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TBD-catalyzed α -sulfenylation of cyclic ketones: desymmetrization of 4-substituted cyclohexanones

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ABSTRACT

A low loading of triazabicyclo[4.4.0]dec-5-ene (TBD) catalyzes the α -sulfenylation reaction of ketones employing tetramethylthiuram disulfide (TMTDS) as electrophilic reagent. This methodology is mild, effective and straightforward, rendering the desired products in high yield. Prochiral 4-substituted cyclohexanones can be desymmetrized with remarkable diastereoselectivity following this protocol. The dithiocarbamoyl function was shown to be easily removed upon reduction, affording thiols (1-mercaptan-2-ols).

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1. Introduction

Sulfur-containing organic structures, particularly carbonyl compounds, constitute an important class of ligands, display pharmacological properties, and are useful intermediates in synthetic chemistry.¹ The formation of C–S bonds α to a carbonyl function (ketones or aldehydes) is a challenging task. Of the methods employed in their preparation organocatalytic protocols, either chiral or non-chiral, are especially attractive.² The advantages are sound and convincing: processes that avoid the use of metals and take place typically under mild and straightforward conditions, some of them affording products with high enantiomeric excess. The sulfur-based electrophilic reagents 1-3 have been commonly used for such transformations (Fig. 1). Disadvantaging, only reagent 2 (Ar=Ph) is commercially available. Recently, Enders and co-workers have reported the use of tetramethylthiuram disulfide (TMTDS, 4, Fig. 1) in the first basepromoted α -sulfering of aldehydes and ketones that employs this electrophile.³ TMTDS, a very cheap available reagent.⁴ was previously employed in the synthesis of aromatic and heteroaromatic thiols from functionalized Grignard⁵ or zinc reagents.⁶ Considering our interest in the development of organocatalytic processes assisted by guanidines and guanidinium salts,⁷ in this paper we present an efficient α -sulfenylation reaction of cyclic ketones employing triazabicyclo[4.4.0]dec-5-ene (TBD, **5**, Fig. 1) as organocatalyst, and TMTDS as electrophilic reagent.



Fig. 1. Reagents 1–3, employed in organocatalyzed α -sulfenylation reactions of aldehydes and ketones. Structures of TMTDS (**4**) and TBD (**5**).

2. Results and discussion

Guanidines, being extensively used as organocatalysts, present a rich chemistry.⁸ Recently we have reported a novel Al₂O₃/TBDcatalyzed aldol/retro-aldol reaction that allows preparing dynamic



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combinatorial libraries that exhibit complex system behaviour.⁹ Continuing with our research program we decided to investigate the ability of this readily available guanidine base on the electrophilic sulfenylation of ketones employing TMTDS, 4, as electrophilic reagent. The reaction of TMTDS with a 10-fold excess of cyclohexanone, in the presence of 10 mol % TBD, 5, for 120 h, at 20 °C, was adopted as a model system. In a preliminary study we scrutinized the role of different common organic solvents, and water, on the course of this reaction (Table 1). No reaction took place with water, non-polar organic solvents, acetonitrile or isopropanol (Table 1, entries 1-5). Moderate conversion was observed in the case of methanol and dimethylformamide (Table 1, entries 6 and 7), whereas dimethyl sulfoxide (Table 1, entry 8), or the absence of solvent (Table 1, entry 9), afforded a mixture of the corresponding mono- and α, α' -disulferilated ketones, **6a** and **7**¹⁰ respectively, with nearly full conversion, strongly favouring product **6a**. Under neat conditions, rising up the temperature to 30 °C implied a considerable diminution of reaction time¹¹ with a negligible decrease in the ratio 6a/7 (Table 1, entry 10). Moreover, at 30 °C, the catalyst loading could be conveniently reduced to 5 mol % (Table 1, entry 11).

co-workers³ (A: TMTDS (1 equiv), ketone (10 equiv), pyrrolidine (0.3 equiv), NEt₃ (2 equiv) in CH₃CN/CH₂Cl₂ (3:1, 0.5 M) at -20 °C, for 6 days; or alternatively B: TMTDS (1 equiv), ketone (10 equiv), neat, 50 °C). Following either of these protocols A or B, the corresponding α -sulfenylated ketones were all isolated in inferior yield compared to Table 2.

Considering the efficiency of our catalytic system we decided to study the possibility of exploring the α -sulfenylation of prochiral 4-substituted cyclohexanones. Although desymmetrization reactions are usual in enzymatic transformations, there are few examples of desymmetrizations using well-established chemical organic systems.¹² Granting conditions in which products can be obtained with high stereoselectivity, these reactions are a powerful method for the stereocontrolled preparation of complex synthetic structures. Initially we explored the α -sulfenylation reaction of 4-methylcyclohexanone, a readily available ketone liquid at the mild temperature of our reaction (30 °C). To our delight, without altering our standard conditions the sulfenylated product **6e** could be isolated in high yield displaying a substantial *syn*-diastereoselectivity (Table 3, entry 1). 4-Ethyl- and 4-propylcyclohexanone were simi-

7

Table 1

Screening of solvents and reaction conditions on the TBD-catalyzed α -sulfenylation of cyclohexanone^a



Entry	Solvent	6a/7	Conversion ^b (%)
1	H ₂ O		0
2	CH_2Cl_2	_	0
3	Toluene	_	0
4	CH ₃ CN	_	0
5	<i>i</i> -PrOH	_	0
6	MeOH	88:12	43
7	DMF	85:15	63
8	DMSO	83:17	>99
9 ^c	Neat	98:2	94
10 ^d	Neat	96:4	99
11 ^e	Neat	97:3	99

^a General reaction conditions: cyclohexanone (4.0 mmol), TMTDS (0.4 mmol), TBD (0.04 mmol), stirred at 20 °C, for 120 h, unless otherwise stated.

^b Conversion of TMTDS (limiting reagent) to sulfenylated ketones **6a**+**7** as determined by ¹H NMR spectroscopy on crude reaction mixtures.

