

Reaction of Thioketones with (*R*)-2-Vinyloxirane: Regio- and Stereoselective Formation of (*S*)-4-Vinyl-1,3-oxathiolanes

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The reactions of 4,4'-dimethoxythiobenzophenone (**1**), 9H-xanthene-9-thione (**2**), and adamantane-2-thione (**3**) with (*R*)-2-vinyloxirane [(*R*)-**6**] in the presence of SiO₂ in anhydrous CH₂Cl₂ at 0 °C or room temperature afforded the corresponding 4-vinyl-1,3-oxathiolane derivatives (*S*)-**7**, (*S*)-**9**, and (*S*)-**11**, respectively. The analogous BF₃-catalyzed reactions of (*R*)-**6** with 1,1,3,3-tetramethylindane-2-thione (**4**) and 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**5**) in anhydrous CH₂Cl₂ at –65 °C or –78 °C yielded the corresponding spi-

rocyclic 1,3-oxathiolanes (*S*)-**12** and (*S*)-**14**, respectively. The structures of (*S*)-**9** and (*S*)-**12** were established by X-ray crystallography. In all cases, the nucleophilic thiocarbonyl S atom attacked predominantly C(2) of the Lewis acid-activated (*R*)-2-vinyloxirane ring with inversion of the configuration through an S_N2-type mechanism.

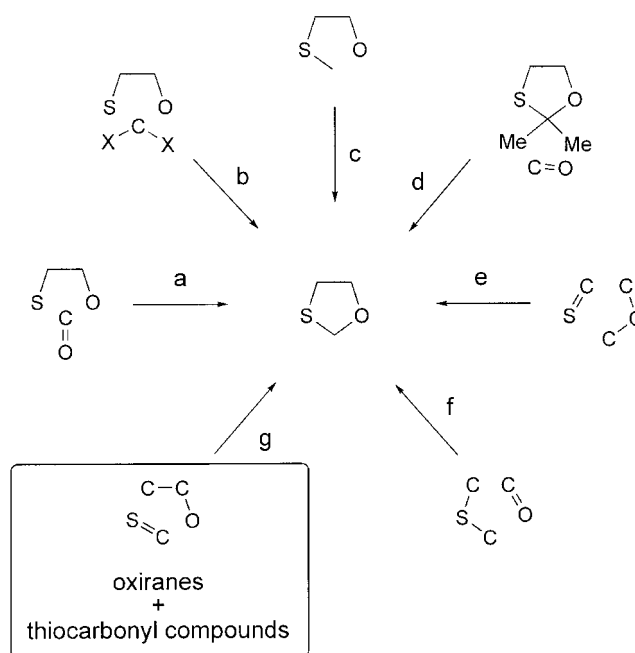
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Introduction

In recent years, interest in 1,3-oxathiolanes has increased remarkably. On the one hand, some nucleoside analogues containing a 1,3-oxathiolane ring instead of a sugar moiety show antiviral activities against HIV.^[1–4] Another clinically effective drug is (±)-*cis*-2-methylspiro[1,3-oxathiolane-5,3'-quinuclidine] hydrochloride hemihydrate, which has been developed in Japan for treatment of the symptoms of dry mouth.^[5,6] On the other hand, 1,3-oxathiolanes are versatile carbonyl protecting groups in organic synthesis, because they can easily be removed under essentially neutral conditions to generate the carbonyl functionality.^[7–9] The chemoselective protection of aldehydes in the presence of ketone groups and of aliphatic ketones in the presence of aromatic ketones has been reported recently.^[10,11]

Because of many important applications, convenient and efficient syntheses of 1,3-oxathiolanes are still sought after. The methodologies reported so far are summarized in Scheme 1.

The most widely used procedure for preparing 1,3-oxathiolanes is the acid-catalyzed condensation (acetalization) of 2-sulfanylethan-1-ols and carbonyl compounds (*path a*; see^[10,12]). *Path b* represents the base-catalyzed nucleophilic substitution of dihalomethane derivatives by 2-sulfanylethan-1-ols,^[13,14] and *path c* shows the electrochemical



Scheme 1.

chemoselective α -acetoxylation of β' -hydroxy sulfides followed by a cyclization in the presence of BF₃·Et₂O.^[15] *Path d* concerns the acid-catalyzed exchange reaction between 2,2-dimethyl-1,3-oxathiolanes and a nonvolatile carbonyl compound.^[7a] This procedure has been improved recently by use of solid acid catalysts under microwave irradiation conditions in the absence of a solvent.^[16] *Paths e* and *f* relate to 1,3-dipolar cycloadditions between carbonyl ylides and thiocarbonyl groups and between thiocarbonyl ylides

