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Synthesis of Thiabicyclic Heterocycles Through Free Radical Cyclization of β-Thioacrylates

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Abstract—8-Aza-3-thiabicyclo[4.3.0]nonanes **7** and **8**, 3-thiabicyclo[4.4.0]decanes **18**, and 8-thiabicyclo[4.3.0]nonanes **31** were obtained from monocyclic precursors through free radical cyclizations involving a β-thioacrylate system as radical acceptor and a thionocarbonate as radical precursor. Oxidative sulfur extrusion in 3-thiabicyclo[4.4.0]decanes **18** afforded methyl (2-isopropenyl-5-methylcyclohexyl)-2-propenoates **35**.

Introduction

The development of a method for temporary sulfur connection and its application to the synthesis of (−)-α-kainic acid and to the stereocontrolled functionalization of (−)-carvone was recently reported.[1–5] This method involves three parts: (i) anchoring stage, in which two reactants are linked through a sulfur connector; (ii) intramolecular cyclization through the formation of a new carbon–carbon bond as part of a sulfur-containing ring; (iii) disconnecting stage in which the temporary sulfur linker is removed. As part of a study directed towards the further development of temporary sulfur connection, methods for the construction of some bicyclic sulfur-containing systems were investigated. These compounds are of interest as synthetic intermediates as well as target compounds for studying their properties.[6–8] In this paper efficient syntheses of thiabicyclic compounds through free radical cyclization of β-thioacrylates are reported.

Results and Discussion

Radical-mediated cyclizations are extensively used for the construction of heterocyclic systems.[9] Although there are no previous reports on the free radical cyclization of β-thioacrylates, β-alkoxyacrylates were found to be efficient radical acceptors for the synthesis of oxacycles.[10,11] Scheme 1 describes the synthesis of conformationally restricted kainoids **7** and **8**.[8] Pyrrolidine derivative **6**, carrying the β-thioacrylate function as radical acceptor and the thionocarbonate function as radical precursor was designed as a key intermediate. It was prepared in a few stages starting from the anti-Markovnikov addition of methyl 2-mercaptopropionate to the isopropenyl group of **1**.[2] The resulting sulfides **2** (mixture of C-1′ epimers) were selectively oxidized to sulfoxides **3**. Sulfoxides which carry an acidic methylene group in a β-position undergo facile thermolysis to give the corresponding sulfenic acids. The emerging sulfenic acid can be trapped in situ by alkenes or alkynes.[12] Extension of this reaction allowed the metathetic transformation of sulfoxides **3** into α,β-unsaturated sulfoxides **5** by heating the former with excess of methyl propiolate. Selective reduction with Lawesson's reagent of the unsaturated sulfoxide **3** to the corresponding thioenolate,[13] was followed by desilylation and thionocarbonation to give the desired β-thioacrylate-thionocarbonate derivatives **6**. *n*-Bu_3SnH/AIBN induced free radical cyclization of thionocarbonates **6** (1:1 mixture of two epimers at C-1′) gave two individual products **7** and **8**. ^1H NMR spectra indicate that compounds **7** and **8** have opposite configuration, not only at C-7, but also at C-3a. Relative stereochemistry at position C-3a of isomers **7** and **8** was established on the basis of the values of $J_{H3a-H7a}$, which are 11.3 Hz for **7** and 5.5 Hz for **8**. The large difference in coupling constants, J_{H3-H3a}=0 Hz vs. 9 Hz in isomers **7** and **8**, indicates an opposite configuration at C-3 and C-3a. These values led us to assign to 3-H and 3a-H a *trans*-configuration in compound **7** and *cis* in compound **8**. Moreover, relative stereochemistry at positions C-3a, C-4, and C-7 in isomers **7** and **8** was confirmed by NOE-difference ^1H NMR. Irradiation at 7a-H in **7** resulted in NOE response at 3a-H (4.8%) and 7-H (11.2%). Irradiation at 3a-H in **7** resulted in NOE response at 7a-H (2%) and 4-H (2.6%). NOE experiments for isomer **8** showed that irradiation at 3a-H revealed NOE difference at 7-H (6.7%), 4-H (4.5%) and no response at 7a-H. While irradiation at 3-H revealed NOE difference at 4-H (6.3%). These data indicate the *cis*-configuration of 3a-H and 7a-H, and the *trans*-configuration of 3-H and 3a-H in thiopyranopyrrole **7** and opposite configurations in isomer **8**.

Keywords: cyclization; radicals and radical reactions; sulfoxides; sulfur heterocycles.

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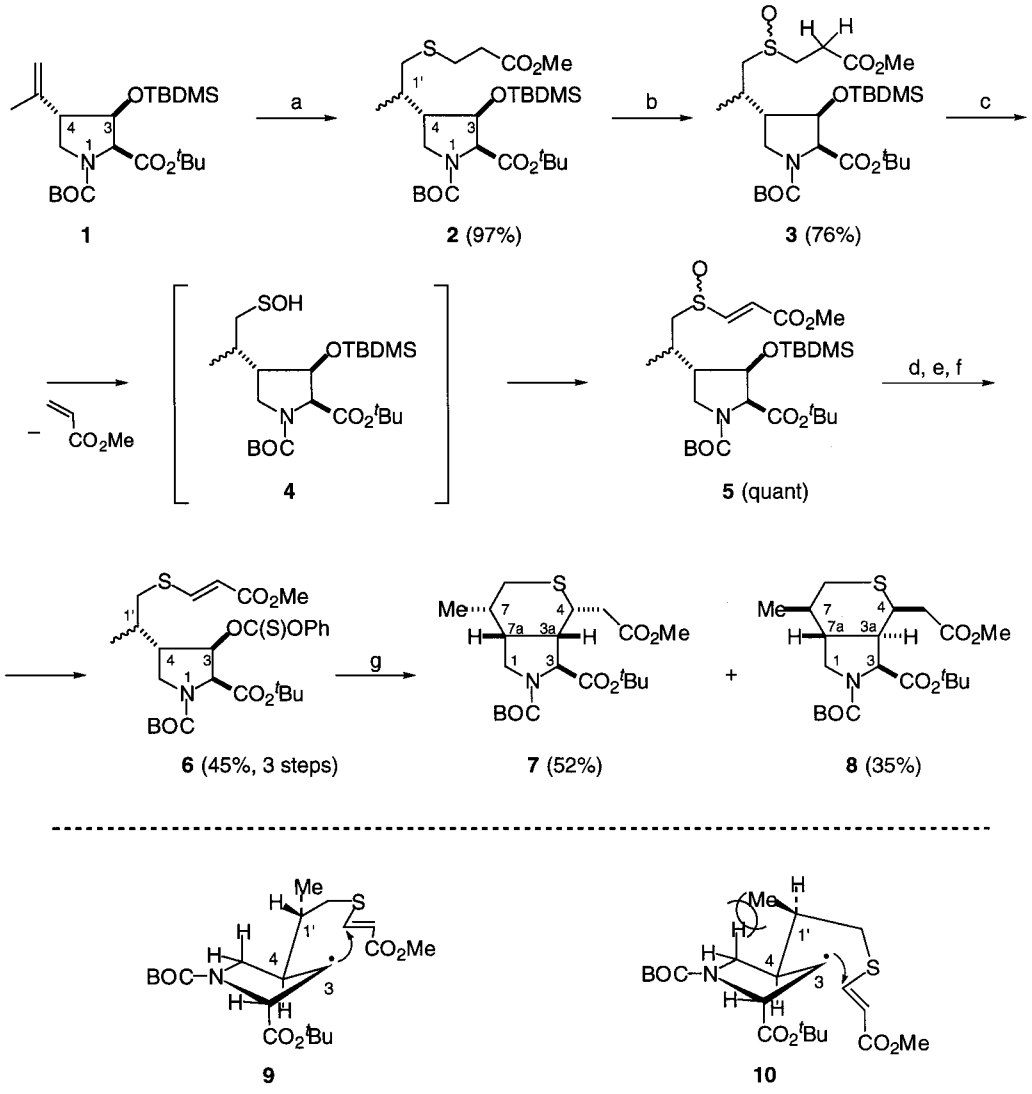
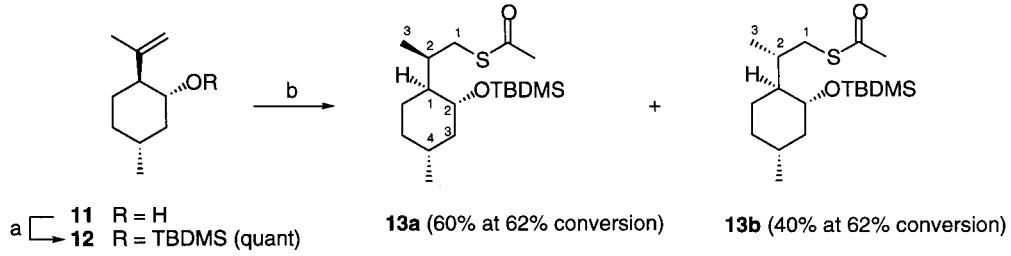


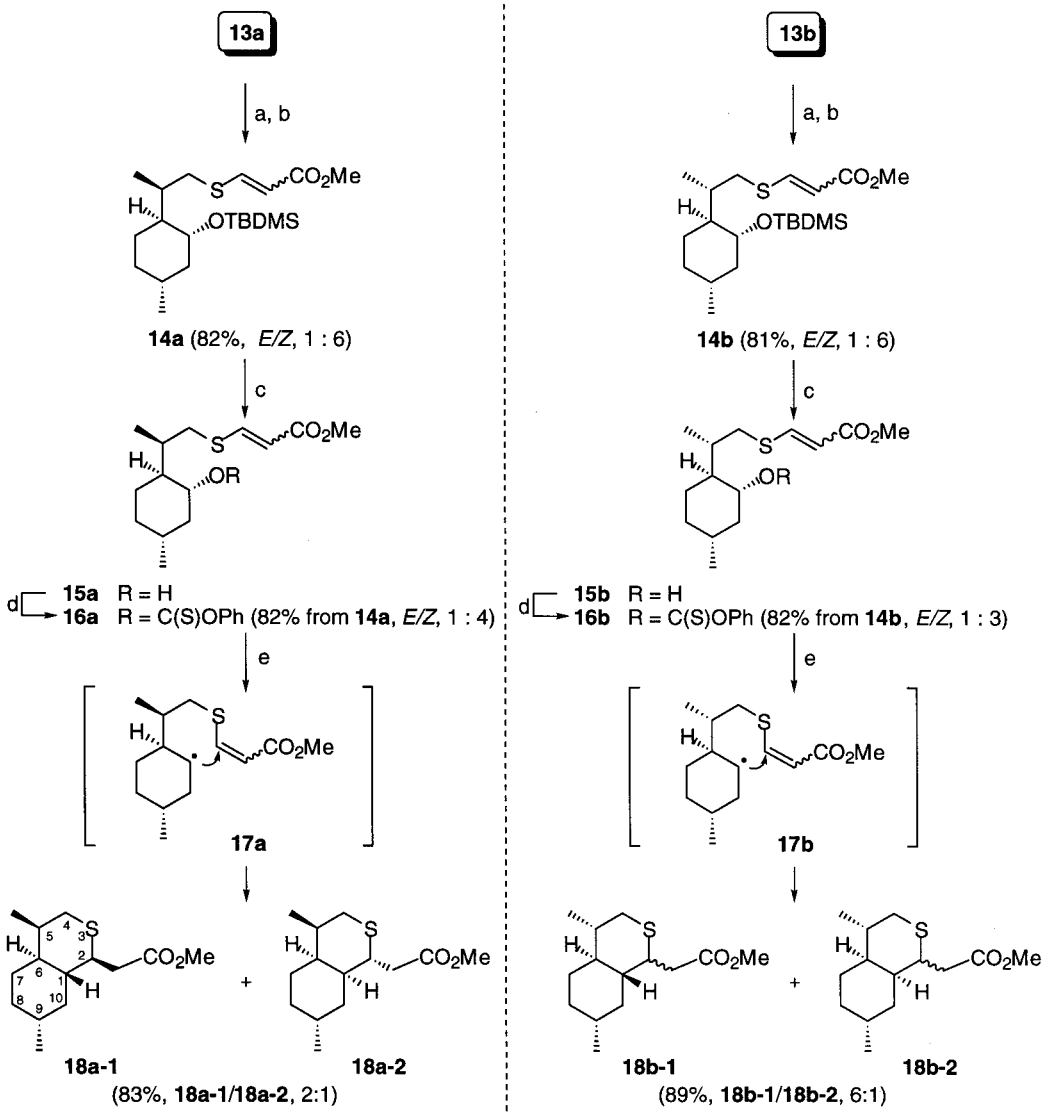
Scheme 1. *Reagents and conditions*: (a) $HSCH_2CH_2CO_2Me$, AIBN, THF, 60°C, 4.5 h; (b) *m*-CPBA, CH_2Cl_2, −60°C, 2 h; (c) $HC{\equiv}CCO_2Me$, toluene, reflux, 2 h; (d) Lawesson's reagent, THF, −10°C, 50 min; (e) Bu_4NF, AcOH, THF, room temp., 20 h; (f) *n*-BuLi, PhOC(S)Cl, THF, −78°C→room temp., 3 h; (g) *n*-Bu_3SnH, AIBN, toluene, 100°C, 1.5 h.