^c No solvent was used in the reaction apart from the excess of cyclohexanone, acting as reagent and reaction medium.

^d Reaction carried out at 30 °C for 24 h.

^e Reaction carried out at 30 °C for 24 h, employing 5 mol % of TBD catalyst.

With optimum conditions at hand (Table 1, entry 11) we decided to explore the scope and limitations of our electrophilic α -sulfenylation reaction on simple cyclic ketones. Cyclopentanone, tetrahydropyranone and acetone were used as starting materials (Table 2). All the corresponding α -sulfenylated products were isolated in excellent yield. α, α' -Disulfenylated byproducts were only observed in reaction mixtures where cyclohexanone, cyclopentanone or acetone was employed, and could be easily removed by flash chromatography. Unfortunately, linear ketones (symmetrical, non-symmetrical, linear or branched) proved to be unsuccessful substrates for this transformation. It is worth noting that analogous products **6a**–**c** can be prepared according to the methodology of Enders and larly desymmetrized, products **6f** and **6g**, respectively, being obtained with comparable yield and *syn*-selectivity (Table 3, entries 2 and 3). Solid ketones can be also employed as substrates for this desymmetrization reaction. In this later case solid mixtures consisting of TBD, TMTDS, and a 10-fold excess of the corresponding ketone were heated up at a temperature moderately above ketone's melting point. Following this procedure 4-*tert*-butyl- and 4-phenylcyclohexanone afforded their corresponding α -sulfenylated products, **6h** and **6i**, in high yield and excellent diastereoselectivity (Table 3, entries 4 and 5). Other functionalized solid ketones were also conveniently sulfenylated (Table 3, entries 6 and 7). In all cases the diastereoisomeric ratio (dr) of products **6e**–**i** was determined by

Table 2

Scope of the $\alpha\text{-sulfenylation reaction of ketones}^a$



^a General conditions: ketone (4.0 mmol), TMTDS (0.4 mmol), TBD (0.02 mmol), stirred at 30 °C, for 24 h, unless otherwise stated.

^b Isolated yield of analytically pure products.

^c Reaction time: 72 h.

high-field ¹H NMR spectroscopy (300 MHz) on crude reaction mixtures by deconvoluting and comparing the integral values for the resonance of the C2 proton for the *syn-* and *anti*-diastereoisomers. The stereochemical assignment was made feasible by 2D NMR and NOE experiments, where it was observed a strong spatial contact between the H₁ and H₂ protons in products **6e–i**, which presumably adopt the chair-like structure illustrated in Fig. 2, with both substituents occupying a thermodynamically-favoured equatorial position.

 α -Sulfenylated cyclohexanone **6a** was adopted as a model substrate to study the conversion of the thiocarbamate group into various thio derivatives. Originally we pursued the deprotection of **6a** to the corresponding 2-thiol ketone. Knochel's method (NaOH, or KOH, in MeOH),⁵ applied to aromatic non-functionalized substrates, proved to be fruitless on our model compound 6a. Changes in the nature of the base or solvent were likewise ineffective. These unfavourable results motivated us to consider the feasibility of reducing the ketone moiety on **6a** to the secondary alcohol **8a** prior to the deprotection of the thiocarbamoyl function (Table 4). Accordingly, when α -sulfenylated cyclohexanone 6a, dissolved in dry THF, was treated with an equimolar amount of LiAlH₄ (1 M, in dry Et_2O) at $-20 \degree C$ for 16 h the corresponding 1-hydroxy-2-thyocarbamoylcyclohexane 8a was obtained with full conversion and a dr of 71:29, biasing the product with a relative 1,2-trans disposition. Lowering the reaction temperature delivered a notable increment of diastereoselection, being particularly favourable at -78 °C (Table 4, entries 2 and 3). Reacting further product **8a**, retaken in THF, with LiAlH₄ at room temperature gave rise, after purification, to *trans*-1-mercaptocyclohexan-2-ol (**9a**) verified from the spectroscopic data present in the literature.¹³ Hence, it confirmed the correct stereochemical assignment of 1-hydroxy-2thiocarbamoylcyclohexane 8a.

A collection of previously prepared α -sulfenylated ketones (**6a**,**b**, **6e**-**i**, **6k**) was subjected to analogous reaction conditions to afford their homologous 1-hydroxy-2-carbamoyl derivatives **8a**,**b**, **8e**-**i**,

8k in very high isolated yield (Table 5). Moreover, all products **8a,b**, **8e–i** present a remarkable dr favouring the 1,2-trans diastereoisomer with no exception. Worth considering are products **8e–i** in which the relative stereochemistry of three different stereogenic centres has been fixed (Table 5, entries 3–7).

The stereochemical assignment of products **8e–i** was done by analogy to the reduction of 2-carbamoylcyclohexanone **6a** to its corresponding alcohol **8a**, discussed above. Nonetheless, 2D NMR and NOE experiments on products **8e–i** revealed a large transoid ${}^{3}J_{H-H}$ coupling constant for H₁–H₂ protons (10–15 Hz), along with a through-space relation between their H₂ and H₄ protons, which satisfies the chair-like structure outlined in Fig. 3.

From the bases of the procedure for the stereoselective reduction of our α -sulfenylated ketones shown in Table 5 we developed a one-pot protocol for the full deprotection of the family of compounds **6**. Initially, ketone **6i**, available as a single pure diastereoisomer, was chosen as a paradigm. A solution of ketone **6i**, in dry THF, was treated with an equimolar amount of LiAlH₄ (1 M in Et₂O) at -78 °C, for 16 h before it was allowed to get room temperature. Further addition of LiAlH₄, and stirring for 5 h rendered thiol **9i** in excellent yield and total diastereoselectivity, after quenching and purification by flash chromatography. The same one-pot sequence was successfully applied on ketones **6e**–**h** (Table 6). Remarkably, products **9f**–**h** were isolated in a diastereopure form after purification. The thiol groups on compounds **9** could be conveniently transformed into other functions according to procedures well documented in the literature.