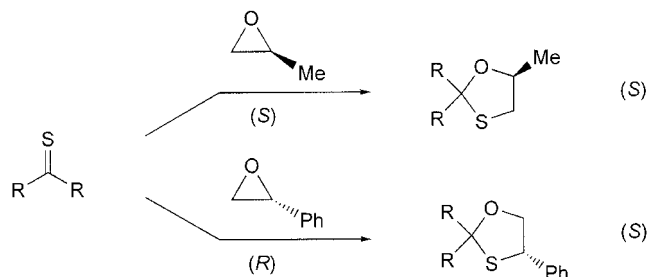
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and carbonyl compounds, respectively. The 1,3-dipolar species can be generated by the pyrolysis of oxiranes possessing electron-withdrawing groups^[17] and by the extrusion of N₂ from 2,5-dihydro-1,3,4-thiadiazoles.^[18] Other very useful precursors of carbonyl and thiocarbonyl ylides are silicon-based synthons such as chloromethyl (trimethylsilyl)methyl ethers or their sulfur analogues, which readily react with CsF through a 1,3-elimination process to generate the corresponding reactive ylides in situ, and these then undergo [3+2] cycloadditions with C=S or C=O groups to give the 1,3-oxathiolanes.^[19,20] As is generally the case in 1,3-dipolar cycloadditions, regio- and stereoselectivity are important aspects of these 1,3-oxathiolane syntheses.

The novel synthetic approach to 1,3-oxathiolanes through the Lewis acid-catalyzed reaction of thioketones and thiolactones with oxiranes (*path g*) has been investigated thoroughly over the last few years.^[21–28] The results reported so far for this reaction indicate that it proceeds with high regio- and stereoselectivity by an S_N2-type mechanism (Scheme 2). In the case of 2-alkyl-substituted oxiranes, the nucleophilic thiocarbonyl S atom reacts preferentially at C(3) to give the 5-substituted 1,3-oxathiolanes with retention of the configuration at C(2) of the oxirane. On the other hand, 2-phenyloxirane is attacked mainly at C(2) with inversion of the configuration to yield the 4-phenyl-substituted products. Similar reactions have been observed with 1,3-thiazole-5(4*H*)-thiones,^[29,30] with cyclic trithiocarbonates,^[31] and with a rhodanine derivative.^[32]



Scheme 2.

The reaction of 2-vinyloxirane with thiocarbonyl compounds, which could lead to five- or seven-membered heterocycles, has not been reported so far. With the aim of further extending the scope of the reactions of thioketones with oxiranes, reactions of 4,4'-dimethoxythiobenzophenone (**1**), 9*H*-xanthene-9-thione (**2**), adamantane-2-thione (**3**), 1,1,3,3-tetramethylindane-2-thione (**4**), and

2,2,4,4-tetramethyl-3-thioxocyclobutanone (**5**) with (*R*)-vinyloxirane [(*R*)-**6**] were carried out. In this paper, the results of these reactions are described.

Results and Discussion

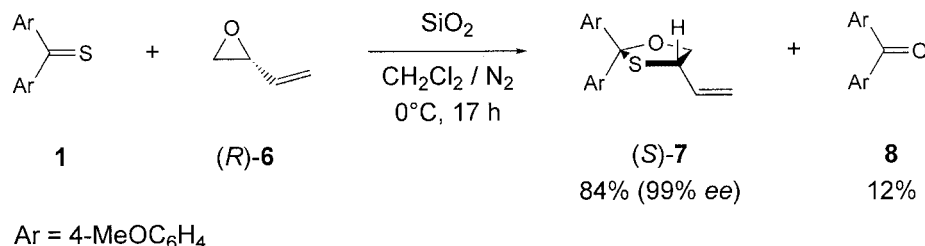
The reaction of 4,4'-dimethoxythiobenzophenone (**1**) with (*R*)-2-vinyloxirane [(*R*)-**6**] at a molar ratio of 1:2 was carried out in anhydrous CH₂Cl₂ in the presence of SiO₂ at 0 °C under N₂.^[33] After stirring for 17 h, filtration, and usual workup by column chromatography (CC), the 1,3-oxathiolane (*S*)-**7** and 4,4'-dimethoxybenzophenone (**8**) were obtained in 84 and 12% yields, respectively (Scheme 3). The enantiomeric excess of (*S*)-**7** (99% *ee*) was determined by analytical HPLC (Chiralcel OD-H, hexane/*i*PrOH, 400:1).

The structure of (*S*)-**7** was assigned on the basis of ¹H and ¹³C NMR spectra, and by comparison of these spectra with those described previously.^[22] The absolute configuration of (*S*)-**7** has been proposed by assuming that the ring-opening of (*R*)-**6** takes place through nucleophilic attack of the thiocarbonyl S atom at C(2) of the oxirane and cleavage of the O–C(2) bond with inversion of the configuration at C(2).^[34]

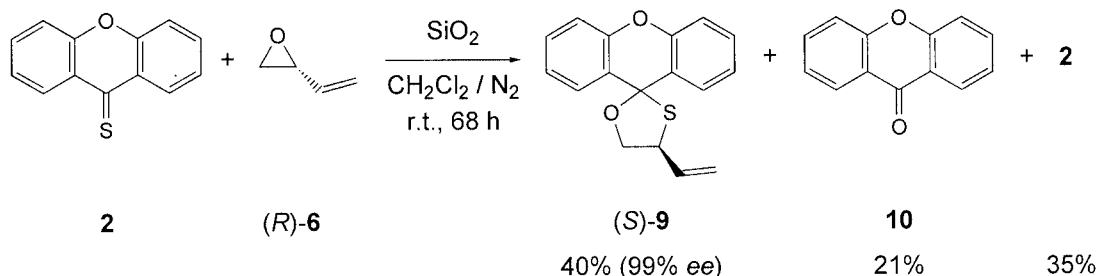
The analogous reaction of 9*H*-xanthene-9-thione (**2**) with (*R*)-**6** (molar ratio 1:2) in anhydrous CH₂Cl₂ at room temperature in the presence of SiO₂ occurred much more slowly. After 68 h, the spirocyclic compound (*S*)-**9** and xanthone (**10**) were obtained in 40 and 21% yields, respectively. In addition, a 35% yield of the starting material **2** was recovered (Scheme 4). The 1,3-oxathiolane derivative (*S*)-**9** was almost enantiomerically pure (99% *ee*, HPLC, Chiralcel OD-H, hexane/*i*PrOH, 250:1).