Formation of two, rather than four isomers, is attributed to a different directive effect of the C-1′ methyl group in the two C-1′ epimers **6**. Indeed, molecular models examination of intermediate radical **9** indicates the absence of any significant non-bonding interaction at the transition state leading to *cis*-fused product **7**. In contrast, in intermediate radical **10**, non-bonding interaction between the C-1′ methyl group and ring hydrogen atoms are lower at the transition state leading to *trans*, rather than to the *cis*-fused product, therefore formation of compound **8** is favored. In conclusion, stereoselectivities in the free radical cyclizations of the two C-1′ epimeric thionocarbonates **6** are very high and antithetical.

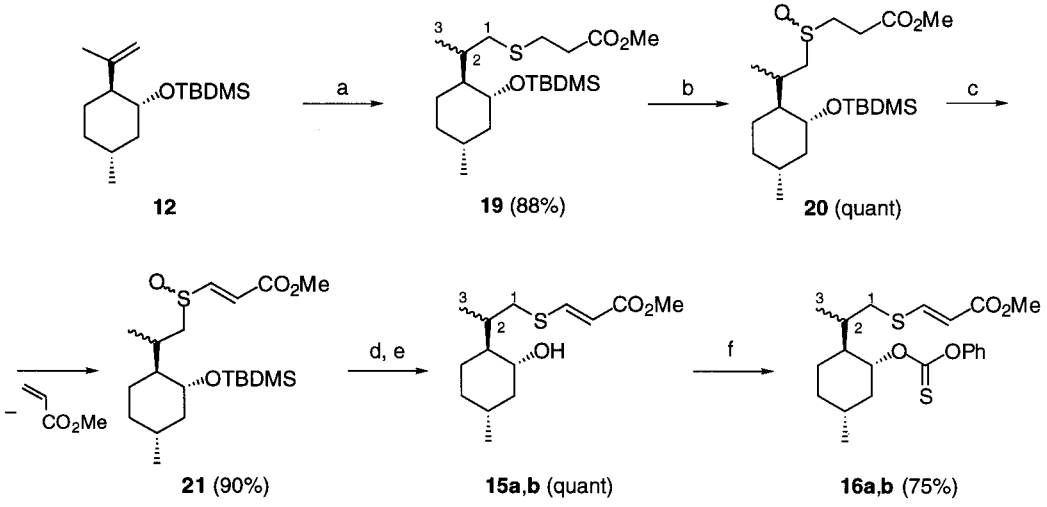
In another line of research, β-thioacrylates **16a** and **16b** were synthesized and their free radical cyclization studied (Schemes 2 and 3). Light-induced addition of thiolacetic acid to *tert*-butyl(dimethylsilyl)isopuelegol **12** afforded



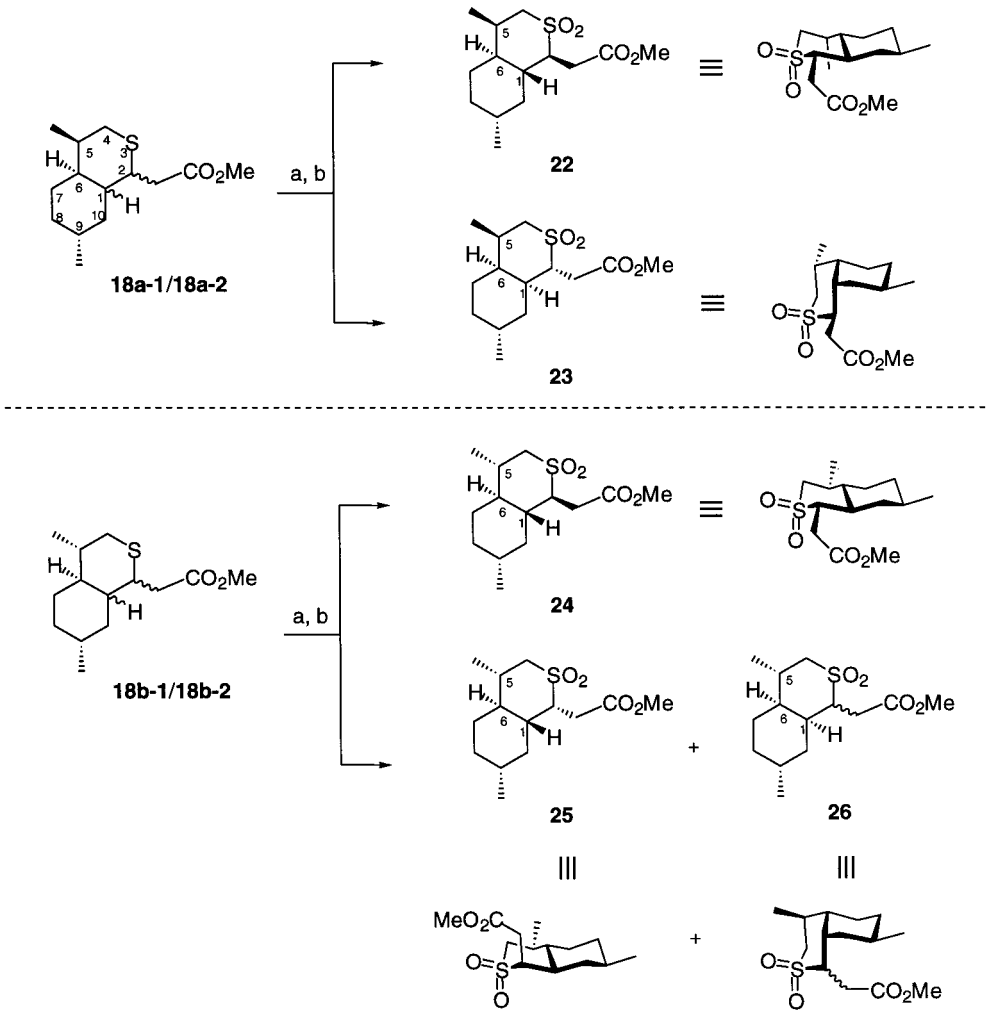
Scheme 2. *Reagents and conditions*: (a) TBDMSTf, 2,6-lutidine, CH_2Cl_2, −72°C, 1 h; (b) HSC(O)Me, longwave UV lamp, 72 h.



Scheme 3. *Reagents and conditions*: (a) KOH, MeOH, 0°C→room temp., 1.5 h; (b) HC≡CCO$_2$Me, MeOH–H$_2$O (10:1), Et$_3$N, 0°C→room temp., 24 h; (c) Bu$_4$NF, THF, room temp., ca. 12 h; (d) PhOC(S)Cl, DMAP, pyridine, THF, 0°C→room temp., ca. 12 h; (e) *n*-Bu$_3$SnH, AIBN, toluene, 95°C, 1.5 h.



Scheme 4. *Reagents and conditions*: (a) HSCH$_2$CH$_2$CO$_2$Me, AIBN, THF, 60°C, 8 h; (b) *m*-CPBA, CH$_2$Cl$_2$, −60°C, 4.5 h; (c) HC≡CCO$_2$Me, toluene, reflux, 2 h; (d) NaI, (CF$_3$CO)$_2$O, acetone, 0°C, 30 min; (e) Bu$_4$NF, THF, room temp., 22 h; (f) PhOC(S)Cl, DMAP, pyridine, THF, 0°C→room temp., ca. 12 h.

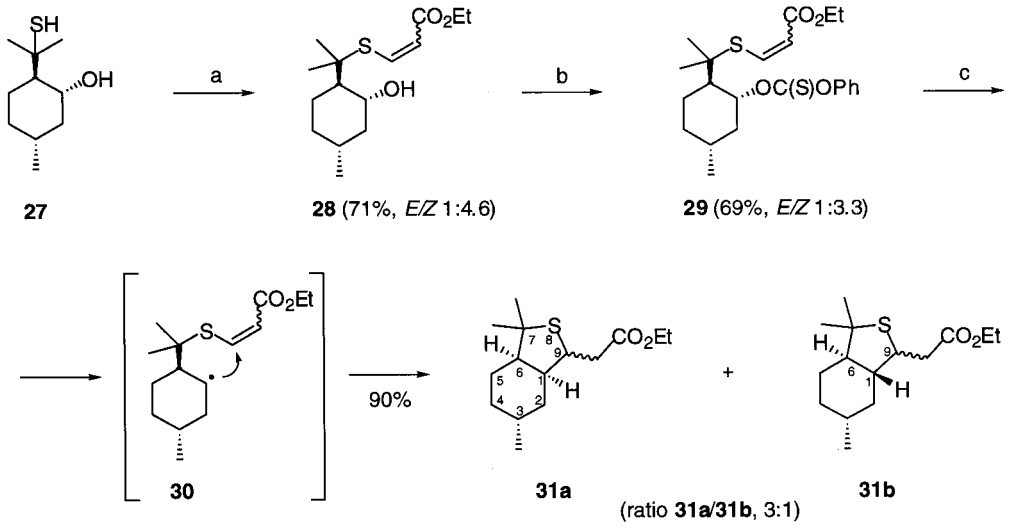


Scheme 5. *Reagents and conditions*: (a) *m*-CPBA, EtOAc, 0°C→room temp., 4 h; (b) MPLC.

epimeric acetylsulfides **13** (Scheme 2), which were chromatographically separated into the two diastereomers **13a** and **13b**. Each of these diastereomers was subjected to the series of reactions detailed in Scheme 3. Thus, deacetylation followed by base-induced addition of the resulting thiols to methyl propiolate, afforded β-thioacrylates **14a** and **14b**. Desilylation to **15a** and **15b** followed by thionocarbonation affords the corresponding β-thioacrylate-thionocarbonate derivatives **16a** and **16b**. *n*-Bu_3SnH/AIBN induced free radical cyclization of thionocarbonates **16a** and **16b** afforded respectively thiabicyclic compounds **18a** and **18b** in high yields. The absence of any monocyclic reduced compound deriving from direct hydrogen atom transfer from *n*-Bu_3SnH to incipient radicals **17a** and **17b** indicate that the 6-*exo* ring closure proceeds at high rate. Thus, 6-*exo* ring closure of cyclohexyl radicals **17a** and **17b** proceeds at the same high regioselectivity as that of the azacyclopentyl carbon-centered radicals **9** and **10**, but at rather lower stereoselectivity.

The two diastereomeric menthol derivatives **16a**,**b** were also obtained by the method based on acrylate/propiolate metathesis as described in Scheme 4. Thus, TBDMS-isopulegol **12** was converted in 60% overall yield into β-thioacrylate-thionocarbontes **16a**,**b**.