3. Conclusion

Summarizing, we have developed a simple and efficient protocol for the α -sulfenylation of cyclic ketones. This procedure employs inexpensive tetramethylthiuram disulfide as sulfenylating

Table 3

Desymmetryzation of 4-substituted cyclohexanones^a



^a General conditions: ketone (4.0 mmol), TMTDS (0.4 mmol), TBD (0.02 mmol), stirred at 30 °C, for 72 h, unless otherwise stated.

^b Diastereoisomeric ratio of products as determined by ¹H NMR spectroscopy on crude reaction mixtures.

^c Isolated yield of analytically pure products.

^d Reaction time: 48 h.

^e Reaction temperature: 55 °C.

^f Reaction temperature: 80 °C.

^g Reaction temperature: 65 °C.



Fig. 2. Stereochemical assignment of compounds 6e-i.

reagent and catalytic amounts of TBD, a readily available guanidine base, under solvent-free conditions and at mild temperatures. This methodology has been successfully implemented on different prochiral 4-substituted cyclohexanones rendering the corresponding 2-thiocarbamoyl-4-substituted derivatives with high yield and relative *syn*-diastereoselectivity. The thiocarbamoyl group of the α -sulfenylated ketones can be conveniently unmasked, upon reduction of the ketone function in a process that occurs with good stereochemical control. Chiral guanidines, acting as catalysts for the sulfenylation reaction, are currently being investigated in our laboratory, and the results will be reported in due course.

4. Experimental section

4.1. General considerations

All commercially available reagents and solvents were used without further purification unless otherwise stated. Flash chromatography of reaction products was carried out using Silica 60A, particle size 230–400 micron (Merck). Analytical thin layer chromatography (TLC) was performed on DC-Alufolien Kieselgel 60F₂₅₄ 0.2 mm plates (Merck) and compounds were visualized by UV

Table 4

Table 5

Reduction of ketones 6a,b, 6e-i, 6k^a

Screening of temperatures on the reduction of the ketone functional group on α -sulfenylated derivative **6a**^a



Entry	Temperature (°C)	Conversion (%)	dr (trans/cis) ^b
1	-20	99	71:29
2	-40	99	85:15
3	-78	99	92:8

^a General conditions: ketone **6a** (0.3 mmol), LiAlH₄ (1 M in dry Et₂O, 0.3 mL, 0.3 mmol), dry THF (3 mL), stirred at the indicated temperature for 16 h. ^b Diastereoisomeric ratio (trans/cis) of 1-hydroxy-2-thiocarbamoyl product **8a** as determined by ¹H NMR spectroscopy on crude reaction mixtures.



LiAlH₄ (1M in Et₂O)

 a General conditions: ketone (0.3 mmol), LiAlH_4 (1 M in dry Et_2O, 0.3 mL, 0.3 mmol), dry THF (3 mL), stirred at $-78\ ^\circ C$ for 16 h.

^b Diastereoisomeric ratio (trans/cis) of 1-hydroxy-2-thiocarbamoyl products, as determined by ¹H NMR on pure products **8**. Diastereoisomeric ratio refers to the relative disposition of the C–OH and C–SR centres.

^c Isolated yield of analytically pure products.



Fig. 3. Stereochemical assignment of compounds 8e-i.

Table 6

One-pot protocol for the reduction of ketones $\mathbf{6e}{-i^{\mathrm{a}}}$



 a General conditions: ketone (0.3 mmol), LiAlH_4 (1 M in dry Et_2O, 0.3 mL, 0.3 mmol), dry THF (3 mL), stirred at $-78\ ^\circ C$ for 16 h, then LiAlH_4 (0.45 mmol), $-78\ ^\circ C$ to rt, 5 h.

^b Diastereoisomeric ratio (trans/cis) of pure products **9**, referring to the relative disposition of the C–OH and C–SH centres, as determined by ¹H NMR spectroscopy. ^c Isolated yield of analytically pure products.

^d Product isolated as a single diastereoisomer.

fluorescence or 5% phosphomolybdic acid in methanol. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC-300, a Bruker DPX-300 or a Bruker AMX-400 spectrometer, using deuterated solvents and were referenced internally to the residual solvent peak ($\delta_{\rm H}$ =7.26 ppm, $\delta_{\rm C}$ =77.36 ppm) signal.¹⁴ Coupling constants (*J*values) are given in hertz (Hz). The DEPT 135 technique was used to assign methylene (CH₂) signals. Chemical shifts are reported as follows: value (description of absorption, coupling constant(s) where applicable, number of protons). 2D NMR experiments (COSY, HMBC, HMQC) and NOE experiments (NOESY) were used to determine the stereochemistry of products. Mass spectrometry was performed on an Agilent 5973N A spectrometer (MS) or a Finnigan-Mat 95-S spectrometer (HRMS) employing in both cases the electrospray ionization technique on positive mode (ES⁺).

4.2. Standard procedure for the α -sulfenylation of liquid ketones (SP1)

Triazabicyclo[4.4.0]dec-5-ene **5** (0.02 mmol, 3.0 mg) and tetramethylthiuram disulfide **4** (0.4 mmol, 96 mg) were weighed together inside a screw-capped test tube. Ketone (4.0 mmol) was added to the mixture and the resulting suspension was stirred inside a water bath at 30 °C. The reaction progress was followed up by TLC before it was quenched with NH₄Cl (aq satd), extracted with DCM (2×15 mL) and washed again with NaHCO₃ (aq satd 2×10 mL). The combined organic liquors were dried (MgSO₄). Solvents and excess of ketone were eliminated under high vacuum. Crude reaction products were purified by flash chromatography on silica gel.

4.3. Standard procedure for the α -sulfenylation of solid ketones (SP2)

Triazabicyclo[4.4.0]dec-5-ene **5** (0.02 mmol, 3.0 mg) and tetramethylthiuram disulfide **4** (0.4 mmol, 96 mg) were weighed together inside a screw-capped test tube. Solid ketone (4.0 mmol) was added to the mixture and heated at the melting point temperature of the corresponding ketone. The reaction progress was followed up by TLC before it was quenched with NH₄Cl (aq satd), extracted with DCM (2×15 mL) and washed again with NaHCO₃ (aq satd 2×10 mL). The combined organic liquors were dried (MgSO₄). Solvents were eliminated under reduced pressure and crude reaction products were purified by flash chromatography on silica gel.

