Reaction of Optically Active Oxiranes with Thiofenchone and 1-Methylpyrrolidine-2-thione: Formation of 1,3-Oxathiolanes and Thiiranes

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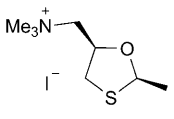
The $SnCl_4$-catalyzed reaction of (−)-thiofenchone (=1,3,3-trimethylbicyclo[2.2.1]heptane-2-thione; **10**) with (*R*)-2-phenyloxirane ((*R*)-**11**) in anhydrous CH_2Cl_2 at −60° led to two spirocyclic, stereoisomeric 4-phenyl-1,3-oxathiolanes **12** and **13** *via* a regioselective ring enlargement, in accordance with previously reported reactions of oxiranes with thioketones (*Scheme 3*). The structure and configuration of the major isomer **12** were determined by X-ray crystallography. On the other hand, the reaction of 1-methylpyrrolidine-2-thione (**14a**) with (*R*)-**11** yielded stereoselectively (*S*)-2-phenylthiirane ((*S*)-**15**) in 56% yield and 87–93% ee, together with 1-methylpyrrolidin-2-one (**14b**). This transformation occurs *via* an S_N2-type attack of the S-atom at C(2) of the aryl-substituted oxirane and, therefore, with inversion of the configuration (*Scheme 4*). The analogous reaction of **14a** with (*R*)-2-{[(triphenylmethyl)oxy]methyl}oxirane ((*R*)-**16b**) led to the corresponding (*R*)-configured thiirane (*R*)-**17b** (*Scheme 5*); its structure and configuration were also determined by X-ray crystallography. A mechanism *via* initial ring opening by attack at C(3) of the alkyl-substituted oxirane, with retention of the configuration, and subsequent decomposition of the formed 1,3-oxathiolane with inversion of the configuration is proposed (*Scheme 5*).

1. Introduction. – Derivatives of 1,3-oxathiolanes, for example, the muscarine analog **1** as a cholinergic agonist, have been known as biologically active compounds for many years (see, *e.g.*, [1]). However, the interest in these heterocycles increased impressively in recent times. In particular, the nucleoside analogs of type **2** became the focus of many medicinal chemists because of their remarkable activity as nucleoside-analog reverse transcriptase inhibitors (nRTIs), which found application in the treatment of hepatitis B and HIV (see, *e.g.*, [2]).



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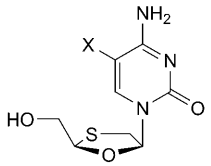
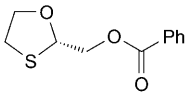


Lamivudine (**2a**) X = H
Emtricitabine (**2b**) X = F



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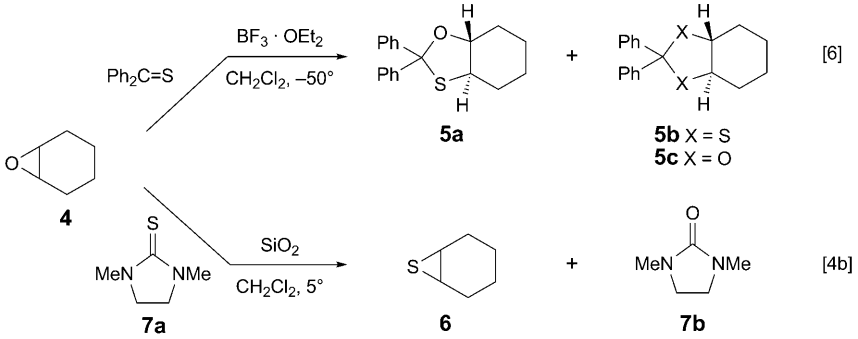
For this reason, new synthetic approaches and optimizations of known syntheses for 1,3-oxathiolanes are of current interest [3]. The most common approach is the reaction of a carbonyl compound with 2-sulfanylethanol [3b–3g]. In this manner, optically

[1]) Present address: Verlag Helvetica Chimica Acta AG, Hofwiesenstrasse 26, CH-8042 Zürich.

active 2-(acyloxymethyl)-1,3-oxathiolanes of type **3** have been obtained after an enzyme-catalyzed kinetic resolution of the racemate [3e]. Some years ago, we have elaborated a regio- and stereoselective formation of 1,3-oxathiolanes *via* the *Lewis* acid-catalyzed reaction of thiocarbonyl compounds with oxiranes [4]. Analogous ring enlargement reactions have been reported to occur with CS_2 [3h] and thioacetamide [3i]. Whereas the SiO_2-catalyzed reaction of thioketones with (*S*)-2-methyloxirane yielded (*S*)-5-methyl-1,3-oxathiolane with retention of the configuration of the oxirane, the reaction with (*R*)-2-phenyloxirane led to (*S*)-4-phenyl-1,3-oxathiolane with inversion of the configuration [5a]. Similar results were obtained in the reactions with thionolactones [5b]. These findings can be rationalized by a regioselective S_N2-type mechanism.