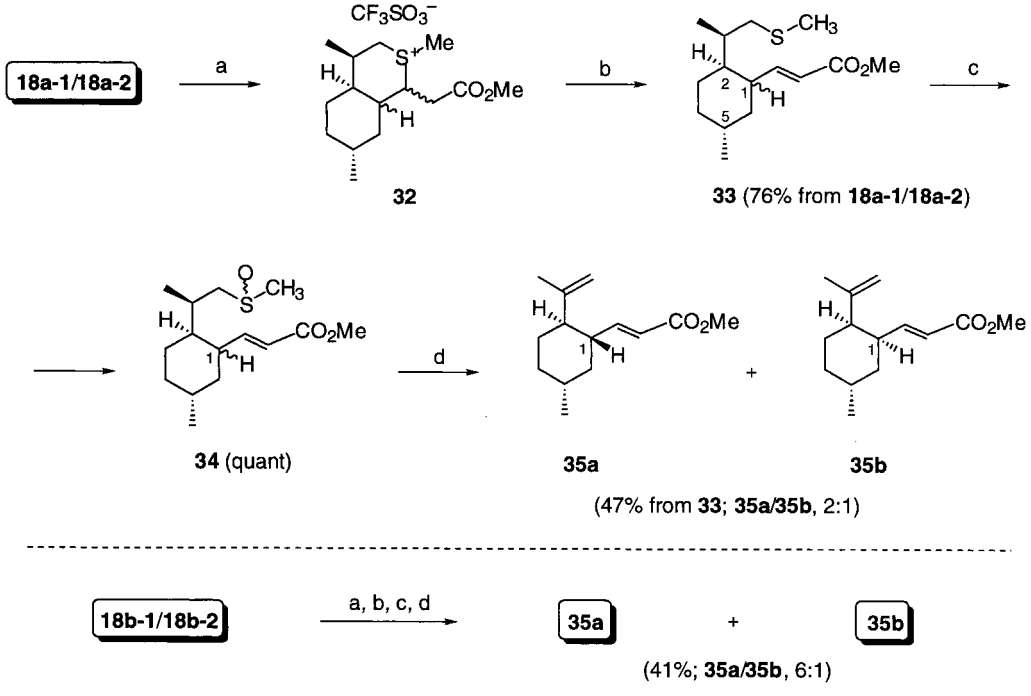
To elucidate the stereochemistry[7] of the inseparable 2:1 mixture of two thiabicyclo[4.4.0]decanes **18a-1** and **18a-2**, these compounds were oxidized with *m*-CPBA (Scheme 5) to the corresponding *trans*-fused bicyclic sulfone **22** (major isomer) and *cis*-fused bicyclic sulfone **23** (minor isomer) (separated by MPLC). The stereochemistry of sulfones **22** and **23** was established by detailed NMR analysis which included spin decoupling experiments, 1D- (^1H, ^{13}C/DEPT), and 2D-NMR spectra ($^1H/^1H$, COSY, $^1H/^{13}C$ HMQC). The same approach was used to elucidate the stereochemistry of the mixture of thiabicyclo[4.4.0]decanes **18b-1** and **18b-2**. It was found that the product of cyclization of **16b** consists of two *trans*-fused bicyclic isomers **18b-1**, which are epimers at C-2, and two *cis*-fused bicyclic isomers **18b-2** also epimeric at C-2. A 6:1 ratio of *trans*-fused to *cis*-fused isomers **18b-1** and **18b-2** was established on the grounds of the NMR spectra of their degradation products **35** (Scheme 7, **18b→35**). It was found that the NMR spectra for these compounds are identical to those obtained from the degradation of cyclic sulfides **18a** (Scheme 7, **18a→35**). Indeed, oxidation of thiabicyclo[4.4.0]decanes **18b-1** and **18b-2** gave, after separation, pure *trans*-fused sulfones **24** and **25** and a mixture of sulfone **25** with *cis*-fused sulfones **26** (epimers at C-2) where sulfone **25** constitutes the major component. 1,6-*cis*



Scheme 6. *Reagents and conditions*: (a) $HC{\equiv}CCO_2Et$, $EtOH–H_2O$ (15:1), Et_3N, 0°C→room temp., ca. 12 h. (b) PhOC(S)Cl, DMAP, pyridine, THF, 0°C→room temp., ca. 12 h. (c) *n*-Bu_3SnH, AIBN, toluene, 95°C, 1 h.

and 1,6-*trans* configuration assignments for compounds **22**–**26** was derived from spin coupling constants of the C-1 and C-6 protons, where $J_{H1eqH6ax}$ (*cis*)<$J_{H1axH6ax}$ (*trans*). 1,6-*cis* Compounds **23** and **26** and 1,6-*trans* compounds **22**, **24**, and **25** exhibited upon irradiation of the C-2 protons the following relevant coupling constants: $J_{H1eqH6ax}\approx 0$ Hz in compounds **23** and **26** and $J_{H1axH6ax}=10.0–10.9$ Hz in sulfones **22**, **24**, and **25**. The ^1H NMR spectra of sulfones **23**, **24** and **25** exhibited characteristic signals of C-5 methyl groups at 1.03–1.07 ppm. The corresponding signals for isomers **22** and **26** are further downfield and are 1.19, 1.20, and 1.31 ppm. This pattern derives from the deshielding effect of SO_2 group on the juxtaposed 5-CCH_3 H-atoms and constitutes a simple diagnostic tool to differentiate between epimers at position C-5.

Opposite stereoselectivity was observed in the 5-*exo* ring closure of cyclohexyl radical **30**. Its precursor, β-thioacrylate-thionocarbonte **29**, was prepared from thiol **27** as described in Scheme 6. A key mercaptane **27** was prepared from (+)-pulegone by a known procedure.[14] Addition of mercaptan **27** with ethyl propiolate using catalytic amount of triethylamine led to a β-thioacrylate **28** in good yield. This compound was acetylated with chlorothionoformate to give radical precursor **29**. 5-*exo* Intramolecular radical cyclization reaction of **29** (*n*-Bu_3SnH/AIBN) afforded 8-thiabicyclo[4.3.0]nonane derivative **31** (90% yield) as a



Scheme 7. *Reagents and conditions*: (a) $CF_3SO_3CH_3$, CH_2Cl_2, −10°C→room temperature, 2.5 h. (b) ^{t}BuOK, THF, 0°C→room temperature, 2 h; (c) *m*-CPBA, EtOAc, −60°C→−40°C, 4 h; (d) $H_2C{=}CHCO_2Me$, toluene, 180°C, 62 h.

6:1.5:1.5:1 mixture of four diastereomers (epimers at C-1 and C-9). The ratio 3:1 of 1,6-*cis*-fused bicyclic sulfide **31a** to 1,6-*trans*-fused bicycle **31b** was determined by NMR on the grounds of the spin coupling constants where $J_{H1eqH6ax}$ (*cis*)<$J_{H1axH6ax}$ (*trans*).

Oxidative sulfur extrusion in thiabicyclic compounds like **7**, **8**, **18a**,**b** and **31a**,**b** would restore the isopropenyl group and thus complete a process by which the hydroxyl group present in starting materials like **1** and **11** is substituted by an acrylic ester system through temporary sulfur connection. This is exemplified in Scheme 7 for compounds **18a** and **18b**. Thus, *S*-methylation of **18a-1/18a-2** with methyl trifluoromethanesulfonate to sulfonium **32**,[15] followed by base induced retro-Michael ring opening, afforded methyl acrylate **33**. Oxidation of the sulfide **33** to sulfoxide **34** using *m*-CPBA and subsequent pyrolysis in a sealed tube in toluene at 180°C produced isopropenyl-acrylate derivatives **35**. Similarly the same two *cis*/*trans* isopropenyl-acrylates **35** were obtained from thiabicyclo[4.4.0]decanes **18b-1/18b-2**.

Conclusion

Metathesis of acrylates with propiolates in (alkoxycarbonylethyl)alkyl sulfoxides like **3** and **20** constitutes an excellent method for the preparation of the corresponding β-sulfoxyacrylates like **5** and **21**. *n*-Bu_3SnH/AIBN induced free radical cyclization of β-thioacrylates like **6**, **16a**,**b** and **29** affords fused thiabicyclic compounds like **7**, **8**, **18a**,**b** and **31a**,**b** in high yields. These compounds may serve as intermediates for syntheses through temporary sulfur connection (e.g. Scheme 7). Bicyclic kainoid derivatives like **7** and **8** are of interest for the preparation of neuroexcitatory amino acids.[8]

Experimental

Thin layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60 F-254). Flash-chromatographic separations were performed on silica gel (Merck, Kieselgel 60, 230–400 Mesh ASTM). Medium-pressure liquid chromatography (MPLC) was performed on glass columns (Büchi, B-685, d=26 mm, l=460 mm) with LiChroprep™ 60 (particle size 15–25 μm). Light-induced reaction was performed by using BLAK-RAY® lamp, Model B-100AP, λ=310–400 nm (λ_{max}=365 nm). Unless otherwise stated NMR spectra were recorded in $CDCl_3$ on Bruker AMX-400 (400 MHz) spectrometer using TMS as an internal standard (chemical shifts in ppm). Infrared spectra (IR) were recorded on Nicolet Protege 460 FT-IR spectrometer. Elementary analyses were performed by the microanalytical laboratory of the Hebrew University, Jerusalem. High resolution mass spectra (HRMS) were recorded using a VG 7070e high resolution mass spectrometer. Solvents and glassware were dried and deoxygenated by conventional methods, and all reactions were performed in atmosphere of argon.

Di(*tert*-butyl) (2*S,3*R**,4*S**)-3-*tert*-butyldimethylsilyloxy-4-{1-methyl-2-[(*E*)-2-methyloxycarbonyl-1-ethenylsulfinyl]ethyl}tetrahydro-1*H*-1,2-pyrroledicarboxylate (5).** *a. Mercaptan addition.* A mixture of pyrrolidine **1**[2] (732 mg, 1.66 mmol), methyl β-mercaptopropionate (300 mg, 2.5 mmol), AIBN (68 mg, 0.42 mmol), and THF (0.5 mL) was stirred under argon in a sealed tube at 60°C for 4.5 h. The reaction mixture was evaporated, the residue was dissolved in xylene and evaporated to afford compound **2** (pale yellow oil, 900 mg, 97%) as a 1:1 mixture of two diastereomers. IR (film): ν_{max} 1702, 1739 cm^{-1}. ^1H NMR: (2 diastereomers, 2 conformers): δ 0.10–0.16 (m, 6H); 0.88 (s, 9H); 0.93–0.96 (m, 3H); 1.43–1.47 (m, 18H); 1.75–2.00 (m, 1H); 2.26 (m, 8H); 3.50–3.75 (m, 4H); 4.05–4.25 (m, 2H). The product was used without further purification in the next step.

b. Oxidation. To a solution of sulfide **2** (890 mg, 1.6 mmol) in CH_2Cl_2 (10 mL) at −60°C under argon was added dropwise for 20 min a solution of *m*-CPBA (326 mg of 85% reagent, 1.6 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred during 2 h at −60°C, slowly warmed to room temperature, washed with 5% aqueous $NaHCO_3$ (2×5 mL), dried, and evaporated. The residue was chromatographed (MPLC) to afford a mixture of four isomeric sulfoxides **3** (pale yellow oil, 703 mg, 1.22 mmol, 76%) and starting sulfide **2** (oil, 199 mg, 0.35 mmol, 22%). **3**: IR (film): ν_{max} 1701, 1739 cm^{-1}. ^1H NMR (4 diastereomers, 2 conformers): δ 0.11–0.19 (m, 6H); 0.88–089 (m, 9H); 1.05–1.30 (m, 3H); 1.42–1.47 (m, 18H); 2.20–3.21 (m, 9H); 3.50–3.80 (m, 4H); 4.10–4.30 (m, 2H). Anal. Calcd for $C_{27}H_{51}NO_8SSi$ (577.85): C, 56.12; H, 8.90; N, 2.42; S, 5.55. Found: C, 56.20; H, 8.74; N, 2.50; S, 5.74.

c. Sulfoxide metathesis. A mixture of sulfoxide **3** (320 mg, 0.56 mmol), methyl propiolate (0.5 mL, 5.9 mmol), and toluene (3 mL) was refluxed for 2 h. The reaction mixture was evaporated to dryness to afford unsaturated sulfoxide **5** as an oil with quantitative yield. IR (film): ν_{max} 1702, 1735, 1610 cm^{-1}. ^1H NMR (4 diastereomers, 2 conformers): δ 0.00–0.08 (m, 6H); 0.75–0.80 (m, 9H); 0.90–1.18 (m, 3H); 1.30–1.36 (m, 18H); 2.25–3.15 (m, 5H); 3.40–3.75 (m, 4H); 4.01–4.10 (m, 2H); 6.52–6.58 (m, 1H); 7.45–7.50 (m, 1H). Anal. Calcd for $C_{27}H_{49}NO_8SSi$ (575.83): C, 56.32; H, 8.58; N, 2.43; S, 5.57. Found: C, 56.01; H, 8.53; N, 2.18; S, 5.44.