4.4. Standard procedure for the stereoselective ketone reduction of α -sulfenylated ketones 6 (SP 3)

Either α -sulfenylated ketones **6a,b**, **6f**–**k** (0.30 mmol), dissolved in dry THF (3.0 mL) at -78 °C, were treated with LiAlH₄ (1 M in dry Et₂O, 0.30 mmol, 0.3 mL), and stirred for 16 h. The reaction was quenched with EtOAc (1 mL) and filtered through a pad of Celite. The organic liquors were washed with 1 M HCl (aq), extracted with Et₂O (2×15 mL), and dried over MgSO₄. Solvents and volatiles were evaporated under vacuum. Purification by flash chromatography on silica gel yielded pure alcohols **8a,b**, **8f–k**.

4.5. Standard procedure for the one-pot full reduction of α -sulfenylated ketones 6 (SP 4)

Either α -sulfenylated ketone **6** (0.3 mmol), dissolved in dry THF (3.0 mL) at -78 °C, was treated with LiAlH₄ (1 M in dry Et₂O, 0.30 mmol, 0.3 mL), and stirred for 16 h. After this time the reaction mixture was cooled to room temperature and powdered LiAlH₄ (17 mg, 0.45 mmol) was added. After 5 h of stirring the reaction mixture was quenched with EtOAc and filtered through a pad of Celite. The organic liquors were washed with 1 M HCl (aq), extracted with Et₂O (2×15 mL), and dried over MgSO₄. Solvents and

volatiles were evaporated under vacuum. Purification by flash chromatography on silica gel yielded pure compounds **9**.

4.6. Synthesis of 2-(dimethylaminothiocarbonylthio) cyclohexanone (6a)³

Prepared in 84% yield according to SP1. White solid. Purified by flash chromatography (hexane/EtOAc, 5:1). ¹H NMR (300 MHz, CDCl₃): δ 4.97 (dd, *J*=6.0, 12.0 Hz, 1H), 3.53 (s, 3H), 3.41 (s, 3H), 2.59–2.49 (m, 3H), 2.19–2.09 (m, 1H), 1.99–1.64 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ 206.2 (C), 195.3 (C), 62.5 (CH), 45.7 (CH₃), 42.5 (CH₂), 41.9 (CH₃), 35.4 (CH₂), 27.8 (CH₂), 25.9 (CH₂); MS (ES⁺): *m/z* (%)=220 (7) [M+H]⁺, 242 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₉H₁₆NOS₂]⁺ 218.0591, found 218.0669.

4.7. Synthesis of 2-(dimethylaminothiocarbonylthio) cyclopentanone (6b)³

Prepared in 93% yield according to SP1. Brown solid. Purified by flash chromatography (hexane/EtOAc 10:1). ¹H NMR (300 MHz, CDCl₃): δ 4.73(t, *J*=9.0 Hz, 1H), 3.50 (s, 3H), 3.35 (s, 3H), 2.70–2.58 (m, 1H), 2.49–2.40 (m, 1H), 2.33–2.20 (m, 1H), 2.14–2.07 (m, 1H), 2.00–1.85 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 213.8 (C), 195.2 (C), 57.8 (CH), 46.2 (CH₃), 41.8 (CH₃), 37.3 (CH₂), 31.1 (CH₂), 20.7 (CH₂); MS (ES⁺): *m/z* (%)=228 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₈H₁₄NOS₂]⁺ 204.0439, found 204.0511.

4.8. Synthesis of 3-(dimethylaminothiocarbonylthio) tetrahydro-4H-pyran-4-one (6c)³

Prepared in 94% yield according to SP1. Yellow solid. Purified by flash chromatography (hexane/Et₂O 2:1). ¹H NMR (300 MHz, CDCl₃): δ 5.16 (dd, *J*=10.6, 6.9 Hz, 1H), 4.45 (ddd, *J*=11.9, 7.1, 0.9 Hz, 1H), 4.35–4.27 (m, 1H), 3.79 (td, *J*=11.6, 2.9 Hz, 1H), 3.59 (t, *J*=10.7 Hz, 1H), 3.53 (s, 3H), 3.40 (s, 3H), 2.93–2.81 (m, 1H), 2.62–2.56 (m, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 201.7 (C), 193.6 (C), 72.4 (CH₂), 68.4 (CH₂), 60.7 (CH), 46.0 (CH₃), 43.5 (CH₂), 41.9 (CH₃); MS (ES⁺): *m/z* (%)=218 (65), 220 (100), 222 (20); HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₈H₁₄NO₂S₂]⁺ 220.0388, found 220.0468.

4.9. Synthesis of 1-(dimethylaminothiocarbonylthio)propan-2-one (6d)

Prepared in 84% yield according to SP1. Yellow solid. Purified by flash chromatography (hexane/EtOAc 10:1). ¹H NMR (300 MHz, CDCl₃): δ 4.21 (s, 2H), 3.54 (s, 3H), 3.43 (s, 3H), 2.36 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 202.4 (C), 195.8 (C), 47.5 (CH₂), 46.1 (CH₃), 42.0 (CH₃), 28.8 (CH₃); MS (ES⁺): *m*/*z* (%)=176 (45) [M–H]⁺, 178 (100) [M+H]⁺; HRMS (ES⁺): *m*/*z* calcd for [C₆H₁₂NOS₂]⁺ [M+H]⁺ 178.0282, found 178.0353.