The structure of (*S*)-**9** was assigned on the basis of elemental analysis and spectroscopic data, and was confirmed by X-ray crystallography (Figure 1). The crystals of (*S*)-**9** were enantiomerically pure and the absolute configuration of the molecule was determined independently by the diffraction experiment and found to be (4*S*). Therefore, the ring-opening of the oxirane occurred by an S_N2 mechanism.

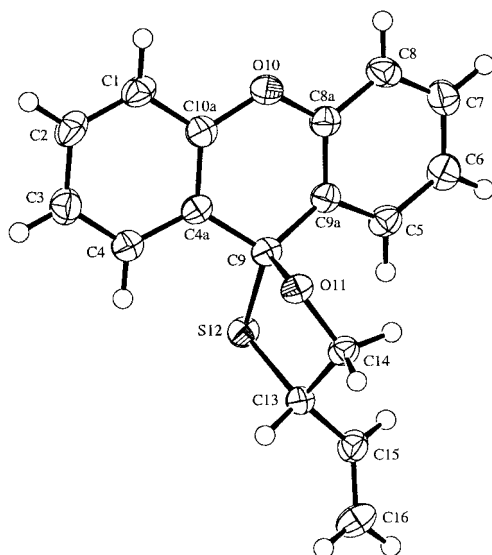
The reaction of adamantane-2-thione (**3**) with (*R*)-**6** in a molar ratio of 1:2 was also carried out in anhydrous CH₂Cl₂ under N₂ and in the presence of SiO₂. Because **3** was more reactive than **2**, a reaction temperature of 0 °C was chosen and the mixture was stirred for 28 h. Filtration and the usual workup by column chromatography (CC) gave the spiroheterocycle (*S*)-**11** in 32% yield, and the start-



Scheme 3.



Scheme 4.

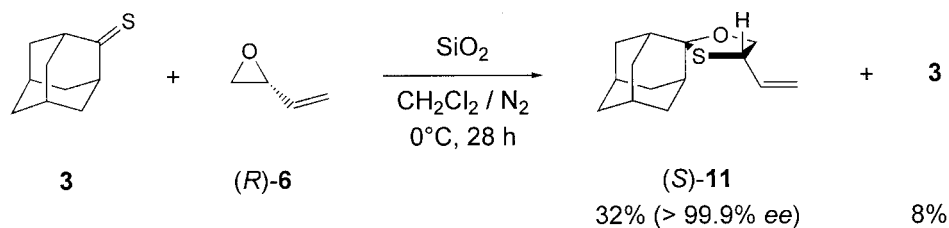

 Figure 1. ORTEP plot^[35] of the molecular structure of (*S*)-**9** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability).

ing material **3** was recovered in 8% yield (Scheme 5). The *ee* value of (*S*)-**11** was determined by analytical HPLC (Chiralcel OD-H, hexane) to be >99.9%.

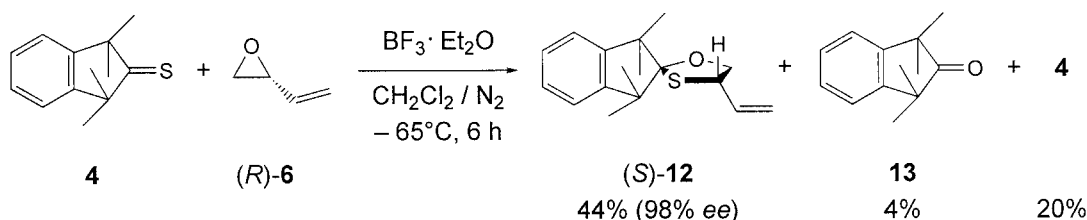
The structure of (*S*)-**11** was again assigned on the basis of elemental analysis and spectroscopic data, and, from the reaction mechanism postulated above, the absolute configuration of (*S*)-**11** was assumed to be (4'*S*).

Under the reaction conditions used for the transformation of **1–3** (i.e., 0–20 °C and SiO_2 as catalyst), only very slow formation of 1,3-oxathiolane was observed with the sterically crowded 1,1,3,3-tetramethylindane-2-thione (**4**). Therefore, a stronger Lewis acid was used: the BF_3 -catalyzed reaction of **4** with (*R*)-**6** (molar ratio 1:4) in anhydrous CH_2Cl_2 at –65 °C for 6 h under N_2 afforded the spirocyclic compound (*S*)-**12** and ketone **13** in 44 and 4% yields, respectively. The starting material **4** was recovered in 20% yield (Scheme 6). The *ee* value of (*S*)-**12** (98%) was determined by analytical HPLC (Chiralcel OD-H, hexane/*i*PrOH, 750:1).

