000, 0.50 mL/min] = 12/14 min. (*S*)-**21h**: $[\alpha]_D^{20}$ = +11.4 [*c* = 1.82, $CHCl_3$, at 90% *ee* (*e.r.* = 95:5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 [d, ^3J = 6.6 Hz, 6 H, *i*Pr(CH_3)$_2$]; 1.15−1.27, 1.30−1.65, 1.65−1.81, 1.83−1.94, 2.17−2.26, 2.28−2.38 (each m, 1 H + 11 H + 2 H + 1 H + 2 H + 1 H, OH/3CH/4CH_2/5CH_2/6CH_2/2′CH_2/3′CH_2/4′CH_2/5′CH_2/6′CH_2); 3.99 (ψ-oct, 1 H, *i*PrCH); 5.56 (br. s, 1 H, NH); 6.30 (br. s, 1 H, 2CH). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.84 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH_3); 0.85 (d, ^3J = 6.6 Hz, 3 H, *i*PrCH_3′); 1.11−1.88, 2.16−2.25, 2.44−2.52 (each m, 15 H + 1 H + 2 H, OH/3CH/4CH_2/5CH_2/6CH_2/2′CH_2/3′CH_2/4′CH_2/5′CH_2/6′CH_2); 4.01 (ψ-oct, 1 H, *i*PrCH); 4.96 (br. d, 1 H, NH); 6.56−6.59 (m, 1 H, 2CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.93, 21.96, 22.2 (3′CH_2/4′CH_2/5′CH_2); 22.7 [*i*Pr(CH_3)$_2$]; 23.1, 25.7 (4CH_2/5CH_2); 32.5 (6CH_2); 34.2, 35.7 (2′CH_2/6′CH_2); 43.6 (*i*PrCH); 47.2 (3CH); 73.2 (1′C); 130.5 (1C); 140.6 (2CH); 165.5 (C=O) ppm. IR (KBr): ṽ = 3458 s [ν(O−H)], 3270 s [ν(N−H)], 2970 m, 2929 s, 2856 m, 1654 s [ν(C=O)], 1524 s [δ(N−H)], 1447 m, 1419 w, 1386 w, 1365 w, 1319 w, 1279 w, 1215 s, 1167 w, 1129 w, 957 m, 874 w, 813 w, 539 w cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 199 (27) [McLafferty {M − cyclohexanone}$^+$]; 171 (3) [McLafferty + retro Diels−Alder {M − cyclohexanone − C_2H_4}$^+$]; 120 (34) [HS(COH)NH-*i*Pr$^+$]; 114 (36); 99 (51) [*c*$C_6H_{10}OH^+$]; 81 (100) [McLafferty {M − cyclohexanone − S(CO)NH-*i*Pr }$^+$]; 79 (44) [{M − *c*C_6H_{11}OH − S(CO)NH-*i*Pr}$^+$]; 77 (12) [Ph$^+$]; 55 (26). MS (ESI {MeOH/$CHCl_3$}, [1.32 kV, 33 V], ES$^+$): *m*/*z* (%) = 320 (100) [M + Na$^+$]; 298 (8) [M + H$^+$]. HR-MS (ESI [MeOH/$CHCl_3$], ES$^+$): $C_{16}H_{27}NO_2S$ (297.46): [M + H$^+$]: calcd. 298.1841; found 298.1829; [M + Na$^+$]: calcd. 320.1660; found 320.1674.