4.10. Synthesis of (2*S**,4*S**)-2-(dimethylaminothiocarbonylthio)-4-methylcyclohexanone (6e)

Prepared in 81% yield according to SP1. Yellow solid. Purified by flash chromatography (hexane/EtOAc 10:1). ¹H NMR (300 MHz, CDCl₃): δ (*syn* diastereoisomer) 5.01 (dd, *J*=13.5, 5.8 Hz, 1H), 3.51 (s, 3H), 3.38 (s, 3H), 2.65–2.43 (m, 3H), 2.17–2.04 (m, 2H), 1.58–1.20 (m, 2H), 1.00 (d, *J*=6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ (*syn* diastereoisomer) 206.4 (C), 195.5 (C), 61.8 (CH), 45.8 (CH₃), 43.3 (CH₂), 42.0 (CH₃), 41.7 (CH₂), 35.8 (CH₂), 32.9 (CH), 21.3 (CH₃); MS (ES⁺): *m/z* (%)=232 (100) [M+H]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₀H₁₈NOS₂]⁺ 232.0752, found 232.0829.

4.11. Synthesis of (25*,45*)-2-(dimethylaminothiocarbonylthio)-4-ethylcyclohexanone (6f)

Prepared in 91% yield according to SP1. Yellow oil. Purified by flash chromatography (hexane/EtOAc, 10:1). ¹H NMR (300 MHz, CDCl₃): δ (*syn* diastereoisomer) 5.02 (dd, *J*=13.6, 5.7 Hz, 1H), 3.53 (s, 3H), 3.41 (s, 3H), 2.61–2.52 (m, 3H), 2.21–2.11 (m, 1H), 1.97–1.85 (m, 1H), 1.51–1.30 (m, 4H), 0.95 (t, *J*=7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃): δ (*syn* diastereoisomer) 206.7 (C), 195.6 (C), 61.9 (CH), 45.8 (CH₃), 42.0 (CH₃), 41.7 (CH₂), 41.1 (CH₂), 39.4 (CH), 33.4 (CH₂), 28.7 (CH₂), 11.9 (CH₃); MS (ES⁺): *m*/*z* (%)=246 (100) [M+H]⁺; HRMS (ES⁺): *m*/*z* calcd for [M+H]⁺ [C₁₁H₂₀NOS₂]⁺ 246.0908, found 246.0980.

4.12. Synthesis of (2S*,4S*)-2-

(dimethylaminothiocarbonylthio)-4-propylcyclohexanone (6g)

Prepared in 84% yield according to SP1. Yellow oil. Purified by flash chromatography (hexane/EtOAc, 10:1). ¹H NMR (300 MHz, CDCl₃): δ (*syn* diastereoisomer) 5.02 (dd, *J*=13.4, 5.7 Hz, 1H), 3.52 (s, 3H), 3.40 (s, 3H), 2.61–2.51 (m, 3H), 2.16–2.05 (m, 1H), 2.16–1.97 (m, 1H), 1.55–1.24 (m, 6H), 0.94–0.89 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ (*syn* diastereoisomer) 206.5 (C), 195.5 (C), 61.9 (CH), 45.7 (CH₃), 41.9 (CH₃), 41.6 (CH₂), 41.3 (CH₂), 38.0 (CH₂), 37.4 (CH), 33.7 (CH₂), 20.5 (CH₂), 14.4 (CH₃); MS (ES⁺): *m/z* (%)=260 (100) [M+H]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₂H₂₂NOS₂]⁺ 260.1065, found 260.1141.

4.13. Synthesis of (2*S**,4*S**)-2-(dimethylaminothiocarbonylthio)-4-(*tert*-butyl)cyclohexanone (6h)

Prepared in 97% yield according to SP2 (reaction temperature: 55 °C). Yellow solid. Purified by flash chromatography (hexane/Et₂O, 3:1). ¹H NMR (300 MHz, CDCl₃): δ (*syn* diastereoisomer) 5.00 (dd, *J*=12.5, 5.1 Hz, 1H), 3.53 (s, 3H), 3.40 (s, 3H), 2.60–2.56 (m, 3H), 2.18–2.14 (m, 1H), 1.85–1.76 (m, 1H), 1.64–1.56 (m, 2H), 0.92 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ (*syn* diastereoisomer) 206.7 (C), 195.5 (C), 62.3 (CH), 47.9 (CH), 45.7 (CH₃), 41.9 (CH₃), 41.7 (CH₂), 36.7 (CH₂), 32.8 (C), 28.6 (CH₂), 27.5 (3×CH₃); MS (ES⁺): *m/z* (%)= 274 (100) [M+H]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₃H₂₄NOS₂]⁺ 274.1221, found 274.1290.

4.14. Synthesis of (2*S**,4*S**)-2-(dimethylaminothiocarbonylthio)-4-phenylcyclohexanone (6i)

Prepared in 95% yield according to SP2 (reaction temperature: 80 °C). Orangish solid. Purified by flash chromatography (hexane/Et₂O, 3:1). ¹H NMR (300 MHz, CDCl₃): δ (*syn* diastereoisomer) 7.37–7.20 (m, 5H), 5.21 (dd, *J*=13.2, 5.7 Hz, 1H), 3.53 (s, 3H), 3.40 (s, 3H), 3.32 (tt, *J*=12.1, 3.5 Hz, 1H), 2.80–2.67 (m, 3H), 2.35–2.28 (m, 1H), 2.10–2.00 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ (*syn* diastereoisomer) 205.7 (C), 195.3 (C), 143.8 (C), 128.9 (2×CH), 127.7 (CH), 127.0 (2×CH), 62.1 (CH), 45.8 (CH₃), 43.9 (CH), 42.4 (CH₂), 42.0 (CH₃), 41.9 (CH₂), 34.7 (CH₂); MS (ES⁺): *m/z* (%)=294 (100) [M+H]⁺, 216 (5) [M–C₆H₅]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₅H₂₀NOS₂]⁺ 294.0908, found 294.0982.