In some cases, *e.g.*, in the BF_3-catalyzed reaction of thiobenzophenone with 1,2-epoxycyclohexane (**4**), in addition to the expected 1,3-oxathiolane **5a**, the corresponding 1,3-dithiolane **5b** and the 1,3-dioxolane **5c** were formed as minor products [6] (*Scheme 1*). It has been shown that **5b** and **5c** are secondary products, and a reaction mechanism *via* the intermediate formation of 1,2-epithiocyclohexane (**6**) and benzophenone was proposed[2]). Under milder conditions, **4** reacted with 1,3-dimethylimidazolidine-2-thione (**7a**) to give **6** and **7b** in high yield [4b].

Scheme 1



Transformations of oxiranes into thiiranes have been known for more than 60 years [7], and several examples have been described. In most of the cases, thiourea was used as the 'S-transfer reagent'. Several new modifications of the procedure have been reported in recent years [8]. Furthermore, the stereochemical course of this transformation, which occurs with inversion of the configuration at both stereogenic centers, has been studied extensively (see, *e.g.*, [9]). For example, the reaction of the optically active oxirane **8** with thiourea in MeOH at room temperature gave stereoselectively the thiirane **9** (*Scheme 2*).

Instead of thiourea, heterocyclic thiones containing the N–C(S)–X moiety (X = N, O, S) [4b][10] as well as thiourethanes [11] can be used as the 'S-transfer reagent'.

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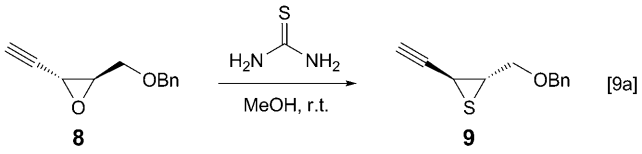
[2]) The reaction of (2*S*,3*S*)-2,3-dimethyloxirane with CS_2 in the presence of Bu_4NBr and an Al(salen) complex at 50° led to (4*R*,5*S*)-4,5-dimethyl-1,3-oxathiolane-2-thione, whereas, at 90°, the corresponding 1,3-dithiolane-2-thione was obtained [3h].

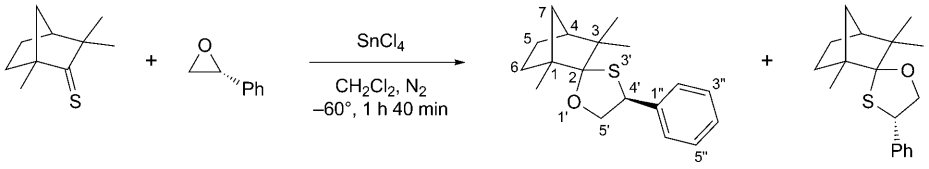
Scheme 2



Here, we report an additional example of the ring enlargement of an optically active oxirane in the reaction with a thioketone and the transformation into optically active thiiranes by using 1-methylpyrrolidine-2-thione as the 'S-transfer reagent'.

2. Results and Discussion. – 2.1. *Reaction of (1*R,*4*S*)-Thiofenchone* (=*(1*R,*4*S*)-1,3,3-Trimethylbicyclo[2.2.1]heptane-2-thione*; **10**) *with (*R*)-2-Phenyloxirane* ((*R*)-**11**). On dropping 0.5 equiv. of $SnCl_4$ into a solution of 1.06 equiv. of **10** and 2 equiv. of (*R*)-**11** in anhydrous CH_2Cl_2 at $-60°$ under an N_2 atmosphere, the orange color of the solution slowly disappeared. After 1 h 40 min, the reaction was quenched by addition of H_2O. Chromatographic separation (CC and HPLC (*Chiralcel OD*)) gave the diastereoisomeric spirocyclic 1,3-oxathiolanes **12** and **13** in 36 and 15% yield, respectively (*Scheme 3*), and two additional impure diastereoisomers in very small amounts.

Scheme 3



The structures of **12** and **13** were determined on the basis of their IR, ^{1}H- and ^{13}C-NMR, and mass spectra. In addition, the structure of **12** was established by a single-crystal X-ray diffraction analysis (*Fig. 1*). The crystals were enantiomerically pure, and the absolute configuration of the molecule has been determined independently by the diffraction experiment, as expected, as (1*R*,2*S*,4*S*,4′*S*), *i.e.*, the S-atom occupies the *exo*- and the O-atom the *endo*-position with respect to the bicycloheptane skeleton. The five-membered heterocycle has an envelope conformation with C(5) as the envelope flap lying 0.587(2) Å from the plane defined by the other four atoms.