***S*-[3-(1-Hydroxy-1-phenylbenzyl)cyclohex-1-enyl] *N*-Isopropylmonothiocarbamate (21i):** Hydroxyalkylations were carried out according to General Procedure D; yields and stereospecificities are given in Table 8. M.p. 130 °C (Et_2O/PE for *rac*-**21i**); m.p. 129 °C [Et_2O/PE for (*S*)-**21i** at 23% *ee* (*e.r.* = 61.5:38.5)]. R_f = 0.14 (Et_2O/PE, 1:3). t_r [ChiraGrohm 2 (2 × 250 mm), *i*PrOH/*n*hexane, 3:97, 0.30 mL/min] = 6/9 min. (*S*)-**21i**: $[\alpha]_D^{20}$ = +21.7 [*c* = 1.39, $CHCl_3$, at 23% *ee* (*e.r.* = 61.5:38.5)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, ^3J = 6.7 Hz, 3 H, *i*PrCH_3); 1.15 (d, ^3J = 7.1 Hz, 3 H, *i*PrCH_3′); 1.40−1.50, 1.52−1.65, 1.78−1.89, 2.17−2.26 (each m, 2 H + 1 H + 1 H + 2 H, 4CH_2/5CH_2/6CH_2); 3.60−3.69 (m, 1 H, 3CH); 3.67 (s, 1 H, OH); 3.92−4.09 (m, 1 H, *i*PrCH); 5.21 (d, ^3J = 7.6 Hz, 1 H, NH); 5.94−5.96 (m, 1 H, 2CH); 7.13 (tt, $^3J_{m\mathrm{Ph},p\mathrm{Ph}}$ = 6.6, $^4J_{o\mathrm{Ph},p\mathrm{Ph}}$ = 1.3 Hz, 1 H, *p*PhCH); 7.17 (tt, 1 H, *p*Ph′CH); 7.22−7.33 (m, 4 H, *m*PhCH/*m*Ph′CH); 7.51 (dm, 2 H, *o*PhCH); 7.62 (dm, 2 H, *o*Ph′CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 [*i*Pr(CH_3)$_2$]; 22.8, 22.9, 33.1 (4CH_2/5CH_2/6CH_2); 44.1 (*i*PrCH); 45.8 (3CH); 79.4 (1′CH); 125.5, 125.9 (*m*PhCH/*m*Ph′CH); 126.2, 126.5 (*p*PhCH/*p*Ph′CH); 128.0 128.3 (*o*PhCH/*o*Ph′CH); 132.7 (1C); 140.4 (2CH); 145.5, 146.9 (PhC/Ph′C); 165.4 (C=O) ppm. IR (KBr): ṽ = 3451 s [ν(O−H)], 3291 s [ν(N−H)], 3059 m, 3029 m, 2971 s, 2933 s, 2873 m, 2832 m, 1655 s [ν(C=O)], 1638 s [ν(C=C_{Ph})], 1528 s [δ(N−H)], 1493 s [ν(C=C_{Ph})], 1447 m, 1388 w, 1366 w, 1321 w, 1216 s, 1168 w, 1007 m, 974 w, 909 s, 869 w, 810 m, 743 s, 728 s, 701 s, 655 w, 638 w, 539 w cm^{-1}. MS (EI [70 eV]): *m*/*z* (%) = 318 (0.2) [M$^+$]; 199 (56) [McLafferty {M − benzophenone}$^+$]; 183 (100) [PhCOHPh$^+$]; 120 (26) [HS(COH)NH-*i*Pr$^+$]; 105 (95) [PhCO$^+$ from benzophenone]; 81 (38) [McLafferty {M − benzophenone − S(CO)NH-*i*Pr }$^+$]; 79 (18) [{M − Ph_2CHOH − S(CO)NH-*i*Pr}$^+$]; 77 (43) [Ph$^+$]; 55 (26). $C_{23}H_{23}NO_2S$ (381.35): calcd. C 72.40, H 7.13, N 3.67; found C 72.12, H 7.01, N 3.33.