4.15. Synthesis of 3-(dimethylaminothiocarbonylthio) tetrahydro-4*H*-thiopyran-4-one (6j)

Prepared in 94% yield according to SP2 (reaction temperature: 65 °C). Brown solid. Purified by flash chromatography (hexane/Et₂O 2:1). ¹H NMR (400 MHz, CDCl₃): δ 5.18 (dd, *J*=11.4, 5.1 Hz, 1H), 3.50

(s, 3H), 3.44–3.38 (m, 1H), 3.38 (s, 3H), 3.10–2.90 (m, 5H); 13 C NMR (75 MHz, CDCl₃): δ 203.8 (br s, C), 194.1 (C), 63.9 (CH), 45.9 (CH₃), 45.6 (CH₂), 42.1 (CH₃), 37.4 (CH₂), 31.1 (CH₂); MS (ES⁺): m/z (%)=236 (100) [M+H]⁺, 242 (39) [M+Na–CH₄]⁺; HRMS (ES⁺): m/z calcd for [M+H]⁺ [C₈H₁₄NOS₃]⁺ 236.0238, found 236.0237.

4.16. Synthesis of 2-(dimethylaminothiocarbonylthio)-4-(1,4-dioxolano)-cyclohexanone (6k)

Prepared in 73% yield according to SP2 (reaction temperature: 80 °C). Yellow solid. Purified by flash chromatography (hexane/Et₂O, 2:1). ¹H NMR (300 MHz, CDCl₃): δ 5.18 (dd, *J*=13.6, 6.0 Hz, 1H), 4.16–4.03 (m, 2H), 3.99–3.94 (m, 2H), 3.47 (s, 3H), 3.36 (s, 3H), 2.88–2.77 (m, 1H), 2.57–2.48 (m, 2H), 2.09–2.00 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 204.5 (C), 194.5 (C), 106.87 (C), 64.9 (CH₂), 64.7 (CH₂), 58.1 (CH), 45.5 (CH₃), 41.7 (CH₃), 40.7 (CH₂), 38.0 (CH₂), 34.7 (CH₂); MS (ES⁺): *m/z* (%)=276 (100) [M+H]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₁H₁₈NO₃ S₂]⁺ 276.0650, found 276.0729.

4.17. Characterization of *syn*-2,6-[bis-(dimethylaminothiocarbonylthio)]cyclohexanone (7)¹⁰

Off-white solid. Purified by flash chromatography (hexane/EtOAc, 5:1). ¹H NMR (400 MHz, CDCl₃): δ 5.28–5.05 (m, 2H), 3.54 (s, 6H), 3.42 (s, 6H), 2.80–2.59 (m, 2H), 2.23–1.94 (m, 2H), 1.95–1.72 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 201.3 (C), 194.8 (2×C), 62.6 (2×CH), 45.4 (2×CH₃), 41.6 (2×CH₃), 35.8 (2×CH₂), 25.9 (CH₂); MS (ES⁺): *m/z* (%)=337 (100) [M+H]⁺; HRMS (ES⁺): *m/z* calcd for [M+H]⁺ [C₁₂H₂₁N₂OS₄]⁺ 337.0537, found 337.0539.

4.18. Synthesis of (15*,25*)-2-hydroxycyclohexyl dimethylcarbamodithioate (8a)

Prepared in 90% yield according to SP3. White solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (trans diastereoisomer) 4.06 (ddd, *J*=15.8, 10.4, 5.8 Hz, 1H), 3.55 (s, 3H), 3.51 (ddd, *J*=14.6, 10.3, 4.3 Hz, 1H), 3.40 (s, 3H), 2.40 (br s, 1H), 2.22–2.13 (m, 1H), 1.83–1.69 (m, 2H), 1.57–1.25 (m, 5H); ¹³C NMR (75 MHz, CDCl₃): δ (trans diastereoisomer) 198.0 (C), 75.0 (CH), 52.2 (CH), 45.9 (CH₃), 42.2 (CH₃), 36.3 (CH₂), 32.2 (CH₂), 26.4 (CH₂), 24.6 (CH₂); MS (ES⁺): *m*/*z* (%)=220 (4) [M+H]⁺, 242 (100) [M+Na]⁺; HRMS (ES⁺): *m*/*z* calcd for [M+Na]⁺ [C₉H₁₇NONaS₂]⁺ 242.0649, found 242.0650.

4.19. Synthesis of (1*S**,2*S**)-2-hydroxycyclopenthyl dimethylcarbamodithioate (8b)

Prepared in 91% yield according to SP3. Off-white solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (trans diastereoisomer) 4.29–4.23 (m, 1H), 3.97 (ddd, *J*=11.1, 8.0, 3.0 Hz, 1H), 3.54 (s, 3H), 3.36 (s, 3H), 2.35–2.25 (m, 1H), 1.98–1.82 (m, 2H), 1.80–1.54 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ (trans diastereoisomer) 198.2 (C), 81.3 (CH), 57.5 (CH), 45.4 (CH₃), 42.2 (CH₃), 34.0 (CH₂), 30.0 (CH₂), 24.1 (CH₂); MS (ES⁺): *m/z* (%)= 228 (100); HRMS (ES⁺): *m/z* calcd for [M+Na]⁺ [C₈H₁₅NONaS₂]⁺ 228.0493, found 228.0487.

4.20. Synthesis (1*S**,2*S**,5*S**)-2-hydroxy-5-methylcyclohexyl dimethylcarbamodithioate (8e)

Prepared in 93% yield according to SP3. White solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 4.12 (ddd, *J*=12.9, 10.6, 4.4 Hz, 1H), 3.55 (s, 3H), 3.48 (ddd, *J*=15.6, 10.8, 4.4 Hz, 1H), 3.40 (s, 3H), 2.21–2.08 (m, 2H), 1.99 (br s, 1H), 1.79–1.71 (m, 1H), 1.70–1.58 (m, 1H), 1.51 (ddd, *J*=24.3, 13.3, 3.7 Hz, 1H), 1.24 (dd, *J*=24.7, 12.8 Hz,

1H), 1.03 (ddd, *J*=25.5, 13.5, 3.4 Hz, 1H), 0.93 (d, *J*=6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ (major diastereoisomer) 198.0 (C), 75.2 (CH), 58.0 (CH), 45.9 (CH₃), 42.2 (CH₃), 40.8 (CH₂), 36.1 (CH₂), 33.3 (CH+CH₂), 22.0 (CH₃); MS (ES⁺): *m*/*z* (%)=234 (10) [M+H]⁺, 256 (100) [M+Na]⁺; HRMS (ES⁺): *m*/*z* calcd for [M+Na]⁺ [C₁₀H₁₉NO-NaS₂]⁺ 256.0806, found 256.0811.