The formation of **12** and **13** was rationalized by a nucleophilic attack of the thiocarbonyl S-atom of **10** at C(2) of (*R*)-**11** according to an S_N2 mechanism, *i.e.*, with inversion of the configuration, leading to the (*S*)-configuration at C(4′), which, in the case of **12**, was confirmed by the X-ray analysis. Based on the results of previously reported reactions, *e.g.*, with thiocamphor [13], the structure **13** was assigned to the minor isomer, *i.e.*, the epimer of **12**.

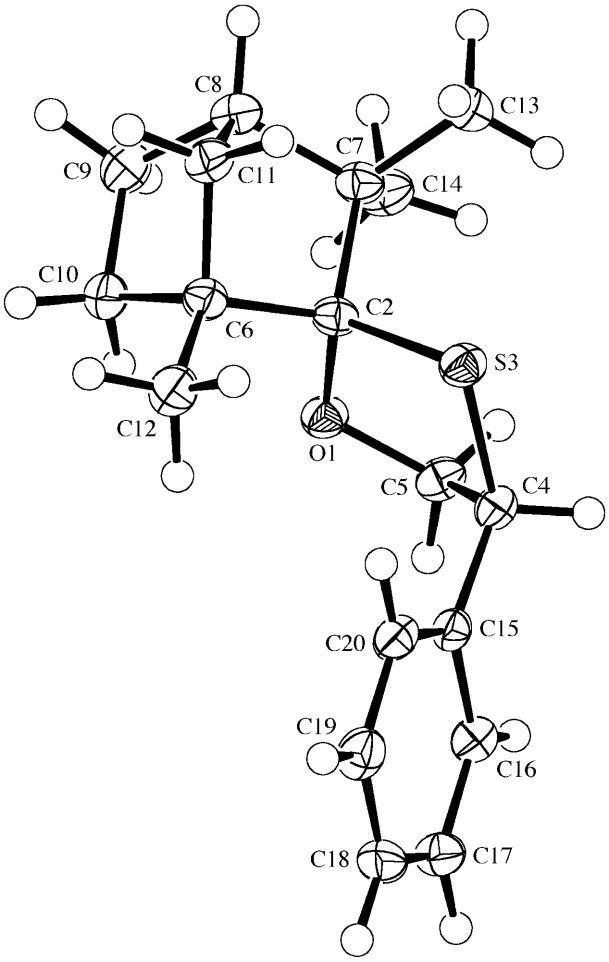


Fig. 1. *ORTEP Plot* [12] *of the molecular structure of* **12** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability)

2.2. *Reaction of 1-Methylpyrrolidine-2-thione* (**14a**) *with* (*R*)-**11**. After addition of 1.0 equiv. of (*R*)-**11** (91% ee) to 1.25 equiv. of **14a** at room temperature, the mixture became warm. Then, dry CH_2Cl_2 was added while stirring, and thin layer chromatography (TLC) showed complete conversion of (*R*)-**11** after 1 h 15 min. After evaporation of the solvent and chromatographic workup, (*S*)-2-phenylthiirane ((*S*)-**15**) was obtained in 55% yield with 92.5% ee (HPLC, *Chiralcel OD-H*) as a colorless oil (*Scheme 4*)[3]).

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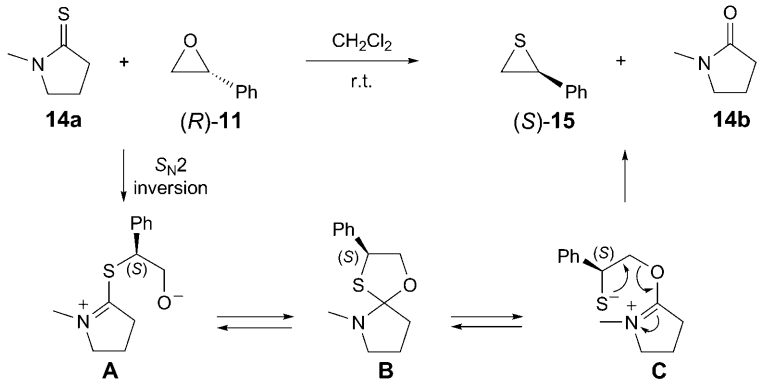
[3]) The transformation of (*R*)-**11** to (*S*)-**15** was described for the first time by *Stewart via* treatment with KSCN [14a]. In 2005, a reaction, in which thiourea, in the presence of SiO_2, was used as 'S-transfer reagent', was reported by *Iranpoor et al.* [14b].