Ni^0-Catalyzed Cross-Coupling Providing Isoterpineol 28: Toluene (3 mL) was added to [1,2-bis(diphenylphosphanyl)ethane]nickel(II) chloride (30 mg, 57 μmol, 15 mol %) and thiocarbamate (+)-**19g** (87 mg, 0.38 mmol, 63% *ee*, *e.r.* = 81.5:18.5) in a Schlenk tube. After careful addition of methylmagnesium bromide solution (0.78 mL 2.9 M in Et_2O, 2.3 mmol, 6.0 equiv.) at room temp., the gray, cloudy reaction mixture was heated to 90 °C in an oil bath for 18 h with stirring. Ether (15 mL) and aqueous HCl (7 mL, 2.0 M) were added at room temp., the phases were separated, and the aqueous layer was extracted with ether (2 × 10 mL). The combined

Table 9. Details of X-ray crystallographic studies

	(+)-(*R*)-**14c**	(−)-(*S*)-**20b**	(−)-(*S*)-**21b**	(+)-(*S*)-**21d**	**21g**
Empirical formula	$C_{11}H_{19}NOS$	$C_{11}H_{19}NOS$	$C_{11}H_{19}NOS$	$C_{17}H_{23}NOS$	$C_{13}H_{23}NO_2S$
Molecular mass	213.33	213.33	213.33	289.42	257.38
Temperature	223(2) K	223(2) K	223(2) K	223(2) K	223(2) K
Wavelength	1.54178 Å	1.54178 Å	1.54178 Å	1.54178 Å	1.54184 Å
Crystal system, space group	orthorhombic, $P2_12_12_1$ (no. 19)	$P2_1$ (no. 4)	triclinic, $P1$ (no. 1)	orthorhombic, $P2_12_12_1$ (no.19)	triclinic, $P\bar{1}$ (no. 2)
Unit cell dimensions	a = 9.685(2) Å b = 12.590(1) Å c = 20.348(3) Å	a = 5.985(4) Å b = 22.318(9) Å, β = 98.90(4)° c = 9.231(4) Å	a = 6.510(1) Å, α = 86.60(2)° b = 9.076(1) Å, β = 88.21(2)° c = 11.169(3) Å, γ = 75.08(1)°	a = 9.892(6) Å b = 11.864(3) Å c = 13.674(2) Å	a = 9.891(2) Å, α = 83.18(1)° b = 12.242(2) Å, β = 69.66(2)° c = 13.659(2) Å, γ = 74.94(1)°
Volume	2481.1(7) Å^3	1218.2(11) Å^3	636.5(2) Å^3	1604.8(11) Å^3	1496.8(4) Å^3
Z, calculated density	8, 1.142 Mg/m^3	4, 1.163 Mg/m^3	2, 1.113 Mg/m^3	4, 1.198 Mg/m^3	4, 1.142 Mg/m^3
Absorption coefficient	2.079 mm^{-1}	2.117 mm^{-1}	2.026 mm^{-1}	1.742 mm^{-1}	1.853 mm^{-1}
F(000)	928	464	232	624	560
Crystal size	0.60 × 0.50 × 0.30 mm	0.25 × 0.20 × 0.20 mm	0.50 × 0.15 × 0.10 mm	0.40 × 0.08 × 0.05 mm	0.45 × 0.10 × 0.05 mm
θ range for data collection	4.13−74.16°	3.96−74.39°	3.97−74.21°	4.93−74.20°	3.45−66.49°
Limiting indices	$-12 \le h \le 0$, $0 \le k \le 15$, $-25 \le l \le 0$	$0 \le h \le 7$, $0 \le k \le 27$, $-11 \le l \le 11$	$-7 \le h \le 8$, $0 \le k \le 11$, $-13 \le l \le 13$	$0 \le h \le 12$, $-14 \le k \le 0$, $0 \le l \le 17$	$-11 \le h \le 11$, $-14 \le k \le 14$, $0 \le l \le 16$
Reflections collected/ unique/observed	2856/2856 [R(int) = 0.00]/2538	2811/2569 [R(int) = 0.015]/2330	2758/2758 [R(int) = 0.000]/2297	1875/1875 [R(int) = 0.000]/1299	5528/5286 [R(int) = 0.047]/2172
Max./min. transmission	0.574/0.369	0.677/0.620	0.823/0.431	0.918/0.542	0.913/0.489
Refinement method	Full-matrix, least squares on F^2	Full-matrix, least squares on F^2	Full-matrix, least squares on F^2	Full-matrix, least squares on F^2	Full-matrix, least squares on F^2
Data/restraints/ parameters	2856/0/266	2569/1/266	2758/3/266	1875/0/187	5286/0/323
Goodness-of-fit on F^2	1.062	1.039	1.086	1.007	1.023
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.054, wR^2 = 0.147	$R1$ = 0.047, wR^2 = 0.123	$R1$ = 0.050, wR^2 = 0.141	$R1$ = 0.045, wR^2 = 0.098	$R1$ = 0.062, wR^2 = 0.103
Absolute structure parameter	0.05(4)	0.02(3)	−0.01(3)	−0.01(4)	−
Extinction coefficient	0.0020(4)	0.007(1)	0.013(2)	−	−
Largest diff. peak/hole	0.35/−0.33 e Å^{-3}	0.26/−0.33 e Å^{-3}	0.25/−0.27 e Å^{-3}	0.26/−0.39 e Å^{-3}	0.25/−0.31 e Å^{-3}

organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. Subsequent FCC (47 mL SiO_2; Et_2O/PE, 1:3) yielded isoterpineol (+)-**28** (53 mg, 0.34 mmol, 91%) as a colorless liquid. Ab initio calculations [aug-SV(p)/BH-LYP and others] indicated the (*S*) absolute configuration for isoterpineol (+)-**28**. R_f = 0.37 (Et_2O/PE, 1:1). t_r (HP 5) = 7.75 min; t_r (HP 1701) = 10.3 min. (+)-(*S*)-**28**: $[\alpha]_D^{20}$ = +24.1 [*c* = 1.10, $CHCl_3$, (*ee* nd)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (s, 3 H, $2CH_3$); 1.16−1.24, 1.18 (m + s, 1 H + 3 H, *n*C*H*H′ + 1-CH_3);* 1.26 (s, 1 H, OH); 1.38−1.54 (m, 1 H, *m*C*H*H′);* 1.67 (s, 3 H, 3′-CH_3); 1.72−1.98 (m, 4 H, 4′CH_2/5′CH_2/6′CH_2);* 2.05−2.16 (m, 1 H, 1′CH); 5.44 (br. s, 1 H, 2′CH); * a definitive assignment of the position is not possible. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 24.3 (5′CH_2/6′CH_2); 24.2 (3′-CH_3); 26.2, 27.9 ($2CH_3$/1-CH_3); 30.0 (4′CH_2); 47.2 (1′CH); 73.0 (1C); 121.4 (2′CH); 136.9 (3′C). MS (EI [70 eV]): *m*/*z* (%) = 154 (3) [M^+]; 139 (6) [{M − CH_3}$^+$]; 136 (3) [{M − H_2O}$^+$]; 96 (78) [retro ene {M − acetone}$^+$]; 81 (69) [retro ene {M − acetone − CH_3}$^+$]; 68 (18); 67 (16); 59 (100) [$CH_3COHCH_3^+$]. GC-HR-MS (EI [70 eV]): $C_{10}H_{18}O$ (154.25): [M − CH_3]: calcd. 139.1123; found 139.1115; [M − H_2O]: calcd. 136.1252; found 136.1287; [M − CH_3 − H_2O]: calcd. 121.1017; found 121.1037.

X-ray Crystallographic Study: Data sets were collected with an Enraf−Nonius CAD4 diffractometer. Programs used: data collection EXPRESS (Nonius B.V., **1994**), data reduction MolEN (K. Fair, Enraf−Nonius B.V., **1990**), structure solution SHELXS-86 and SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr.* **1990**, *A46*, 467−473), structure refinement SHELXL-97 (G. M. Sheldrick, Univ. of Göttingen, **1997**), graphics MoPict 4 (M. Brüggemann, Westfälische Wilhelms-Universität Münster, **2001**). Details are listed in Table 9. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-141924 [(+)-(*R*)-**14c**], -143289 [(−)-(*S*)-**20b**], -143290 [(−)-(*S*)-**21b**], -141448 [(+)-(*S*)-**21d**], and -141081 (**21g**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[31] By General Procedure B, as given in the Exp. Sect. The same lithiation conditions were employed for alkylations in General Procedure C.