4.21. Synthesis of (15*,25*,55*)-5-ethyl-2-hydroxycyclohexyl dimethylcarbamodithioate (8f)

Prepared in 90% yield according to SP3. White solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 4.11 (ddd, *J*=12.8, 10.5, 4.0 Hz, 1H), 3.56 (s, 3H), 3.49 (ddd, *J*=15.2, 10.8, 4.4 Hz, 1H), 3.40 (s, 3H), 2.23–2.14 (m, 2H), 1.95–1.72 (m, 2H), 1.56–1.36 (m, 2H), 1.31–1.15 (m, 3H), 1.04–0.91 (m, 1H), 0.89 (t, *J*=7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ (major diastereoisomer) 197.8 (C), 75.3 (CH), 58.0 (CH), 45.8 (CH₃), 42.1 (CH₃), 39.8 (CH), 38.4 (CH₂), 36.0 (CH₂), 30.7 (CH₂), 29.2 (CH₂), 11.8 (CH₃); MS (ES⁺): *m/z* (%)=248 (4) [M+H]⁺, 270 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+Na]⁺ [C₁₁H₂₁NONaS₂]⁺ 270.0962, found 270.0968.

4.22. Synthesis of (1*S**,2*S**,5*S**)-2-hydroxy-5-propylcyclohexyl dimethylcarbamodithioate (8g)

Prepared in 95% yield according to SP3. White solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 4.11 (ddd, *J*=13.0, 10.5, 4.0 Hz, 1H), 3.55 (s, 3H), 3.53–3.44 (m, 1H), 3.39 (s, 3H), 2.22–2.12 (m, 2H), 1.88–1.41 (m, 5H), 1.38–1.14 (m, 4H), 0.98 (ddd, *J*=25.3, 13.4, 3.5 Hz, 1H), 0.88 (t, *J*=7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ (major diastereoisomer) 197.9 (C), 75.3 (CH), 58.1 (CH), 45.8 (CH₃), 42.1 (CH₃), 38.8 (CH₂), 38.7 (CH₂), 37.8 (CH), 36.0 (CH₂), 31.1 (CH₂), 20.3 (CH₂), 14.4 (CH₃); MS (ES⁺): *m*/*z* (%)=284 (100) [M+Na]⁺; HRMS (ES⁺): *m*/*z* calcd for [M+Na]⁺ [C₁₂H₂₃NONaS₂]⁺ 284.1119, found 284.1125.

4.23. Synthesis of (1*S**,2*S**,5*S**)-5-*tert*-butyl-2hydroxycyclohexyl dimethylcarbamodithioate (8h)

Prepared in 95% yield according to SP3. Yellow solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 4.14–4.04 (m, 1H), 3.55 (s, 3H), 3.47 (ddd, *J*=15.3, 10.8, 4.5 Hz, 1H), 3.40 (s, 3H), 2.29 (br s, 1H), 2.27–2.16 (m, 2H), 1.86–1.78 (m, 1H), 1.53–1.41 (m, 1H), 1.34–1.24 (m, 2H), 1.15–1.03 (m, 1H), 0.87 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ (major diastereoisomer) 197.9 (C), 75.3 (CH), 58.7 (CH), 48.3 (CH), 45.8 (CH₃), 42.1 (CH₃), 36.3 (CH₂), 33.6 (CH₂), 32.7 (C), 27.8 (3×CH₃), 25.5 (CH₂); MS (ES⁺): *m/z* (%)=276 (15) [M+H]⁺, 298 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+Na]⁺ [C₁₃H₂₅NONaS₂]⁺ 298.1275, found 298.1278.

4.24. Synthesis of (1*S**,2*S**,5*S**)-2-hydroxy-5-phenylcyclohexyl dimethylcarbamodithioate (8i)

Prepared in 96% yield according to SP3. Yellow solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 7.33–7.27 (m, 2H), 7.23–7.17 (m, 3H), 4.29 (ddd, *J*=12.8, 10.6, 3.9 Hz, 1H), 3.63 (ddd, *J*=15.0, 10.6, 4.4 Hz, 1H), 3.56 (s, 3H), 3.39 (s, 3H), 2.80 (tt, *J*=12.0, 3.4 Hz, 1H), 2.39–2.28 (m, 1H), 2.02–1.94 (m, 1H), 1.76 (dd, *J*=25.4, 12.7 Hz, 1H), 1.74–1.51 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ (major diastereoisomer) 197.5 (C), 145.2 (C), 128.7 (2×CH), 126.9 (2×CH), 126.6 (CH), 74.6 (CH), 58.1 (CH), 45.8 (CH₃), 44.3 (CH), 42.1 (CH₃), 39.8 (CH₂), 36.2 (CH₂), 32.1 (CH₂); MS (ES⁺) *m/z* (%)=318 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+Na]⁺ [C₁₅H₂₁NONaS₂]⁺ 318.0962, found 318.0959.