Di(*tert*-butyl) (2*S,3*R**,4*S**)-3-phenoxythiocarbonyloxy-4-{1-methyl-2-[(*E*)-2-methyloxycarbonyl-1-ethenylsulfanyl]ethyl}tetrahydro-1*H*-1,2-pyrroledicarboxylate (6).** *a. Sulfoxide reduction.* A mixture of unsaturated sulfoxide **5** (541 mg, 0.94 mmol), Lawesson's reagent (378 mg, 0.54 mmol), and THF (10 mL) was stirred at −10°C for 50 min. After TLC revealed full consumption of starting material, the reaction was diluted with hexane (15 mL) and the formed suspension was filtered through silica gel (2 cm). The filtrate was evaporated and the residue was chromatographed (MPLC) to afford a corresponding unsaturated sulfide (oil, 304 mg, 60%). IR (film): ν_{max} 1582, 1707, 1739 cm^{-1}. ^1H NMR (270 MHz, 2 diastereomers, 2 conformers): δ 0.13–0.25 (m, 6H); 0.87, 0.89 (2×s, 9H); 0.96–1.19 (m, 3H); 1.43–1.48 (m, 18H); 1.90–2.10, 2.50–3.15 (m, 5H); 3.50–3.80 (m, 4H); 4.09–4.22 (m, 2H); 5.68–5.77 (m, 1H); 7.62–7.68 (m, 1H).

b. Desilylation. A mixture of the unsaturated sulfide (260 mg, 0.46 mmol), AcOH (27 mg, 0.46 mmol), and Bu_4NF (1 M solution in THF, 1 mL) was kept for 20 h, diluted with 1:1 EtOAc/hexane mixture (5 mL) and chromatographed (flash chromatography, EtOAc/hexane, 1:1). Fractions containing the corresponding alcohol were combined, evaporated (IR (film): ν_{max} 1581, 1683, 1703, 1737, 3447 cm^{-1}), and used at the next stage.

c. Thionocarbonation. A solution of the alcohol and phenanthroline (ca. 1 mg) in THF was cooled to −78°C, and a solution of *n*-BuLi (1.6 M solution in hexane, 0.4 mL, 0.54 mmol) was added followed by the neat PhOC(S)Cl. After 1.5 h at −78°C the reaction mixture was slowly warmed to room temperature, and stirred 1.5 h at 25°C. The reaction mixture was diluted with hexane (4 mL), the formed suspension was filtered through silica (4 cm). The filtrate was evaporated and purified by MPLC (EtOAc/hexane, 3:7) to afford thionocarbonate **6** (yellow-red oil, 190 mg, 0.33 mmol, 45% from unsaturated sulfoxide **5**). ^{1}H NMR (2 diastereomers, 2 conformers): δ 1.11, 1.26 (2×d, *J*=6.9 Hz, 3H); 1.44–1.51 (m, 18H); 2.6–3.0 (m, 4H); 3.20, 3.90 (2×m, 1H); 3.70, 3.71 (2×d, 3H); 4.62, 4.64 (2×d, major, *J*=6.2 Hz), 4.73 (m, minor), total 1H; 5.75 (m, 2H); 7.09–7.45 (m, 5H); 7.62 (m, 1H). Anal. Calcd for $C_{28}H_{39}NO_8S_2$ (581.74): C, 57.81; H, 6.76; N, 2.41; S, 11.02. Found: C, 57.49; H, 6.73; N, 2.07; S, 10.95.

Di(*tert*-butyl) (3*S,3a*S**,4*R**,7*S**,7a*R**)- and di(*tert*-butyl) (3*S**,3a*R**,4*S**,7*R**,7a*R**)-7-methyl-4-methyloxycarbonylmethylperhydrothiopyrano[3,4-*c*]pyrrole-2,3-dicarboxylates (7) and (8).** A solution of thionocarbonate **6** (155 mg, 0.27 mmol), *n*-Bu_3SnH (100 mg, 0.35 mmol), AIBN (11 mg, 0.07 mmol) in toluene (15 mL) was heated at 100°C for 1.5 h. The reaction mixture was washed with 5 N NaOH to remove PhOH, aqueous $NaHCO_3$, dried, and evaporated. The residue was dissolved in MeCN (30 mL) and extracted with hexane to remove organotin compounds. The MeCN solution was evaporated and the residue was separated by MPLC (EtOAc/hexane, 2:3) to afford two isomers. High R_f isomer—compound **7** (amorphous colorless solid, 60 mg, 52%). IR (film): ν_{max} 1702, 1742 cm^{-1}. ^{1}H NMR (C_6D_6, 2 conformers): δ 0.39 (d, *J*=6.9 Hz, major), 0.44 (d, *J*=6.9 Hz), total 3H; 1.41 (s, 9H); 1.53 (s, minor), 1.54 (s, major), total 9H; 1.76 (m, 2H); 2.09 (m, 1H); 2.31 (dd, *J*=5.8, 11.3 Hz, 1H); 2.39 (dd, *J*=8.8, 15.8 Hz, minor), 2.41 (dd, *J*=8.8, 15.8 Hz, major), total 1H; 2.58 (m, major), 2.70 (m, minor), total 1H; 2.73 (dd, *J*=2.4, 15.8 Hz, minor), 2.74 (dd, *J*=3.4, 15.8 Hz, major), total 1H; 3.10 (m, 2H); 3.35 (s, major), 3.36 (s, minor), total 3H; 3.60 (dd, *J*=8.5, 10.1 Hz, minor), 3.77 (dd, *J*=8.5, 10.6, major), total 1H; 4.31 (s, major), 4.50 (s, minor), total 1H. Anal. Calcd for $C_{21}H_{35}NO_6S$ (429.57): C, 58.72; H, 8.21; N, 3.26; S, 7.46. Found: C, 58.79; H, 8.21; N, 3.26; S, 7.46. Low R_f isomer—compound **8** (oil, 41 mg, 35%). IR (film): ν_{max} all identical to high R_f isomer. ^{1}H NMR (C_6D_6, 2 conformers): δ 0.47 (d, *J*=6.4 Hz, major), 0.55 (d, *J*=6.4 Hz, minor), total 3H; 1.13 (m, 1H); 1.26 (m, 1H); 1.54 (s, major), 1.58 (s, minor), total 18H; 1.77 (dd, *J*=3.7, 14.1 Hz, major), 1.84 (dd, *J*=3.8, 14.1 Hz, minor), total 1H; 1.91 (dd, *J*=11.1, 14.0 Hz, major), 1.93 (dd, *J*=10.1, 14.0 Hz, minor), total 1H; 2.29 (ddd, *J*=2.8, 5.5, 9.4 Hz, major), 2.36 (ddd, *J*=3.6, 5.5, 8.9 Hz, minor), total 1H; 2.44 (dd, *J*=7.4, 15.9 Hz, major), 2.51 (dd, *J*=7.3, 15.8 Hz, minor), total 1H; 2.68 (dd, *J*=7.7, 15.8 Hz, minor), 2.69 (dd, *J*=7.6, 15.9 Hz, major), total 1H; 3.31 (dd, *J*=5.0, 11.0, major), 3.32 (dd, *J*=5.0, 11.0, minor), total 1H; 3.36 (s, major), 3.38 (s, minor), total 3H; 3.47 (dd, *J*=2.0, 10.7, minor), 3.77 (d, *J*=11.2 Hz, major), total 1H; 3.56 (dt, *J*=3.5, 7.5 Hz, minor), 3.63 (dt, *J*=2.8, 7.5 Hz, major), total 1H; 4.68 (d, *J*=9.4 Hz, major), 4.78 (d, *J*=8.7 Hz, minor), total 1H. Anal. Calcd for $C_{21}H_{35}NO_6S$ (429.57): C, 58.72; H, 8.21; N, 3.26; S, 7.46. Found: C, 58.39; H, 8.43; N, 3.03; S, 7.38.

(2*R*)- and (2*S*)-2-[(1*S*,2*R*,4*R*)-2-*tert*-Butyldimethylsilyloxy-4-methylcyclohexyl]propyl ethanethioates (13a) and (13b). To a cold (−72°C) solution of (−)-isopulegol **11** (5.0 mL, 29.5 mmol) in methylene chloride (40 mL) were added in rapid succession 2,6-lutidine (5.2 mL, 44.5 mmol) and *tert*-butyldimethylsilyl triflate (7.5 mL, 32.6 mmol). The reaction mixture was stirred at the same temperature for 1 h. The temperature was allowed to rise to 0°C, and hexane (75 mL) was added. The emulsion was washed with 1 N HCl (25 mL), saturated $NaHCO_3$ (2×50 mL), dried ($NaHCO_3$ and Na_2SO_4), and evaporated. Flash chromatography (hexane) afforded the silylated alcohol **12** (7.91 g, quant.) as a colorless oil. ^{1}H NMR (250 MHz): δ 0.01, 0.04 (2×s, 6H); 0.86 (s, 9H); 0.91 (d, *J*=6.4 Hz, 3H); 0.98–1.11 (m, 1H); 1.24–1.53 (m, 2H); 1.57–1.67 (m, 3H); 1.69 (s, 3H); 1.84–1.97 (m, 2H); 3.49 (ddd, *J*=10.3, 10.3, 4.4 Hz, 1H); 4.75 (br s, 2H). ^{13}C NMR: δ −4.6, 17.4, 20.2, 21.7, 25.2, 29.9, 31.0, 33.7, 44.5, 52.9, 72.7, 110.4, 147.2. HRMS (CI) Calcd for $C_{16}H_{32}OSi$ (MH^+): 269.2301. Found: (MH^+): 269.2307. The silylated alcohol **12** (2.473 g, 9.2 mmol) and thiolacetic acid (2.7 mL, 37.8 mmol) were deoxygenated and the reaction mixture was irradiated with a longwave UV lamp for 72 h. An excess of thiolacetic acid was removed in vacuum. The residue was purified by flash chromatography (toluene–hexane, 1:1) to give recovered starting compound **12** (945 mg, 3.5 mmol, 38%) and two separated sulfides **13a** (yellow-red oil, 1.175 g, 3.4 mmol, 60% based on reacted **12**) and **13b** (yellow oil, 786 mg, 2.3 mmol, 40% based on reacted **12**).

13a: yellow–red oil, IR (neat): ν_{max} 2954, 2925, 2850, 1690, 1258, 1095 cm^{-1}. ^{1}H NMR: δ 0.05, 0.07 (2×s, 6H); 0.87 (s, 9H); 0.90 (d, *J*=6.6 Hz, 3H); 0.79–1.08 (m, 3H); 0.95 (d, *J*=7.0 Hz, 3H); 1.28 (m, 1H); 1.38 (m, 1H); 1.62–1.68 (m, 2H); 1.88 (m, 1H); 2.15 (m, 1H); 2.70 (dd, *J*=12.7, 10.9 Hz, 1H); 2.95 (dd, *J*=12.7, 3.7 Hz, 1H); 3.50 (ddd, *J*=10.3, 10.3, 4.3 Hz, 1H). ^{13}C NMR: δ −4.8, −3.6, 17.5, 18.0, 22.2, 24.6, 26.0, 30.6, 31.5, 31.8, 31.9, 34.5, 45.4, 50.3, 71.9, 196.2. HRMS (CI) Calcd for $C_{18}H_{37}O_2SSi$ (MH^+): 345.2284. Found (MH^+): 345.2288.

13b: yellow oil, IR (neat): ν_{max} 2962, 2923, 2869, 1706, 1262, 1106 cm^{-1}. ^{1}H NMR: δ 0.02, 0.05 (2×s, 6H); 0.81 (d, *J*=7.0 Hz, 3H); 0.86 (s, 9H); 0.89 (d, *J*=6.5 Hz, 3H); 0.93–1.05 (m, 3H); 1.29–1.44 (m, 2H); 1.55 (dddd, *J*=13.0, 3.3, 3.3, 3.3 Hz, 1H); 1.63 (m, 1H); 1.85 (m, 1H); 2.21 (dddd, *J*=21.4, 7.1, 7.1, 2.2 Hz, 1H); 2.77 (dd, *J*=13.1, 7.6 Hz, 1H); 2.87 (dd, *J*=13.1, 7.6 Hz, Hz, 1H); 3.37 (ddd, *J*=10.2, 10.2, 4.3 Hz, 1H). ^{13}C NMR: δ −4.9, −3.6, 13.5, 18.0, 22.3, 23.0, 25.9, 30.6, 31.2, 31.6, 34.2, 34.6,

45.2, 47.8, 71.7, 195.9. HRMS (CI) Calcd for $C_{18}H_{37}O_2SSi$ (MH^+): 345.2284. Found (MH^+): 345.2272.