The structure of (*S*)-**12** was assigned on the basis of elemental analysis and spectroscopic data, particularly NMR experiments (HSQC, HSQC-TOCSY, and HMBC), and was established by X-ray crystallography (Figure 2). The crystals of (*S*)-**12** were enantiomerically pure, and the absolute configuration of the molecule was determined independently by the diffraction experiment and found to be (4'*S*). There are two symmetry independent molecules in the asymmetric unit. Both are of the same enantiomorph and



Scheme 5.



Scheme 6.

have almost identical conformations, with a r.m.s. fit of the corresponding atoms of 0.06 Å.

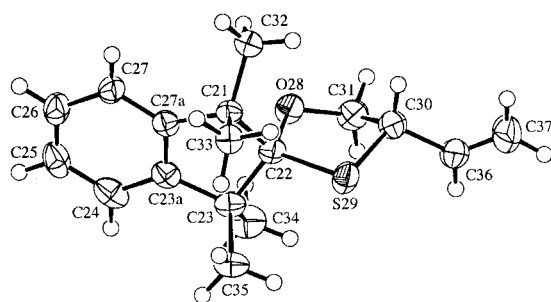


Figure 2. ORTEP plot^[35] of the molecular structure of one of the two symmetry-independent molecules of (*S*)-**12** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability).

In analogy to the experiment with **4**, the reaction of 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**5**) with (*R*)-**6** (molar ratio 1:2) in anhydrous CH₂Cl₂ at –78 °C under N₂ was catalyzed with BF₃. After 45 min and the usual workup, the spirocyclic 1,3-oxathiolane (*S*)-**14** was obtained in 71% yield with 99.6% *ee* (HPLC, Chiralcel OD-H, hexane/*i*PrOH, 400:1) (Scheme 7).

The structure of (*S*)-**14** was assigned as usual, and it has been assumed that the molecules have the (7*S*) configuration.

Conclusions

The nucleophilic attack of the thiocarbonyl S atom at the Lewis acid-activated (*R*)-2-vinyloxirane [(*R*)-**6**] could occur, in principle, at C(2) and C(3) through an S_N2 mechanism to give 1,3-oxathiolanes, or at C(2') through an S_N2' mechanism to afford seven-membered heterocycles. However, the results presented show that, in all cases, the ring-enlarged product is formed by the nucleophilic attack of the thiocarbonyl S atom at C(2) of the Lewis acid-complexed (*R*)-2-vinyloxirane ring through an S_N2-type mechanism (Scheme 8). The stereoselectivity is very high (98–99.9%

ee), and the inversion has been demonstrated in the cases of (*S*)-**9** and (*S*)-**12** by X-ray crystallography. Therefore, the reaction proceeds analogously to that reported for thiocarbonyl compounds with (*R*)-2-phenyloxirane.^[23–26,30]

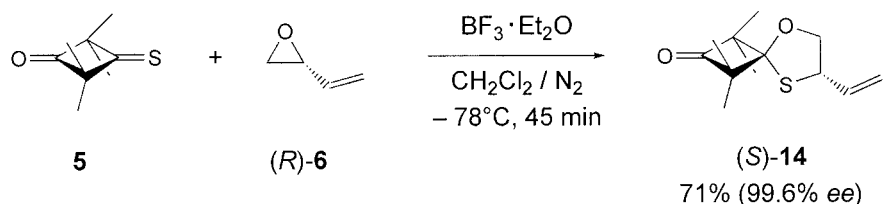
The thiocarbonyl ion **A** is a likely intermediate in the nucleophilic attack of the thiocarbonyl S atom at the C(2) atom (O–C(2) cleavage) of the activated (*R*)-**6**. Cyclization of **A** by the intramolecular addition of the O atom gives the expected 1,3-oxathiolane (*S*)-**15**. The formation of ketones **8**, **10**, and **13** can be explained by the hydrolysis of the corresponding intermediates of type **A**. An alternative explanation is the Lewis acid-catalyzed decomposition of (*S*)-**15**, which produces the carbonyl compound and 2-vinylthiirane (for analogous reactions see^[21,29,31]).

In order to obtain both high regio- and stereoselectivity and high yield, a weak Lewis acid (e.g., SiO₂) is recommended for the reaction of (*R*)-**6** with aromatic and reactive aliphatic thioketones such as **1**, **2**, and **3**, but a strong Lewis acid (e.g., BF₃·Et₂O) is needed for the reaction with sterically hindered thioketones such as **4** and **5**.