4.25. Synthesis of (1*S**,6*S**)-6-hydroxy-3-oxocyclohexyl dimethylcarbamodithioate ethylene ketal (8k)

Prepared in 87% yield according to SP3. Reddish solid. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (trans diastereoisomer) 4.34 (ddd, *J*=12.4, 9.9, 4.3 Hz, 1H), 4.05–3.89 (m, 4H), 3.60 (ddd, *J*=14.3, 10.0, 4.4 Hz, 1H), 3.53 (s, 3H), 3.38 (s, 3H), 2.79 (br s, 1H), 2.23 (ddd, *J*=13.1, 4.0, 3.1 Hz, 1H), 2.14–2.08 (m, 1H), 1.86–1.72 (m, 3H), 1.69–1.57 (m, 1H); ¹³C NMR (75 MHz, CDCl₃): δ (trans diastereoisomer) 197.4 (C), 108.1 (C), 73.7 (CH), 64.8 (CH₂), 64.7 (CH₂), 54.9 (CH), 45.8 (CH₃), 42.1 (CH₃), 39.1 (CH₂), 33.0 (CH₂), 32.1 (CH₂); MS (ES⁺): *m/z* (%)=300 (100) [M+Na]⁺; HRMS (ES⁺): *m/z* calcd for [M+Na]⁺ [C₁₁H₁₉NO₃NaS₂]⁺ 300.0704, found 300.0697.

4.26. Synthesis of (1*S**,2*S**)-2-mercaptocyclohexanol (9a)¹³

Prepared in 94% yield according to SP4. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (300 MHz, CDCl₃): δ (trans diastereoisomer) 3.20 (ddd, *J*=14.0, 10.0, 4.3 Hz, 1H), 2.58–2.44 (m, 1H), 2.22–2.04 (m, 2H), 1.97 (br s, 1H), 1.85–1.65 (m, 2H), 1.42 (d, *J*=9.2 Hz, 1H), 1.39–1.19 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ (trans diastereoisomer) 77.0 (CH), 48.0 (CH), 36.8 (CH₂), 34.3 (CH₂), 26.9 (CH₂), 25.0 (CH₃).

4.27. Synthesis of (1*S**,2*S**,4*S**)-2-mercapto-4methylcyclohexan-1-ol (9e)

Prepared in 87% yield according to SP4. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ (major diastereoisomer) 3.18 (ddd, *J*=14.7, 10.4, 4.4 Hz, 1H), 2.59–2.51 (m, 1H), 2.30 (br s, 1H), 2.14–2.03 (m, 2H), 1.77–1.66 (m, 1H), 1.57–1.45 (m, 1H), 1.41 (d, *J*=9.3 Hz, 1H), 1.38–1.28 (m, 1H), 1.14–0.99 (m, 2H), 0.90 (d, *J*=6.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ (major diastereoisomer) 77.0 (CH), 47.6 (CH), 45.3 (CH₂), 33.9 (CH₂), 33.6 (CH), 33.5 (CH₂), 21.9 (CH₃).

4.28. Synthesis of (1*S**,2*S**,4*S**)-2-mercapto-4ethylcyclohexan-1-ol (9f)

Prepared in 83% yield according to SP4. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ 3.18 (ddd, *J*=14.7, 10.4, 4.4 Hz, 1H), 2.58–2.49 (m, 1H), 2.38 (s, 1H), 2.19–2.14 (m, 1H), 2.11–2.05 (m, 1H), 1.82–1.76 (m, 1H), 1.43 (d, *J*=9.2 Hz, 1H), 1.36–1.19 (m, 4H), 1.10–0.95 (m, 2H), 0.88 (d, *J*=7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 77.2 (CH), 47.7 (CH), 43.0 (CH₂), 40.2 (CH), 33.9 (CH₂), 31.1 (CH₂), 39.3 (CH₂), 11.9 (CH₃).

4.29. Synthesis of (1*S**,2*S**,4*S**)-2-mercapto-4propylcyclohexan-1-ol (9g)

Prepared in 91% yield according to SP4. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1). ¹H NMR (400 MHz, CDCl₃): δ 3.17 (ddd, *J*=14.7, 10.3, 4.3 Hz, 1H), 2.59–2.48 (m, 2H), 2.17–2.11 (m, 1H), 2.09–2.03 (m, 1H), 1.80–1.74 (m, 1H), 1.43 (d, *J*=9.1 Hz, 1H), 1.40–1.24 (m, 4H), 1.20–1.12 (m, 2H), 1.09–0.94 (m, 2H), 0.86 (t, *J*=7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 77.2 (CH), 47.7 (CH), 43.3 (CH₂), 38.8 (CH₂), 38.2 (CH), 33.9 (CH₂), 31.5 (CH₂), 20.4 (CH₂), 14.6 (CH₃).

4.30. Synthesis of (1*S**,2*S**,4*S**)-2-mercapto-4-*tert*-butylcyclohexan-1-ol (9h)

Prepared in 88% yield according to **SP4**. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃): δ 3.16 (ddd, *J*=14.7, 10.3, 4.4 Hz, 1H), 2.59–2.49 (m, 1H), 2.40 (br s, 1H), 2.23–2.08 (m, 2H), 1.85–1.73 (m, 1H), 1.46 (d, *J*=9.2 Hz,

1H), 1.34–1.23 (m, 1H), 1.21–1.05 (m, 3H), 0.86 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 77.2 (CH), 48.8 (CH), 48.4 (CH), 38.1 (CH₂), 34.2 (CH₂), 32.7 (C), 27.9 (3×CH₃), 25.9 (CH₂).

4.31. Synthesis of (1*S**,2*S**,4*S**)-2-mercapto-4-phenylcyclohexan-1-ol (9i)

Prepared in 93% yield according to SP4. Colourless oil. Purified by flash chromatography (hexane/EtOAc, 3:1); ¹H NMR (400 MHz, CDCl₃): δ 7.33–7.29 (m, 2H), 7.23–7.19 (m, 3H), 3.34 (td, *J*=10.2, 4.4 Hz, 1H), 2.79–2.62 (m, 2H), 2.57 (br s, 1H), 2.39–2.30 (m, 1H), 2.27–2.16 (m, 1H), 2.03–1.87 (m, 1H), 1.73–1.55 (m, 3H), 1.51 (d, *J*=9.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 145.3 (C), 128.8 (2×CH), 127.0 (2×CH), 126.7 (CH), 76.7 (CH), 47.7 (CH), 44.8 (CH), 44.1 (CH₂), 34.2 (CH₂), 30.5 (CH₂).

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Supplementary data

A copy of the spectra of all the compounds described in this manuscript. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.05.124.

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