Methyl (*E/Z*)-3-[(2*R*)-2-((1*S*,2*R*,4*R*)-2-*tert*-butyldimethylsilyloxy-4-methylcyclohexyl)propylsulfanyl]-2-propenoate (14a). To thioate **13a** (1.20 g, 3.5 mmol) at 0°C was added a deoxygenated solution of KOH (0.25 g, 4.4 mmol) in methanol (2.5 mL). The temperature was allowed to rise to room temperature and the reaction mixture was stirred for 1.5 h (TLC control). The reaction mixture was quenched with 15 mL of a phosphate buffer (pH 5.5) and hexane (10 mL) was added. The aqueous layer was extracted with hexane (3×30 mL). The combined hexane solution was dried over Na_2SO_4 and evaporated to afford deprotected thiol (1.05 g, quant.). The crude thiol was dissolved in MeOH–H_2O mixture (10:1, 10 mL), cooled to 0°C and methyl propiolate (0.43 mL, 5.0 mmol) and catalytic amount of triethylamine (2 drops of a mixture: 1 drop of NEt_3 in 10 drops of MeOH) were added. The reaction mixture was stirred for 24 h at room temperature, diluted with benzene (100 mL) and evaporated. The residue was purified by flash chromatography (EtOAc/hexane, 1:20) to give the unsaturated sulfide **14a** (oil, 1.11 g, 82% from **13a**) as a mixture of two isomers (*E/Z*, 1:6). IR (neat): ν_{max} 2954, 2924, 2854, 1701, 1577, 1255, 1162 cm^{-1}. ^1H NMR (*E/Z* isomers): δ 0.05, 0.07 (2×s, *E*), 0.07, 0.08 (2×s, *Z*), total 6H; 0.88 (s, 9H); 0.83–1.06 (m, 3H); 0.90 (d, *J*=6.7 Hz, 3H); 1.04 (d, *J*=7.0 Hz, 3H); 1.37 (m, 2H); 1.63 (m, 2H); 1.90 (m, 1H); 2.19 (m, 1H); 2.53 (dd, *J*=12.6, 10.4 Hz, *Z*), 2.54 (dd, *J*=10.8, 10.8 Hz, *E*), total 1H; 2.90 (dd, *J*=11.7, 4.0 Hz, *E*), 2.90 (dd, *J*=11.4, 4.4 Hz, *Z*), total 1H; 3.50 (ddd, *J*=10.4, 10.4, 4.2 Hz, 1H); 5.71 (d, *J*=15.1 Hz, *E*), 5.81 (d, *J*=10.2 Hz, *Z*), total 1H; 7.13 (d, *J*=10.2 Hz, *Z*), 7.74 (d, *J*=15.1 Hz, *E*), total 1H. ^{13}C NMR (*E/Z* isomers): δ −4.41 (*E*), −4.20 (*Z*), −3.55 (*E*), −3.39 (*Z*), 16.70 (*Z*), 17.34 (*E*), 18.05 (*E/Z*), 22.18 (*E/Z*), 25.32 (*E*), 25.76 (*Z*), 25.94 (*E*), 26.00 (*Z*), 31.52 (*Z*), 32.04 (*E*), 33.82 (*E/Z*), 34.48 (*Z*), 35.69 (*E*), 40.41 (*E/Z*), 45.37 (*E*), 45.45 (*Z*), 49.45 (*Z*), 49.93 (*E*), 51.11 (*Z*), 51.32 (*E*), 72.07 (*E*), 72.22 (*Z*), 111.89 (*Z*), 112.78 (*E*), 148.13 (*E*), 151.82 (*Z*), 167.10 (*E/Z*). HRMS (CI) Calcd for $C_{20}H_{39}O_3SSi$ (MH^+): 387.2389. Found (MH^+): 387.2330.

Methyl (*E/Z*)-3-[(2*S*)-2-((1*S*,2*R*,4*R*)-2-*tert*-butyldimethylsilyloxy-4-methylcyclohexyl)propylsulfanyl]-2-propenoate (14b). Compound **14b** (oil, 661 mg, 81%) was obtained as a mixture of two isomers (*E/Z*, 1:6) from thioate **13b** (727 mg, 2.1 mmol) as described above for the synthesis of **14a**, after purification by flash chromatography (EtOAc/hexane, 1:20). IR (neat): ν_{max} 2951, 2927, 2856, 1707, 1579, 1256, 1166 cm^{-1}. ^1H NMR (*E/Z* isomers): δ 0.03, 0.05 (2×s, 6H); 0.86 (s, 9H); 0.86 (d, *J*=7.1 Hz, *Z*), 0.87 (d, *J*=7.1 Hz, *E*), total 3H; 0.89 (d, *J*=6.5 Hz, *Z*), 0.90 (d, *J*=6.5 Hz, *E*), total 3H; 0.96–1.06 (m, 2H); 1.23–1.54 (m, 4H); 1.63 (m, 1H); 1.87 (m, 1H); 2.37 (m, 1H); 2.61–2.76 (m, 2H); 3.40 (ddd, *J*=10.3, 10.3, 4.3 Hz, *E*), 3.41 (*J*=10.2, 10.2, 4.3 Hz, *Z*), total 1H; 5.72 (d, *J*=15.1 Hz, *E*), 5.82 (d, *J*=10.2 Hz, *Z*), total 1H; 7.08 (d, *J*=10.2 Hz, *Z*), 7.69 (d, *J*=15.1 Hz, *E*), total 1H. ^{13}C NMR (*E/Z* isomers): δ −4.86 (*E/Z*), −3.66 (*E/Z*), 12.96 (*Z*), 13.45 (*E*), 17.99 (*E/Z*), 22.23 (*E/Z*), 22.95 (*E*), 23.08 (*Z*), 25.79 (*E*), 25.85 (*Z*), 30.29 (*E*), 31.42 (*Z*), 31.48 (*E*), 31.60 (*Z*), 34.19 (*Z*), 38.05 (*E*), 42.30 (*E/Z*), 45.15 (*E/Z*), 47.88 (*Z*), 48.04 (*E*), 51.12 (*Z*), 51.28 (*E*), 71.69 (*E*), 71.79 (*Z*), 112.32 (*Z*), 113.26 (*E*), 147.39 (*E*), 150.93 (*Z*), 167.11 (*E/Z*). HRMS (CI) Calcd for $C_{20}H_{39}O_3SSi$ (MH^+): 387.2389. Found (MH^+): 387.2330.

Methyl (*E/Z*)-3-[(2*R*)-2-((1*S*,2*R*,4*R*)-2-phenoxythiocarbonyloxy-4-methylcyclohexyl)propylsulfanyl]-2-propenoate (16a). *Method A.* A mixture of compound **14a** (1.10 g, 2.84 mmol) and tetrabutylammonium fluoride (1 M solution in THF, 7.1 mL) was stirred at room temperature overnight. The solution was poured into 35 mL of a phosphate buffer (pH 5.8) and extracted with ethyl acetate (3×30 mL). The organic layer was dried (Na_2SO_4), the solvent was evaporated, and flash chromatography (EtOAc/hexane, 3:7) of the residue gave alcohol **15a** (oil, 774 mg, quant.). ^1H NMR (250 MHz, *E/Z* isomers): δ 0.68–1.02 (m, 3H); 0.80 (d, *J*=6.5 Hz, 3H); 0.95 (d, *J*=6.9 Hz, 3H); 1.13–1.39 (m, 2H); 1.49–1.57 (m, 2H); 1.85 (br d, *J*=12.0 Hz, 1H); 2.07 (m, 1H); 2.43 (dd, *J*=13.0, 9.9 Hz, 1H); 2.92 (dd, *J*=13.0, 4.4 Hz, *Z*), 2.96 (dd, *J*=13.0, 4.4 Hz, *E*), total 1H; 3.39 (ddd, *J*=10.5, 10.5, 4.2 Hz, 1H); 3.60 (s, *E*), 3.61 (s, *Z*), total 3H; 5.71 (d, *J*=15.1 Hz, *E*), 5.72 (d, *J*=10.2 Hz, *Z*), total 1H; 7.11 (d, *J*=10.2 Hz, *Z*), 7.60 (d, *J*=15.1 Hz, *E*), total 1H. To a solution of alcohol **15a** (767 mg, 2.82 mmol), pyridine (1.0 mL, 12.9 mmol), and DMAP (69 mg, 0.56 mmol) in THF (5 mL) at 0°C was added by syringe pump a solution of phenyl chlorothionoformate (2.0 mL, 9.28 mmol) in THF (2 mL). The addition was complete within 30 min. The temperature was allowed to rise to room temperature and the reaction mixture was stirred overnight. The reaction mixture was diluted with hexane (12 mL) and the formed suspension was filtered trough silica gel (4.5 cm). The filtrate was evaporated and purified by MPLC (EtOAc/hexane, 1:9) to afford phenoxythiocarbonyl derivative **16a** (red oil, 944 mg, 82%) as a mixture of two isomers (*E/Z*, 1:4). IR (neat): ν_{max} 2952, 2928, 2869, 1707, 1581, 1498, 1292, 1208, 1167 cm^{-1}. ^1H NMR (*E/Z* isomers): δ 0.85–0.99 (m, 1H); 0.95 (d, *J*=6.5 Hz, 3H); 1.06 (d, *J*=6.9 Hz, *E*), 1.07 (d, *J*=6.9 Hz, *Z*), total 3H; 1.08–1.29 (m, 2H); 1.52 (m, 1H); 1.69–1.87 (m, 3H); 1.99 (m, 1H); 2.26–2.34 (m, 1H); 2.50 (dd, *J*=13.2, 10.4 Hz, *Z*), 2.60 (dd, *J*=13.2, 10.4 Hz, *E*), total 1H; 2.94 (dd, *J*=13.2, 4.2 Hz, *Z*), 2.99 (dd, *J*=13.2, 4.2 Hz, *E*), total 1H; 3.66 (s, *E*), 3.72 (s, *Z*), total 3H; 5.23 (ddd, *J*=10.9, 10.9, 4.4 Hz, *E*), 5.26 (ddd, *J*=10.9, 10.9, 4.4 Hz, *Z*), total 1H; 5.76 (d, *J*=15.2 Hz, *E*), 5.81 (d, *J*=10.1 Hz, *Z*), total 1H; 7.04–7.08 (m, 2H); 7.24–7.29 (m, 1H); 7.35–7.42 (m, 2H); 7.11 (d, *J*=10.1 Hz, *Z*), 7.68 (d, *J*=15.2 Hz, *E*), total 1H. ^{13}C NMR (*E/Z* isomers): δ 16.78 (*Z*), 16.94 (*E*), 22.28 (*E/Z*), 26.33 (*Z*), 27.16 (*E*), 31.60 (*E*), 31.66 (*Z*), 34.40 (*Z*), 35.38 (*E/Z*), 37.19 (*E*), 39.77 (*E/Z*), 40.68 (*E/Z*), 46.69 (*E*), 46.73 (*Z*), 51.58 (*Z*), 51.73 (*E*), 84.83 (*E*), 84.98 (*Z*), 112.92 (*Z*), 113.89 (*E*), 122.36 (*Z*), 122.43 (*E*), 126.91 (*E*), 127.00 (*Z*), 129.88 (*E*), 129.95 (*Z*), 147.87 (*E*), 151.66 (*Z*), 153.66 (*E/Z*), 166.03 (*E*), 167.42 (*Z*), 194.47 (*E*), 194.75 (*Z*). HRMS (CI) Calcd for $C_{21}H_{29}O_4S_2$ (MH^+): 409.1507. Found (MH^+): 409.1497.

Methyl (*E/Z*)-3-[(2*S*)-2-((1*S*,2*R*,4*R*)-2-phenoxythiocarbonyloxy-4-methylcyclohexyl)propylsulfanyl]-2-propenoate (16b). *Method A.* Compound **16b** (red oil, 456 mg, 67%) was obtained as a mixture of two isomers (*E/Z*, 1:4)

from sulfanylpropenoate **14b** (644 mg, 1.67 mmol) as described above for the synthesis of **16a**, after purification by MPLC (EtOAc/hexane, 1:9), through the intermediacy of **15b**: ^{1}H NMR (250 MHz, *E*/*Z* isomers): δ 0.71–1.04 (m, 3H); 0.83 (d, *J*=6.4 Hz, 3H); 0.86 (d, *J*=6.7 Hz, 3H); 1.27–1.39 (m, 2H); 1.46 (m, 1H); 1.59 (m, 1H); 1.91 (br d, *J*=12.0 Hz, 1H); 2.31 (m, 1H); 2.56–2.74 (m, 2H); 3.32 (ddd, *J*=10.4, 10.4, 4.3 Hz, 1H); 3.63 (s, *E*), 3.65 (s, *Z*), total 3H; 5.67 (d, *J*=15.1 Hz, *E*), 5.75 (d, *J*=10.2 Hz, *Z*), total 1H; 7.07 (d, *J*=10.2 Hz, *Z*), 7.64 (d, *J*=15.1 Hz, *E*), total 1H.