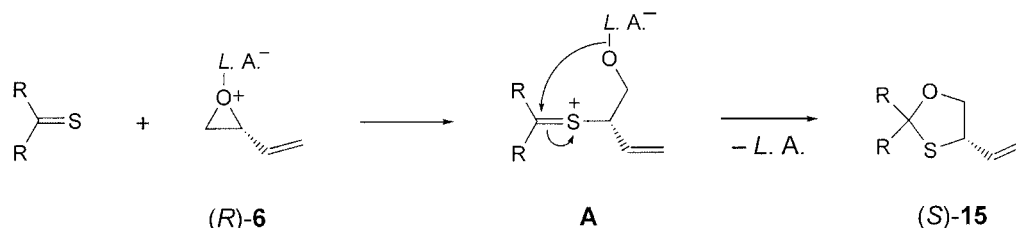
Experimental Section

General: See.^[36] The thioketones **1**,^[37] **2**,^[38] **3**,^[39] **4**,^[40] and **5**^[41] were prepared by thionation of the corresponding ketones by literature procedures. Optical rotations: Perkin–Elmer 241 polarimeter (*c* = 1, in THF). IR spectra: film or KBr (cm^{–1}). NMR spectra: at 300 (¹H) and 75.5 MHz (¹³C) in CDCl₃, if not otherwise stated. Enantiomeric excesses (*ee*) were determined by analytical HPLC on a Chiralcel OD-H column.

General Procedure for the Reactions of 4,4'-Dimethoxythiobenzophenone (1), 9*H*-Xanthene-9-thione (2), and Adamantane-2-thione (3) with (*R*)-2-Vinyloxirane [(*R*)-6**]:** Silica gel (SiO₂, Uetikon-Chemie Chromatographie C-560 (4.5 g) was added at 0 °C or at room temperature to a solution of **1**, **2**, or **3** (ca. 1 mmol) and (*R*)-**6** (ca. 2 mmol) in dry CH₂Cl₂ (15 mL) under N₂. After the suspension had been stirred at 0 °C or room temperature for 17–68 h, the mixture was filtered and the residue was washed with AcOEt (4×). Then, the combined filtrate was evaporated in vacuo, and the prod-



Scheme 7.



Scheme 8.

ucts were separated by column chromatography (CC; SiO₂; hexane/AcOEt, hexane/Et₂O, or hexane/CH₂Cl₂).

General Procedure for the Reactions of 1,1,3,3-Tetramethylindane-2-thione (4**) and 2,2,4,4-Tetramethyl-3-thioxocyclobutanone (**5**) with (*R*)-2-Vinyloxirane [(*R*)-**6**]:** BF₃·Et₂O (0.5 equiv.) was added at –65 °C or –78 °C under N₂ to a solution of **4** or **5** (ca. 1 mmol) in dry CH₂Cl₂ (10–15 mL), leading to little change in the color of the soln. After the mixture had been stirred for 15 min at –65 °C or –78 °C, respectively, (*R*)-**6** (2 equiv.) was added dropwise, whereupon the color of the solution changed moderately. Then, the reaction was quenched by addition of H₂O (4 mL) or aqueous NaHCO₃ solution (5%), and the mixture was washed with saturated aqueous NaCl solution (3×). The organic layers were combined and dried over MgSO₄, and the solvents were evaporated in vacuo. The products were separated by column chromatography (CC; SiO₂, hexane/CH₂Cl₂ or hexane/Et₂O).

(*S*)-2,2-Bis(4-methoxyphenyl)-4-vinyl-1,3-oxathiolane [(*S*)-7**]:** Treatment of **1** (258 mg, 1 mmol) with (*R*)-**6** (140 mg, 2 mmol) and SiO₂ (4.5 g) at 0 °C, 17 h, and CC (SiO₂, hexane/AcOEt, 4:1) yielded (*S*)-**7** (276 mg, 84%) and 4,4'-dimethoxybenzophenone (**8**, 30 mg, 12%).

Data for (*S*)-7**:** Colorless oil. $[\alpha]_D^{25} = -105.5$ (99% *ee*). ¹H NMR: $\delta = 7.45$ (AA' of AA'XX', *J* = 8.9 Hz, 2 arom. H), 7.38 (AA' of AA'XX', *J* = 8.9 Hz, 2 arom. H), 6.84 (XX' of AA'XX', *J* = 8.9 Hz, 2 arom. H), 6.82 (XX' of AA'XX', *J* = 8.9 Hz, 2 arom. H), 5.87–5.75 (m, CH=CH₂), 5.18 (d-like, *J* ≈ 16.9 Hz, 1 H of =CH₂), 5.04 (dd, *J* = 9.9, 1.1 Hz, 1 H of =CH₂), 4.38–4.23 [m, H–C(4), 1 H–C(5)], 3.86–3.77 [m, 1 H–C(5)], 3.80, 3.79 (2 s, 2 Me) ppm. ¹³C NMR: $\delta = 159.0$, 158.9 (2 s, 2 arom. C), 136.7, 136.6 (2 s, 2 arom. C), 136.4 (d, CH=CH₂), 128.4, 128.1 (2 d, 4 arom. CH), 116.5 (t, CH=CH₂), 113.1 (d, 4 arom. CH), 100.3 [s, C(2)], 74.2 [t, C(5)], 55.2 (q, 2 Me), 54.8 [d, C(4)] ppm. IR (film): $\tilde{\nu} = 3076$ w, 3036 w, 3001 w, 2956 m, 2933 m, 2908 w, 2870 w, 2836 m, 1635 w, 1607 s, 1583 m, 1508 s, 1463 m, 1441 m, 1415 m, 1303 s, 1250 s, 1172 s, 1113 m, 1066 s, 1034 s, 988 m, 921 m, 879 w, 824 s, 793 m, 730 w cm^{–1}. CI-MS (NH₃): 331 (6), 330 (18), 329 (83) [M + H]⁺, 244 (17), 243 (100). C₁₉H₂₀O₃S (328.43): calcd. C 69.48, H 6.14, S 9.76; found C 69.27, H 6.20, S 9.85.