[32] The given stereospecificity refers to the transmission of enantioenrichment for the overall process of lithiation and electrophilic substitution. We expect that lithiation should proceed with absolute stereospecificity, in consequence the given stereospecificity should result from a combination of the configurational stability of dilithiated species and the enantiospecificity of the electrophilic substitution step.

[33] For methylation of dianion **9**, other Me^+ sources such as F_3CSO_3Me were not applicable.

[34] This property of thiocarbamate **21b** might be used to prepare larger quantities (> 1 mmol) of high enantiomeric purity.

[35] This can be regarded as additional evidence that inversion of the carbanionic center in **16** (or **9** and **17**) is not the rate-determining step of racemization, because the presence of an excess of Li^+ should facilitate the inversion by an associative process (S_E2 process).

[36] This procedure turned out to be extremely efficient for the *ortho*-lithiation of aromatic *N*-isopropylcarbamates, see: M. Kauch, D. Hoppe, *Can. J. Chem.* **2001**, *79*, 1736−1746.

[37] The absolute configurations were assigned in analogy with methylation of cyclohexenyllithium compounds (*R*)-**9** and (*S*)-**16**.

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[51] TURBOMOLE (Vers. 5.3): R. Ahlrichs, M. Bär, H.-P. Baron, R. Bauernschmitt, S. Böcker, M. Ehrig, K. Eichkorn, S. Elliott, F. Furche, F. Haase, M. Häser, H. Horn, C. Huber, U. Huniar, M. Kattannek, C. Kölmel, M. Kollwitz, K. May, C. Ochsenfeld, H. Öhm, A. Schäfer, U. Schneider, O. Treutler, M. von Arnim, F. Weigend, P. Weis, H. Weiss, Universität Karlsruhe, **2000**.
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[58] (***(AUTHOR: The meaning of this sentence is unclear! Can it be rephrased?))*** The determined experimental [α] values have been corrected to 100% *ee* by assumption of a complete conservation of enantioenrichment by derivatization of **19g** with 63% *ee* towards **28**, the *ee* of the latter could not be detected.
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[62] Synthesized by kinetic resolution of *rac*-**11** with 0.6 equiv. of (+)-(2*R*,3*R*)-DIPT/TIPT/TBHP,[29] at −30 °C/6 d. The (+)-(2*R*,3*R*)-DIPT used showed > 99% *op*.
[63] Determined by CPGC; t_r (DEX β-120, 80 °C) = 82/87 min; the minor enantiomer was not observed for enantioenriched (*R*)-**11**.
[64] Rearrangement of crude *O*-ester (*S*)-**12b** of 68% *ee* (*e.r.* = 84:16) up to 79% *ee* (*e.r.* = 89.5:10.5) from carbamoylation of (*S*)-**10** on a 1-g scale furnished thiocarbamate (*R*)-**14b** in 77−79% yield (FCC) over two steps, showing m.p. 93 °C (Et_2O/PE).
[65] Carbamoylation of *rac*-cyclohept-2-en-1-ol (*rac*-**11**, 1.22 g, 10.0 mmol) according to General Procedure A, followed by rearrangement of the crude carbamoylation product *rac*-**13** by heating for 5 h to 105−110 °C and an additional 2 h to 110 °C, produced *O*-ester *rac*-**13** (90 mg, 0.41 mmol, 3.9%) and *S*-ester *rac*-**15** (1.73 g, 8.11 mmol, 81%), isolated by FCC in good yields over two steps.
[66] Data extracted from spectra of the mixture *syn-anti*-**21e**.

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