16b: IR (neat): ν_{max} 2955, 2931, 2869, 1714, 1582, 1496, 1293, 1199 cm^{-1}. ^{1}H NMR (*E*/*Z* isomers): δ 0.89–1.01 (m, 1H); 0.96 (d, *J*=6.5 Hz, *E*), 0.97 (d, *J*=6.5 Hz, *Z*), total 3H; 0.99 (d, *J*=7.0 Hz, *E*), 1.00 (d, *J*=7.0 Hz, *Z*), total 3H; 1.08–1.31 (m, 2H); 1.54 (m, 1H); 1.63–1.79 (m, 2H); 1.84–1.97 (m, 1H); 2.11–2.25 (m, 1H); 2.33 (m, 1H); 2.67–2.81 (m, 2H); 3.69 (s, *E*), 3.74 (s, *Z*), total 3H; 5.18 (ddd, *J*=10.8, 10.8, 4.4 Hz, *Z*), 5.22 (ddd, *J*=10.8, 10.8, 4.4 Hz, *E*), total 1H; 5.77 (d, *J*=15.1 Hz, *E*), 5.81 (d, *J*=10.1 Hz, *Z*), total 1H; 7.04–7.08 (m, 2H); 7.24–7.29 (m, 1H); 7.35–7.42 (m, 2H); 7.08–7.11 (m, 2H); 7.24–7.31 (m, 1H); 7.35–7.44 (m, 2H); 7.10 (d, *J*=10.1 Hz, *Z*), 7.71 (d, *J*=15.1 Hz, *E*), total 1H. HRMS (CI) Calcd for $C_{21}H_{29}O_4S_2$ (MH^+): 409.1507. Found (MH^+): 409.1500.

Methyl (*E*)-3-[(2*RS*)-2-((1*S*,2*R*,4*R*)-2-phenoxythiocarbonyloxy-4-methylcyclohexyl)propylsulfanyl]-2-propenoates (16a,b). *Method B.* A mixture of compound **12** (750 mg, 2.79 mmol), methyl β-mercaptopropionate (503 mg, 4.18 mmol), AIBN (117 mg, 0.71 mmol) and THF (0.8 mL) was deoxygenated and refluxed under argon for 4.5 h. Then the reaction mixture was cooled to room temperature and additional methyl β-mercaptopropionate (335 mg, 2.79 mmol), AIBN (117 mg, 0.71 mmol) and THF (0.3 mL) were added and the mixture was refluxed for 3.5 h (TLC monitoring). The reaction mixture was evaporated and purified by flash chromatography (EtOAc/hexane, 1:5) to afford sulfide **19** (colorless oil, 954 mg, 88%) as a mixture of two diastereomers at C-2. ^{1}H NMR (250 MHz, epimers at C-2): δ 0.05, 0.07, 0.09 (3×s, 6H); 0.83 (d, *J*=6.9 Hz), 1.02 (d, *J*=6.9 Hz), total 3H; 0.89 (s, 9H); 0.91 (d, *J*=6.9 Hz, 3H); 0.84–1.05 (m, 1H); 1.25–1.48 (m, 3H); 1.63 (m, 2H); 1.88 (m, 1H); 2.05–2.32 (m, 2H); 2.46 (d, *J*=7.5 Hz, 1H); 2.58–2.70 (m, 3H); 2.73–2.80 (m, 2H); 4.43 (ddd, *J*=10.3, 10.3, 4.3 Hz), 4.45 (ddd, *J*=10.3, 10.3, 4.3 Hz), total 1H; 3.70, 3.72 (2×s, 3H). ^{13}C NMR (epimers at C-2): δ −4.55, −3.77, −3.57, 13.34, 17.47, 17.94, 17.99, 19.64, 22.21, 22.79, 25.03, 25.80, 25.94, 26.60, 27.99, 29.92, 31.47, 32.41, 34.22, 34.50, 34.56, 34.80, 35.89, 37.91, 38.20, 45.19, 45.41, 47.45, 50.08, 51.62, 71.79, 71.99, 172.39. To a solution of sulfides **19** (427 mg, 1.1 mmol) in methylene chloride (6 mL) at −60°C under argon was added dropwise for 20 min a solution of *m*-CPBA (348 mg of 54.5% reagent, 1.1 mmol) in methylene chloride (6 mL). The reaction mixture was stirred for 4 h at −60°C and a saturated solution of sodium bisulphite (3 mL) was added. The reaction mixture was slowly warmed to room temperature, washed with 5% aqueous sodium bicarbonate (3×5 mL), dried, and evaporated. The residue was purified by flash chromatography (EtOAc/hexane, gradient from 3:7 to 1:1) to afford sulfoxide **20** (439 mg, quant.) as a mixture of four diastereomers. ^{1}H NMR (250 MHz, 4 diastereomers): δ 0.06, 0.07, 0.09, 0.11 (4×s, 6H); 0.87–1.47 (m, 16H); 1.23–1.55 (m, 3H); 1.65 (m, 2H); 1.82–1.93 (m, 2H); 2.33–3.09 (m, 7H); 4.43 (ddd, *J*=10.2, 10.2, 4.2 Hz), 4.49 (ddd, *J*=10.2, 10.2, 4.2 Hz), total 1H; 3.73 (s, 3H). A mixture of sulfoxides **20** (407 mg, 1.0 mmol), methyl propiolate (0.88 mL, 11 mmol), and toluene (6 mL) was refluxed for 2 h. The reaction mixture was evaporated to dryness and purified by flash chromatography (EtOAc/hexane, 3:7) to afford unsaturated *E*-sulfoxide **21** (362 mg, 90%) as a mixture of four diastereomers. ^{1}H NMR (250 MHz, 4 diastereomers): δ 0.06, 0.08, 0.09, 0.11 (4×s, 6H); 0.84–1.94 (m, 23H); 2.31–3.12 (m, 2H); 3.48 (ddd, *J*=10.3, 10.3, 4.2 Hz, 1H); 3.82, 3.85 (2×s, 3H); 6.67 (d, *J*=15.0 Hz, 1H); 7.62 (d, *J*=15.0 Hz, 1H). HRMS (CI) Calcd for $C_{20}H_{39}O_4SSi$ (MH^+): 403.2338. Found: (MH^+): 403.2320. To a cold (0°C) solution of unsaturated sulfoxide **21** (396 mg, 0.98 mmol) and sodium iodide (367 mg, 2.45 mmol) in acetone (2.5 mL) was added dropwise a solution of trifluoroacetic anhydride (513 mg, 2.44 mmol) in acetone (2.5 mL). The reaction mixture was stirred at 0°C for 30 min, evaporated, dissolved in water, and extracted with diethyl ether. The organic layer was washed with 10% aqueous sodium thiosulfate and water, dried (Na_2SO_4) and evaporated to afford a mixture of silylated and desilylated unsaturated sulfides, which were directly used at the next stage. A mixture of unsaturated sulfides and tetrabutylammonium fluoride (1 M solution in THF, 4.9 mL) was stirred for 22 h, diluted with EtOAc/hexane (1:1, 16 mL), evaporated and purified by flash chromatography (EtOAc/hexane, 3:7) to afford *E*-alcohols **15a**,**b** in a quantitative yield. ^{1}H NMR data of the compound have been compared to the data of the samples **15a** and **15b** obtained from sulfides **14a** and **14b** and are identical with their *E*-isomers. To a solution of alcohols **15a**,**b** (256 mg, 0.94 mmol), pyridine (0.33 mL, 4.3 mmol), and DMAP (23 mg, 0.19 mmol) in THF (2 mL) at 0°C was added by syringe pump a solution of phenyl chlorothionoformate (0.7 mL, 3.25 mmol) in THF (1 mL). The addition was complete within 30 min. The temperature was allowed to rise to room temperature and the reaction mixture was stirred overnight. The reaction mixture was diluted with hexane (5 mL) and the formed suspension was filtered trough silica gel (2.5 cm). The filtrate was evaporated and purified by MPLC (EtOAc/hexane, 1:9) to afford *E*-phenoxythiocarbonyl derivatives **16a**,**b** (red oil, 287 mg, 75%) as a mixture of two isomers (epimers at C-2). ^{1}H and ^{13}C NMR data of the compound have been compared to the data of the samples **16a** and **16b** obtained from alcohols **15a** and **15b** and are identical with their *E*-isomers.

Free radical cyclizations of thionocarbonates 16a and 16b

(1*R*,2*S*,5*R*,6*S*,9*R*)- and (1*S*,2*R*,5*R*,6*S*,9*R*)-5,9-Dimethyl-3-thiabicyclo[4.4.0]decane-2-acetic acid methyl esters (18a-1) and (18a-2). A 0.025 M solution of thionocarbonate **16a** (915 mg, 2.24 mmol) in toluene (90 mL) was placed in a flask equipped with a reflux condenser and a magnetic bar, under argon atmosphere. The solution was heated to 95°C, and individual 0.93 M solution of *n*-Bu_3SnH (1.5 mL, 5.6 mmol, 2.5 equiv.) and a 0.07 M solution AIBN

(68 mg, 0.4 mmol, 0.18 equiv.) in toluene (6 mL) were slowly added (syringe pump, 1 h). The heating at 95°C was continued until disappearance of starting material (TLC). When the reaction was finished, the solvent was removed under vacuum, and the residue was purified by flash chromatography (EtOAc/hexane, 1:9) to afford thiabicyclodecane **18a** (oil, 476 mg, 83%) as a mixture of two isomers (ratio **18a-1/18a-2**, 2:1). ^{1}H NMR (2 isomers): δ 0.54 (ddd, J=11.8, 11.8, 11.8 Hz, major), 0.85–1.70 (m, major+minor), total 8H; 0.81 (d, J=6.5 Hz, minor), 0.86 (d, J=6.5 Hz, major), total 3H; 0.94 (d, J=7.0 Hz, minor), 1.05 (d, J=6.9 Hz, major), total 3H; 1.76–1.85 (m, 1H); 1.90 (ddddt, J=10.5, 10.5, 6.9, 6.9, 6.9 Hz, major), 2.01 (m, 1H, minor), total 1H; 2.14 (dd, J=13.4, 3.4 Hz, minor), 2.21 (dd, J=15.3, 8.4 Hz, minor), 2.26 (dd, J=15.3, 8.6 Hz, major), 2.39 (dd, J=13.3, 3.2 Hz, major), total 2H; 2.68 (dd, J=13.4, 12.1 Hz, minor), 2.71 (dd, J=15.3, 4.9 Hz, minor), 2.78 (dd, J=15.3, 4.5 Hz, major), 3.07 (dd, J=13.2, 2.9 Hz, major), total 2H; 2.86 (ddd, J=10.2, 8.6, 4.6 Hz, major), 3.56 (ddd, J=10.7, 6.7, 3.9 Hz, minor), total 1H; 3.69, 3.70 sh (2×s, 3H). ^{13}C NMR (2 epimers): δ 12.71 (major), 19.39 (*C*H$_2$, minor), 19.98 (minor), 22.74 (major+minor), 26.70 (minor), 30.52 (*C*H$_2$, minor), 31.91 (*C*H$_2$, major), 32.80 (major), 33.02 (major), 34.15 (minor), 34.83 (*C*H$_2$, major), 35.40 (*C*H$_2$, minor), 37.68 (minor), 37.68 (*C*H$_2$, major), 37.91 (*C*H$_2$, major), 38.22 (*C*H$_2$, minor), 38.68 (*C*H$_2$, minor), 38.93 (*C*H$_2$, major), 40.60 (major), 42.81 (minor), 43.95 (major), 44.78 (minor), 45.14 (major), 51.74 (major), 51.78 (minor), 172.41 (minor), 172.48 (major). HRMS (CI) Calcd for $C_{14}H_{25}O_2S$ (MH$^+$): 257.1575. Found (MH$^+$): 257.1560.