(*S*)-4-Vinylspiro[1,3-oxathiolane-2,9'-[9'*H*]xanthene] [(*S*)-9**]:** Treatment of **2** (89 mg, 0.42 mmol) with (*R*)-**6** (59 mg, 0.84 mmol) and SiO₂ (1.9 g) in dry CH₂Cl₂ (6 mL) at room temperature, 68 h, and CC (SiO₂, hexane/Et₂O, 4:1) yielded (*S*)-**9** (48 mg, 40%) and xanthone (**10**, 17 mg, 21%). In addition, 35% of **2** were recovered.

Data for (*S*)-9**:** Colorless crystals. M.p. 72.3–72.9 °C. $[\alpha]_D^{25} = -129.1$ (99% *ee*). ¹H NMR: $\delta = 8.03$ –8.00 (m, 1 arom. H), 7.92–7.89 (m, 1 arom. H), 7.40–7.33 (m, 2 arom. H), 7.25–7.18 (m, 4 arom. H), 6.06–5.94 (m, CH=CH₂), 5.39 (d, *J* = 16.8 Hz, 1 H of =CH₂), 5.23 (d, *J* = 10.0 Hz, 1 H of =CH₂), 4.64–4.57 [m, H–C(4)], 4.50 [dd, *J* = 9.4, 5.7 Hz, 1 H–C(5)], 4.16 [dd, *J* = 9.3, 7.9 Hz, 1 H–C(5)] ppm. ¹³C NMR: $\delta = 151.0$, 150.6 (2 s, 2 arom. C), 133.7 (d, CH=CH₂), 129.6, 129.5, 128.7, 128.0 (4 d, 4 arom. CH), 125.2, 124.4 (2 s, 2 arom. C), 123.3, 123.2 (2 d, 2 arom. CH), 118.5 (t, CH=CH₂), 116.7 (d, 2 arom. CH), 89.0 [s, C(2)], 76.0 [t, C(5)], 55.4 [d, C(4)] ppm. IR (KBr): $\tilde{\nu} = 3084$ w, 3037 w, 3012 w, 2971 w, 2923 w, 2864 m, 1634 w, 1598 s, 1570 m, 1482 m, 1471 s, 1445 s, 1418 m, 1355 w, 1317 s, 1288 s, 1243 s, 1208 m, 1184 m, 1150 m, 1100 m, 1055 s, 1038 m, 991 m, 940 s, 918 m, 884 s, 868 m, 792 m, 757 s, 738 m, 724 m cm^{–1}. ESI-MS (MeOH): 413 (20), 307 (7), 306 (18), 305 (88) [M + Na]⁺, 304 (35), 284 (20), 283 (100) [M + H]⁺, 219 (35), 214 (8), 213 (45), 197 (6). C₁₇H₁₄O₂S (282.36): calcd. C 72.31, H 5.00; found C 72.42, H 5.01.

Crystals of (*S*)-**9** suitable for X-ray crystal structure determination were grown from CH₂Cl₂/hexane.

(*S*)-4'-Vinylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,2'-[1,3]oxathiolane] [(*S*)-11**]:** Treatment of **3** (140 mg, 0.84 mmol) with (*R*)-**6** (117 mg, 1.67 mmol) and SiO₂ (3.8 g) in dry CH₂Cl₂ (9 mL) at 0 °C, 28 h, and CC (SiO₂, hexane/CH₂Cl₂, 10:1) yielded (*S*)-**11** (64 mg, 32%). In addition, 8% of **3** were recovered.

Data for (*S*)-11**:** Colorless oil. $[\alpha]_D^{25} = -153.1$ (99.9% *ee*). ¹H NMR: $\delta = 5.85$ –5.73 (m, CH=CH₂), 5.17 (ddd, *J* = 16.9, 1.3, 0.7 Hz, 1 H of =CH₂), 5.02 (ddd, *J* = 9.9, 1.3, 1.0 Hz, 1 H of =CH₂), 4.22 [dd, *J* = 9.3, 5.4 Hz, 1 H–C(5')], 4.08–4.00 [m, H–C(4')], 3.90 [dd, *J* = 9.3, 6.1 Hz, 1 H–C(5')], 2.19–2.07 (br. m, 4 H), 1.87–1.71 (br. m, 8 H), 1.64–1.56 (br. m, 2 H) ppm. ¹³C NMR (150.9 MHz): $\delta = 137.1$ (d, CH=CH₂), 116.1 (t, CH=CH₂), 103.0 [s, C(2)], 73.7 [t, C(5')], 52.6 [d, C(4')], 40.3, 40.1 [2 d, C(1), C(3)], 37.4 [t, C(6)], 36.8, 36.5, 34.3 [3 t, C(4), C(8), C(9), C(10)], 26.9, 26.2 [2 d, C(5), C(7)] ppm. IR (film): $\tilde{\nu} = 3081$ w, 2910 s, 2854 s, 1636 m, 1469 m, 1451 m, 1417 w, 1373 w, 1358 w, 1350 w, 1309 w, 1276 w, 1249 w, 1226 w, 1197 w, 1174 w, 1103 m, 1084 m, 1046 m, 1019 w, 995 m, 962 m, 917 m, 892 m, 879 w, 851 m, 802 w, 732 w cm^{–1}. CI-MS (NH₃): 239 (5), 238 (14), 237 (88) [M + H]⁺, 169 (12), 168 (100), 151 (8). C₁₄H₂₀OS (236.37): calcd. C 71.14, H 8.53; found C 70.91, H 8.20.

(*S*)-1,1,3,3-Tetramethyl-4'-vinylspiro[indane-2,2'-[1,3]oxathiolane] [(*S*)-12**]:** Treatment of **4** (204 mg, 1 mmol) with (*R*)-**6** (280 mg, 4 mmol) and BF₃·Et₂O (1 mmol) at –65 °C, 6 h, and CC (SiO₂, hexane/CH₂Cl₂, 4:1) yielded (*S*)-**12** (120 mg, 44%) and 1,1,3,3-tetramethylindan-2-one (**13**, 8 mg, 4%). In addition, 20% of **4** were recovered.

Data for (*S*)-12**:** Colorless crystals. M.p. 59.3–59.6 °C. $[\alpha]_D^{25} = -81.1$ (98% *ee*). ¹H NMR (600 MHz): $\delta = 7.23$ –7.16 (m, 4 arom. H), 5.81–5.75 (m, CH=CH₂), 5.34 (d, *J* = 16.9 Hz, 1 H of =CH₂), 5.17 (d, *J* = 10.1 Hz, 1 H of =CH₂), 4.27 [dd, *J* = 8.9, 5.9 Hz, 1 H–C(5')], 4.20–4.16 [m, H–C(4')], 3.80 [t-like, *J* ≈ 8.9 Hz, 1 H–C(5')], 1.43, 1.42, 1.36, 1.35 (4 s, 4 Me) ppm. ¹³C NMR (150.9 MHz): $\delta = 148.5$, 148.1 (2 s, 2 arom. C), 134.3 (d, CH=CH₂), 127.1, 127.0, 122.6, 122.4 (4 d, 4 arom. CH), 118.3 (t, CH=CH₂), 113.9 [s, C(2)], 76.6 [t, C(5')], 53.0 [d, C(4')], 52.2, 51.5 [2 s, C(1), C(3)], 31.9, 30.6, 23.4, 22.2 (4 q, 4 Me) ppm. IR (KBr): $\tilde{\nu} = 3082$ w, 3069 w, 3041 w, 3016 w, 2990 m, 2958 s, 2930 m, 2866 m, 1639 m, 1586 w, 1479 s, 1465 m, 1448 m, 1416 w, 1380 w, 1373 m, 1359 m, 1311 w, 1248 w, 1200 w, 1171 w, 1126 m, 1076 s, 1045 m, 1026 m, 993 m, 984 m, 965 m, 952 m, 912 s, 871 w, 803 w, 754 s, 741 m cm^{–1}. CI-MS (NH₃): 294 (7), 293 (20), 292 (100) [M + NH₄]⁺, 276 (15), 275 (75) [M + H]⁺, 206 (17), 160 (6). C₁₇H₂₂O₂S (274.42): calcd. C 74.40, H 8.08, S 11.68; found C 74.23, H 8.16, S 11.46.

Crystals of (*S*)-**12** suitable for X-ray crystal structure determination were grown from Et₂O/MeOH.

(*S*)-1,1,3,3-Tetramethyl-7-vinyl-5-oxa-8-thiaspiro[3.4]octan-2-one [(*S*)-14**]:** Treatment of **5** (70 mg, 0.45 mmol) with (*R*)-**6** (63 mg, 0.90 mmol) and BF₃·Et₂O (0.22 mmol) at –78 °C, 45 min, and CC (SiO₂, hexane/Et₂O, 30:1) yielded (*S*)-**14** (72 mg, 71%).

Data for (*S*)-14**:** Colorless oil. $[\alpha]_D^{25} = -139.2$ (99.6% *ee*). ¹H NMR: $\delta = 5.81$ –5.70 (m, CH=CH₂), 5.25 (ddd, *J* = 16.9, 1.1, 0.9 Hz, 1 H of =CH₂), 5.10 (ddd, *J* = 10.0, 1.1, 0.4 Hz, 1 H of =CH₂), 4.11 [dd, *J* = 8.8, 5.5 Hz, 1 H–C(6)], 4.07–4.00 [m, H–C(7)], 3.77 [dd, *J* = 8.8, 5.7 Hz, 1 H–C(6)], 1.30, 1.28, 1.19, 1.17 (4 s, 4 Me) ppm. ¹³C NMR: $\delta = 220.9$ [s, C(2)], 136.1 (d, CH=CH₂), 117.0 (t, CH=CH₂), 100.7 [s, C(4)], 76.4 [t, C(6)], 65.6, 65.5 [2 s, C(1), C(3)], 52.2 [d, C(7)], 24.6, 24.0, 17.7, 17.3 (4 q, 4 Me) ppm. IR (film): $\tilde{\nu} = 3085$ w, 2967 m, 2931 w, 2868 w, 1774 s, 1637 w, 1463 m, 1444 w, 1420 w, 1380 w, 1364 w, 1250 w, 1205 w, 1142 w, 1096 s, 1028 m, 986 w,

927 m, 892 w, 811 w, 733 w, 701 w cm⁻¹. CI-MS (NH₃): 228 (13), 227 (100) [M + H]⁺, 156 (18), 71 (5). C₁₂H₁₈O₂S (226.34): calcd. C 63.68, H 8.02, S 14.17; found C 63.51, H 7.89, S 14.08.