(1*R*,2*RS*,5*S*,6*S*,9*R*)- and (1*S*,2*RS*,5*S*,6*S*,9*R*)-5,9-Dimethyl-3-thiabicyclo[4.4.0]decane-2-acetic acid methyl esters (18b-1) and (18b-2). Thiabicyclodecanes **18b** (oil, 228 mg, 89%) were obtained as a mixture of four isomers (ratio **18b-1/18b-2**, 6:1) as described above for the synthesis of **18a**, after purification by flash chromatography (EtOAc/hexane, 1:9). ^{1}H NMR (4 diastereomers): δ 0.57 (ddd, J=12.4, 12.4, 12.4 Hz), 0.71 (ddd, J=12.3, 12.3, 12.3 Hz), 0.64–0.96 (m), total 4H; 0.85 (d, J=6.4 Hz), 0.86 (d, J=6.6 Hz), total 3H; 0.94 (d, J=6.6 Hz), 0.95 (d, J=6.6 Hz), total 3H; 1.12–1.54 (m, 3H); 1.65–2.04 (m, 3H); 2.17–2.27 (m), 2.25 (dd, J=15.5, 8.2 Hz), total 1H; 2.36–2.58 (m), 2.42 (dd, J=13.5, 3.6 Hz), 2.51 (dd, J=13.6, 11.2 Hz), total 2H; 2.63–2.83 (m), 2.70 (dd, J=15.2, 4.8 Hz), 2.77 (dd, J=15.4, 4.9 Hz), total 1H; 2.87–2.99 (m), 2.86 (ddd, J=10.2, 8.3, 5.0 Hz), 3.42 (m), total 1H; 3.68, 3.69. 3.70, 3.72 (4×s, 3H). HRMS (CI) Calcd for $C_{14}H_{25}O_2S$ (MH$^+$): 257.1575. Found (MH$^+$): 257.1557.

Oxidation of 3-thiabicyclo[4.4.0]decanes 18a and 18b to sulfones

General procedure: To a solution of thiabicyclodecanes **18a** or **18b** (51 mg, 0.2 mmol) in ethyl acetate (5 mL) at 0°C was added *m*-CPBA (160 mg of 65% reagent, 3 equiv.), and the reaction mixture was slowly warmed to room temperature and stirred for 4 h. The resulting mixture was poured into EtOAc/hexane (1:1 mixture, 20 mL), washed with saturated sodium bisulphite and $NaHCO_3$ solutions, dried (Na_2SO_4), and evaporated. Flash chromatography (EtOAc/hexane, 3:7) gave the mixture of corresponding sulfones **22** and **23** or **24–26**. The isomers were further separated by MPLC (EtOAc/hexane, 3:7).

(1*R*,2*S*,5*R*,6*S*,9*R*)-5,9-Dimethyl-3,3-dioxo-3-thiabicyclo-[4.4.0]decane-2-acetic acid methyl ester (22). White needles, mp 88–89°C. IR (nujol): ν_{max} 1735, 1300, 1132 cm^{-1}. ^{1}H NMR: δ 0.72 (ddd, J=11.9, 11.9, 11.9 Hz, 1H); 0.89 (d, J=6.5 Hz, 3H); 0.91 (dddd, J=12.8, 12.8, 12.8, 3.4 Hz, 1H); 1.19 (d, J=7.4 Hz, 3H); 1.24–1.38 (m, 2H); 1.47 (dddd, J=11.6, 10.7, 3.4, 3.4 Hz, 1H); 1.54 (dddd, J=12.8, 3.2, 3.2, 3.2 Hz, 1H); 1.64–1.76 (m, 2H); 1.88 (dddd, J=10.9, 10.9, 10.9, 3.5 Hz, 1H); 2.30 (m, 1H); 2.49 (dd, J=17.4, 6.8 Hz, 1H); 3.06 (d, J=14.3 Hz, 1H); 3.07 (dd, J=17.4, 3.4 Hz, 1H); 3.22 (ddd, J=10.9, 6.8, 3.4 Hz, 1H); 3.23 (dd, J=14.3, 5.2 Hz, 1H); 3.73 (s, 3H). ^{13}C NMR: δ 13.24, 22.28, 28.05, 30.54, 31.57, 33.69, 34.15, 38.17, 38.64, 43.62, 52.41, 56.70, 61.95, 171.53. HRMS (CI) Calcd for $C_{14}H_{24}O_4S$ (MH$^+$): 289.1474. Found (MH$^+$): 289.1486.

(1*S*,2*R*,5*R*,6*S*,9*R*)-5,9-Dimethyl-3,3-dioxo-3-thiabicyclo-[4.4.0]decane-2-acetic acid methyl ester (23). White amorphous solid. IR (nujol): ν_{max} 1735, 1296, 1139 cm^{-1}. ^{1}H NMR: δ 0.82 (d, J=6.4 Hz, 3H); 0.94 (dddd, J=12.8, 12.8, 12.8, 3.8 Hz, 1H); 1.05 (d, J=7.1 Hz, 3H); 1.20 (ddd, J=13.9, 12.2, 4.4 Hz, 1H); 1.38 (dddd, J=13.2, 13.2, 13.2, 3.8 Hz, 1H); 1.53 (m, 1H); 1.56–1.67 (m, 2H); 1.68 (dddd, J=13.0, 3.6, 3.6, 3.6 Hz, 1H); 1.86 (m, 1H); 2.21 (m, 1H); 2.46 (dd, J=16.9, 6.8 Hz, 1H); 2.48 (m, 1H); 2.85 (dd, J=15.6, 14.2 Hz, 1H); 2.87 (dd, J=22.4, 14.2 Hz, 1H); 3.09 (dd, J=16.9, 3.8 Hz, 1H); 3.67 (ddd, J=10.7, 6.8, 3.8 Hz, 1H); 3.74 (s, 3H). ^{13}C NMR: δ 18.62, 18.88, 22.28, 26.49, 28.76, 33.07, 34.48, 36.78, 41.21, 41.40, 52.40, 52.42, 54.68, 171.38. HRMS (CI) Calcd for $C_{14}H_{24}O_4S$ (MH$^+$): 289.1474. Found (MH$^+$): 289.1471.

(1*R*,2*S*,5*S*,6*S*,9*R*)-5,9-Dimethyl-3,3-dioxo-3-thiabicyclo-[4.4.0]decane-2-acetic acid methyl ester (24). White needles, mp 148–151°C. IR (nujol): ν_{max} 1736, 1287, 1137 cm^{-1}. ^{1}H NMR: δ 0.72 (ddd, J=11.8, 11.8, 11.8 Hz, 1H);, 0.83–1.02 (m, 3H); 0.90 (d, J=6.5 Hz, 3H); 1.07 (d, J=6.7 Hz, 3H); 1.39 (m, 1H); 1.56–1.78 (m, 3H); 1.97–2.08 (m, 2H); 2.49 (dd, J=17.3, 7.2 Hz, 1H); 2.80 (dd, J=14.0, 12.8 Hz, 1H); 3.07 (dd, J=14.0, 3.4 Hz, 1H); 3.10 (dd, J=17.3, 3.5 Hz, 1H); 3.27 (ddd, J=11.0, 7.2, 3.5 Hz, 1H); 3.75 (s, 3H). ^{13}C NMR: δ 19.39, 22.28, 28.02, 29.64, 32.16, 34.06, 35.17, 37.91, 44.58, 46.81, 52.44, 57.20, 61.00, 171.48. HRMS (CI) Calcd for $C_{14}H_{24}O_4S$ (MH$^+$): 289.1474. Found (MH$^+$): 289.1470.

(1*R*,2*R*,5*S*,6*S*,9*R*)-5,9-Dimethyl-3,3-dioxo-3-thiabicyclo-[4.4.0]decane-2-acetic acid methyl ester (25). White amorphous solid. IR (nujol): ν_{max} 1736, 1301, 1135 cm^{-1}. ^{1}H NMR: δ 0.74 (ddd, J=12.4, 12.4, 12.4 Hz, 1H); 0.83–1.01 (m, 3H); 0.90 (d, J=6.5 Hz, 3H); 1.03 (d, J=6.7 Hz, 3H); 1.48 (m, 1H); 1.56 (dddd, J=12.6, 2.5, 2.5, 2.5 Hz, 1H); 1.75 (m, 1H); 1.94 (m, 1H); 2.05 (dddd, J=12.6, 3.3, 3.3, 3.3 Hz, 1H); 2.30 (m, 1H); 2.64 (dd, J=17.0, 6.1 Hz, 1H); 2.69 (dd, J=14.5, 12.6 Hz, 1H); 2.84 (dd, J=17.0, 6.2 Hz, 1H); 2.85 (d, J=14.5 Hz, 1H); 3.51 (ddd, J=9.6, 6.1, 3.4 Hz, 1H); 3.75 (s, 3H). ^{13}C NMR: δ 19.14, 22.19, 29.86, 30.35, 32.23, 34.37, 35.87, 39.40, 39.83, 41.93,

52.47, 53.60, 60.04, 170.81. HRMS (CI) Calcd for $C_{14}H_{24}O_4S$ (MH^+): 289.1474. Found (MH^+): 289.1477.

(1*S*,2*RS*,5*S*,6*S*,9*R*)-5,9-Dimethyl-3,3-dioxo-3-thiabicyclo-[4.4.0]decane-2-acetic acid methyl esters (26) occur as a mixture with sulfone **25** and exhibited characteristic ^1H NMR peaks at δ 1.20, 1.31 (2×d, J=7.4 Hz, 3H); and 3.02–3.29 (m, 1H).

Ethyl (*E*/*Z*)-3-[1-((1*R*,2*R*,4*R*)-2-hydroxy-4-methylcyclo-hexyl)-1-methylethylsulfanyl]-2-propenoate (28). Thiol **27**[14] (641 mg, 3.4 mmol) was dissolved in EtOH–H_2O mixture (15:1, 10 mL). The temperature was reduced to 0°C and ethyl propiolate (0.5 mL, 4.9 mmol) and catalytic amount of triethylamine (two drops of a mixture: one drop of NEt_3 in 10 drops of EtOH) were added. The reaction mixture was stirred for 12 h at room temperature, diluted with benzene (100 mL) and evaporated. The residue was purified by flash chromatography (EtOAc/hexane, 1:20) to give the unsaturated sulfide **28** (oil, 691 mg, 71%) as a mixture of two isomers (*E*/*Z*, 1:4.6). ^1H NMR (*E*/*Z* isomers): δ 0.85 (m, 1H); 0.89 (d, J=6.5 Hz, *Z*), 0.90 (d, J=6.5 Hz, *E*), total 3H; 0.95–1.16 (m, 2H); 1.27 (t, J=7.1 Hz, 3H); 1.45 (m, 1H); 1.46 (s, *Z*), 1.47 (s, *E*), total 3H; 1.50 (s, *Z*), 1.52 (s, *E*), total 3H; 1.51 (m, 1H); 1.67 (m, 1H); 1.85–1.96 (m, 2H); 2.46 (br s, *Z*), 2.58 (br s, *E*), total 1H; 3.66 (m, 1H); 4.17 (q, J=7.1 Hz, 2H, *E*), 4.18 (q, J=7.1 Hz, 2H, *Z*), total 2H; 5.87 (d, J=10.5 Hz, *Z*), 5.95 (d, J=15.4 Hz, *E*), total 1H; 7.36 (d, J=10.5 Hz, *Z*), 7.87 (J=15.4 Hz, *E*), total 1H. ^{13}C NMR (*E*/*Z* isomers): δ 14.27 (*E*), 14.29 (*Z*); 21.77 (*E*), 21.80 (*Z*); 26.65 (*E*/*Z*); 27.00 (*E*), 27.29 (*Z*); 28.87 (*Z*), 29.27 (*E*); 31.22 (*E*), 31.25 (*Z*); 34.44 (*E*), 34.54 (*Z*); 45.28 (*E*), 45.41 (*Z*); 50.48 (*E*/*Z*); 51.83 (*Z*), 51.94 (*E*); 60.00 (*Z*). 60.21 (*E*); 72.47 (*Z*), 72.55 (*E*); 113.27 (*Z*), 116.40 (*E*); 144.27 (*E*), 144.92 (*Z*); 165.53 (*E*), 166.53 (*Z*). HRMS (CI) Calcd for $C_{15}H_{27}O_3S$ (MH^+): 287.1681. Found (MH^+): 287.1660.