X-ray Crystal Structure Determination of (S)-9 and (S)-12 (Figure 1 and Figure 2):^[42] All measurements were performed on a Nonius KappaCCD area-detector diffractometer^[43] by use of graphite-monochromated Mo-*K*_α radiation (λ, 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. The data collection and refinement parameters are given below, and views of the molecules are shown in Figures 1 and 2. Data reduction was performed with HKL Denzo and Scalepack.^[44] The intensities were corrected for Lorentz and polarization effects, and an absorption correction based on the multi-scan method^[45] was applied. The structures were solved by direct methods with SIR92,^[46] which revealed the positions of all non-H atoms. In (S)-12, there are two symmetry-independent molecules in the asymmetric unit. The atomic coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group with the program PLATON,^[47] but none could be found. The non-H atoms of (S)-9 and (S)-12 were refined anisotropically. All of the H atoms were placed in geometrically calculated positions and refined by use of a riding model in which each H atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 *U*_{eq} of its parent C atom (1.5 *U*_{eq} for the methyl group in (S)-12). The refinement of each structure was carried out on *F*² using full-matrix least-squares procedures, which minimized the function Σ(*wF*_o² - *F*_c²)². A correction for secondary extinction was applied in both cases. In (S)-12, four reflections, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Refinement of the absolute structure parameter^[48] yielded values of -0.05(7) and -0.15(8) for (S)-9 and (S)-12, respectively, which confidently confirms that the refined coordinates represent the true enantiomorph in both cases. Neutral atom scattering factors for non-H atoms were taken from,^[49] and the scattering factors for H atoms were taken from.^[50] Anomalous dispersion effects were included in *F*_c.^[51] The values for *f*' and *f*'' were those of.^[52] The values of the mass attenuation coefficients are those of.^[53] All calculations were performed by use of the SHELXL97^[54] program.

Crystal Data for (S)-9: C₁₇H₁₄O₂S, *M* = 282.36, colorless, tablet, crystal dimensions 0.08 × 0.25 × 0.30 mm³, orthorhombic, space group *P*2₁2₁2₁, *Z* = 4, *a* = 8.9261(3) Å, *b* = 9.7256(4) Å, *c* = 15.6448(4) Å, *V* = 1358.15(8) Å³, *D*_x = 1.381 g·cm⁻³, μ(Mo-*K*_α) = 0.236 mm⁻¹, *T* = 160 K, φ and ω scans, transmission factors (min./max.) 0.906/0.988, 2θ_(max.) = 55°, total reflections measured 27993, symmetry independent reflections 3125, reflections with *I* > 2σ(*I*) 2744, reflections used in refinement 3125, parameters refined 182, *R* (on *F*; *I* > 2σ(*I*) reflections) = 0.0367, *wR*(*F*²) (all reflections) = 0.0853 (*w* = [σ²(*F*_o²) + (0.0407*P*)² + 0.3488*P*]⁻¹, where *P* = (*F*_o² + 2*F*_c²)/3), goodness of fit 1.058, secondary extinction coefficient 0.006(2), final Δ_{max.}/σ 0.001, Δρ (max./min.) = 0.20/-0.29 e·Å⁻³.

Crystal Data for (S)-12: C₁₇H₂₂OS, *M* = 274.42, colorless, prism, crystal dimensions 0.15 × 0.20 × 0.27 mm³, monoclinic, space group *C*2, *Z* = 8, *a* = 19.7743(4), *b* = 8.2890(2), *c* = 19.7925(4) Å, β = 109.813(1)°, *V* = 3052.1(1) Å³, *D*_x = 1.194 g·cm⁻³, μ(Mo-*K*_α) = 0.203 mm⁻¹, *T* = 160 K, φ and ω scans, transmission factors (min./max.) 0.908/0.974, 2θ_(max.) = 55°, total reflections measured 37032, symmetry independent reflections 7017, reflections with *I* > 2σ(*I*) 5175, reflections used in refinement 7013, parameters refined 352, restraints 1, *R* (on *F*; *I* > 2σ(*I*) reflections) = 0.0454, *wR*(*F*²) (all reflections) = 0.1184 (*w* = [σ²(*F*_o²) + (0.0573*P*)² + 0.9687*P*]⁻¹, where *P* = (*F*_o² + 2*F*_c²)/3), goodness of fit 1.042, secondary extinction coefficient 0.0049(6), final Δ_{max.}/σ 0.001, Δρ (max./min.) = 0.20/-0.29 e·Å⁻³.

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