Ethyl (*E*/*Z*)-3-[1-((1*R*,2*R*,4*R*)-2-phenoxythiocarbonyloxy-4-methylcyclohexyl)-1-methylethylsulfanyl]-2-propenoate (29). Compound **29** (red oil, 630 mg, 69%) was obtained as a mixture of two isomers (*E*/*Z*, 1:3.3) from alcohol **28** (619 mg, 2.16 mmol) as described above for the synthesis of **16a**, after purification by MPLC (EtOAc/hexane, 1:9). ^1H NMR (*E*/*Z* isomers): δ 0.88–1.06 (m, 1H); 0.97 (d, J=6.4 Hz, 3H); 1.09–1.38 (m, 2H); 1.29 (t, J=7.1 Hz, *Z*), 1.30 (t, J=7.1 Hz, *E*), total 3H; 1.43 (s, *Z*), 1.46 (*E*), total 3H; 1.54 (m, 1H); 1.58 (s, *Z*), 1.59 (*E*), total 3H; 1.75 (m, 1H); 2.02 (m, 1H); 2.16–2.37 (m, 2H); 4.21 (q, J=7.1 Hz, *Z*), 4.22 (q, J=7.1 Hz, *E*), 5.36 (ddd, J=10.6, 10.6, 4.7 Hz, *E*), 5.37 (ddd, J=10.6, 10.6, 4.7 Hz, *Z*), total 1H; 5.89 (d, J=10.5 Hz, *Z*), 5.97 (d, J=15.4 Hz, *E*), total 1H; 7.30 (d, J=10.5 Hz, *Z*), 7.86 (J=15.4 Hz, *E*), total 1H; 7.08–7.47 (m, 5H). HRMS (CI) Calcd for $C_{22}H_{31}O_4S_2$ (MH^+): 423.1664. Found (MH^+): 423.1653.

(1*S*,3*R*,6*R*,9*RS*)- and (1*R*,3*R*,6*R*,9*RS*)-3,7,7-Trimethyl-8-thiabicyclo[4.3.0]nonane-9-acetic acid ethyl esters (31a) and (31b). The synthesis of 8-thiabicyclo[4.3.0]nonanes **31** was performed starting from thionocarbonate **29** (182 mg, 0.43 mmol), *n*-Bu_3SnH (0.29 mL, 1.08 mmol, 2.5 equiv.), and AIBN (14 mg, 0.09 mmol, 0.2 equiv.) using reaction conditions described for preparation of **18a** to give after flash chromatography (EtOAc/hexane, 1:9) bicyclic sulfide **31** (105 mg, 90%) as a mixture of four diastereomers (6:1.5:1.5:1) with overall ratio of *cis*/*trans* isomers **31a**/**31b**, 3:1. ^1H NMR (4 isomers): δ 0.79–0.91 (m, 1H); 0.87 (d, J=6.4 Hz, major), 0.88 (d, J=6.4 Hz, minor), 0.93 (d, J=6.5 Hz, minor), 0.94 (d, J=6.5 Hz, minor), total 3H; 1.07–1.91 (m, 8H); 1.23 (t, J=7.1 Hz, minor), 1.24 (t, J=7.1 Hz, minor), 1.27 (t, J=7.1 Hz, major), 1.29 (t, J=7.1 Hz, minor), total 3H; 1.39 (s, minor), 1.40 (s, minor), 1.45 (s, major), 1.46 (s, minor), total 3H; 2.12 (m, minor), 2.42 (m, major+minor), 2.93 (m, minor), total 1H; 2.38 (dd, J=16.0, 10.0 Hz, minor), 2.41 (dd, J=16.0, 6.8 Hz, minor), 2.46 (dd, J=16.0, 10.0 Hz, major), 2.66 (dd, J=16.0, 14.6 Hz, minor), 2.68 (dd, J=16.0, 8.5 Hz, minor), 2.82 (dd, J=16.0, 3.8 Hz, major), 2.83 (dd, J=16.0, 3.2 Hz, minor), 2.84 (dd, J=16.0, 4.3 Hz, minor), total 2H; 3.33 (ddd, J=9.9, 9.9, 4.0 Hz, minor), 3.72 (ddd, J=14.6, 7.2, 5.4 Hz, minor), 3.76 (ddd, J=10.5, 10.5, 3.8 Hz, major), 3.89 (ddd, J=11.3, 9.3, 4.0 Hz, minor), total 1H; 4.10–4.20 (4×q, J=7.1 Hz, 2H). ^{13}C NMR (major isomer): δ 14.20, 22.42, 24.43, 26.00, 26.18, 26.83, 34.24, 34.44, 35.20, 42.22, 44.98, 47.35, 53.70, 54.91, 60.60. HRMS (CI) Calcd for $C_{15}H_{27}O_2S$ (MH^+): 271.1732. Found (MH^+): 271.1719.

Methyl (*E*)-3-[(1*RS*,2*R*,5*R*)-5-methyl-2-((1*R*)-1-methyl-2-methylsulfanylethyl)cyclohexyl]-2-propenoate (33). To a solution of in thiabicyclodecanes **18a-1**/**18a-2** (141 mg, 0.55 mmol) in methylene chloride (5 mL) at −10°C was added methyl trifluoromethanesulfonate (0.3 mL, 2.65 mmol). The reaction mixture was warmed to room temperature, stirred for 2.5 h, and evaporated to give sulfonium salt **32** as a dark-brown oil. The crude salt was suspended in THF (4 mL) and cooled to 0°C. Potassium *tert*-butoxide (1.0 M solution in THF, 0.6 mL) was added dropwise. After stirring for 2 h at room temperature (TLC), the reaction mixture was quenched with glacial acetic acid (0.2 mL) and evaporated. The residue was dissolved in water (10 mL) and hexane (10 mL), and aqueous layer was extracted with hexane (2×10 mL). The combined organic layers were dried (Na_2SO_4), the solvent was evaporated, and flash chromatography (EtOAc/hexane, 1:20) of the residue gave the title compound **33** (112 mg, 76%) as a 2:1 mixture of epimers at C-1. IR (neat): ν_{max} 2956, 2919, 2857, 1732, 1659, 1431, 1272, 1173 cm^{-1}. ^1H NMR (2 epimers, major and minor):δ 0.82 (d, J=6.4 Hz, minor), 0.87 (d, J=6.5 Hz, major), total 3H; 0.87–1.09 (m, 3H); 1.24–1.82 (m, 6H); 1.99 (s, major), 2.05 (s, minor), total 3H; 2.11 (dd, J=12.7, 10.5 Hz, major), 2.20 (dddd, 1H, J=10.9, 3.2, 3.2, 3.2 Hz, major), 2.37 (dd, J=12.4, 7.7 Hz, minor), 2.50 (dd, J=12.7, 3.8 Hz, major), 2.61 (dd, J=12.4, 3.4 Hz, minor), 2.73 (m, minor), total 3H; 3.71 (s, major), 3.72 (s, minor), total 3H; 5.80 (d, J=15.6 Hz, major), 5.87 (d, J=15.6 Hz, minor), total 1H; 6.74 (dd, J=15.6, 9.9 Hz, major), 7.19 (dd, J=15.6, 9.9 Hz, minor), total 1H. ^{13}C NMR (2 epimers): δ 15.86 (major), 16.51 (minor), 17.00 (minor), 17.72 (major), 22.25 (major), 22.52 (minor), 25.37 (CH_2, minor), 25.77 (CH_2, major), 26.91 (minor), 32.03 (major), 34.35 (major), 34.86 (CH_2, major), 35.32 (CH_2, minor), 35.77 (minor), 36.94 (CH_2, major), 39.89 (minor), 40.37 (CH_2, minor), 41.86 (CH_2, major), 41.97 (CH_2, minor), 44.11 (major), 44.24 (minor), 46.47 (major), 51.32 (minor+major), 120.39 (major), 121.59 (minor), 150.47 (minor), 153.59 (major), 166.91 (minor), 166.94 (major).

HRMS (CI) Calcd for $C_{15}H_{27}O_2S$ (MH^+): 271.1732. Found (MH^+): 271.1721.

Methyl (*E*)-3-[(1*S*,2*R*,5*R*)- and (*E*)-3-[(1*R*,2*R*,5*R*)-2-isopropenyl-5-methylcyclohexyl]-2-propenoates (35a) and (35b) from sulfide 33. To a solution of sulfide **33** (49 mg, 0.18 mmol) in ethyl acetate (1 mL) at −60°C under argon was added dropwise for 20 min a solution of *m*-CPBA (53 mg of 65% reagent, 0.2 mmol) in ethyl acetate (5 mL). The reaction mixture was stirred for 4 h at −40°C, slowly warmed to room temperature, washed with 5% aqueous $NaHCO_3$ (3×10 mL), dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography (EtOAc/hexane, 3:7) to afford quantitatively a mixture of four isomeric sulfoxides **34** used at the next stage. A solution of **34** (50 mg, 0.17 mmol) and methyl acrylate (2 mL) in toluene (2 mL) was heated at 180°C for 62 h in a sealed tube. The mixture was then evaporated and purified by flash chromatography (EtOAc/hexane, 1:1) to afford title compound **35** (colorless oil, 19 mg, 47%, from **33**) as a mixture of two epimers at C-1 (ratio **35a/35b**, 2:1). ^{1}H NMR (two epimers, **35a**—major and **35b**—minor): δ 0.87 (d, J=6.5 Hz, minor), 0.92 (d, J=6.5 Hz, minor), total 3H; 0.90–1.03 (m, 2H); 1.31–1.51 (m, 2H); 1.62 (s, major), 1.70 (s, minor), total 3H; 1.63–1.90 (m, 3H); 2.04–2.25 (m), 2.81 (m), total 2H; 3.72 (s, major), 3.73 (minor), total 3H; 4.65 (m, minor), 4.70 (m, major), 4.80 (m, minor), total 2H; 5.75 (dd, J=15.7, 1.0 Hz, major), 5.82 (dd, J=15.8, 1.3 Hz, minor), total 1H; 6.79 (dd, J=15.7, 8.4 Hz, major), 7.05 (dd, J=15.8, 8.3 Hz, minor), total 1H. ^{13}C NMR (2 epimers): δ 19.28 (major), 22.27 (minor), 22.38 (major), 22.50 (minor), 25.76 (minor), 27.06 (minor), 31.82 (major), 34.61 (major), 35.15 (minor), 39.57 (minor), 40.59 (major), 40.70 (minor), 43.41 (major), 46.52 (minor), 50.59 (major), 51.31 (minor+major), 110.23 (minor), 111.35 (major), 119.33 (major), 121.15 (minor), 147.68 (minor+major), 150.17 (minor), 153.12 (major), 167.34 (minor+major). HRMS (CI) Calcd for $C_{14}H_{23}O_2$ (MH^+): 223.1698. Found (MH^+): 223.1657.

Methyl (*E*)-3-[(1*S*,2*R*,5*R*)- and (*E*)-3-[(1*R*,2*R*,5*R*)-2-isopropenyl-5-methylcyclohexyl]-2-propenoates (35a) and (35b) from thiabicyclodecanes 18b-1 and 18b-2. To a solution of in thiabicyclodecanes **18b-1/18b-2** (139 mg, 0.55 mmol) in methylene chloride (5 mL) at −10°C was added methyl trifluoromethanesulfonate (0.3 mL, 2.65 mmol). The reaction mixture was warmed to room temperature, stirred for 2.5 h, and evaporated to give a sulfonium salt of thiabicyclodecanes **18b** as a dark-brown oil. The crude salt was suspended in THF (4 mL) and cooled to 0°C. Potassium *tert*-butoxide (1.0 M solution in THF, 0.6 mL) was added dropwise. After stirring for 2 h at room temperature (TLC monitoring), the reaction mixture was quenched at 0°C with glacial acetic acid (0.1 mL) and diluted with ethyl acetate (10 mL), washed with water (3×10 mL). Aqueous layer was additionally extracted with ethyl acetate (2×5 mL) and combined organic layers were dried (Na_2SO_4) and filtered. The solution of sulfide obtained was cooled to −60°C and a solution of *m*-CPBA (53 mg of 65% reagent, 0.6 mmol) in ethyl acetate (5 mL) was added dropwise over 20 min. The reaction mixture was stirred for 4 h at −40°C, slowly warmed to room temperature, washed with 5% aqueous $NaHCO_3$ (3×15 mL), dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography (EtOAc/hexane, 2:3) to afford a mixture of four diastereomeric sulfoxides used at the next stage. A solution of sulfoxides (98 mg, 0.34 mmol) and methyl acrylate (4 mL) in toluene (4 mL) was heated at 180°C for 62 h in a sealed tube. The mixture was evaporated and purified by flash chromatography (EtOAc/hexane, 1:1) to afford title compound **35** (colorless oil, 32 mg, 41%, from **11b**) as a mixture of two epimers at C-1 (ratio **35a/35b**, 6:1). ^{1}H NMR data of the compound have been compared to the data of the sample obtained from sulfide **33** and are identical.

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