Scheme 4



In an analogous experiment, 1.0 equiv. of (*R*)-**11** was added to a solution of 1.05 equiv. of **14a** in dry CH_2Cl_2 at 0°. The mixture was stirred at 0° for 1 h and then left to warm to room temperature; TLC control indicated only partial conversion of (*R*)-**11**. Then, CH_2Cl_2 (3 ml) and SiO_2 (2 g) were added to the mixture, and stirring at room temperature was continued for 30 h. After this time, no (*R*)-**11** could be detected by TLC, and usual workup by column chromatography on silica gel gave (*S*)-**15** in 56% yield with 87.6% ee (HPLC, *Chiralcel OD-H*).

A reaction mechanism for the stereoselective S-transfer reaction is proposed in *Scheme 4* (see also [4b])[4]). The ring opening of (*R*)-**11** by nucleophilic attack of the S-atom of **14a** at C(2) occurs *via* inversion of the configuration, leading to the intermediate zwitterion **A** [5b][16]. Ring closure gives the spirocyclic 1,3-oxathiolane **B**, which undergoes rearrangement to yield the new zwitterion **C**. The latter then decomposes to give the isolated product (*S*)-**15** and 1-methylpyrrolidin-2-one (**14b**).

2.3. *Reaction of* **14a** *with (*RS*)-2-[(*tert*-Butoxy)methyl]oxirane* ((*RS*)-**16a**). The SiO_2-catalyzed reaction of **14a** with (*RS*)-**16a** (molar ratio 1.1:1) in dry CH_2Cl_2 at room temperature for 3.5 h afforded *2-[(*tert*-butoxy)methyl]thiirane* ((*RS*)-**17a**) in 62.8% yield after purification by column chromatography on silica gel (hexane/Et_2O 13:1 and 10:1; *Scheme 5*).

2.4. *Reaction of* **14a** *with (*R*)-2-[(Triphenylmethoxy)methyl]oxirane* ((*R*)-**16b**). In an analogous manner, the reaction of **14a** and (*R*)-**16b** (molar ratio 1.2:1) in dry CH_2Cl_2 at room temperature in the presence of SiO_2 yielded, after 1 d, stereoselectively (*R*)-2-[(triphenylmethoxy)methyl]thiirane ((*R*)-**17b**) in 87.3% yield with $[\alpha]_D^{21} = +4.2$ ($c = 1.0$, CH_2Cl_2) (*Scheme 5*)[5]). Unfortunately, the determination of the ee value of (*R*)-**17b** by means of HPLC (*Chiralcel OD-H*) failed.

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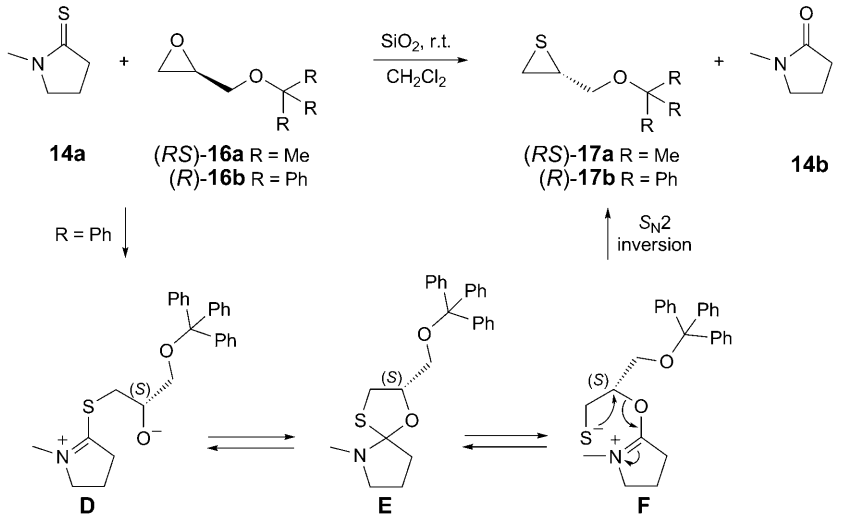
[4]) A detailed experimental and computational study of the mechanism of the transformation (*R*)-**11** → (*S*)-**15** with NH_4SCN in H_2O was published recently by *Schreiner* and co-workers [15].

[5]) This transformation, by using thiourea in MeOH, was reported by *Harfouche et al.* [17]. The authors claimed to have obtained (*R*)-**17b** from (*R*)-**16b**, but in their Scheme 1, they presented the (*S*)-enantiomers. Furthermore, the melting point of (*R*)-**17b** was given as 65–66° and the $[\alpha]_D$ value of the isolated product as −26.5° ($c = 1$, CH_2Cl_2). In our case, (*R*)-**17b** showed a melting point of 108.6–109.6°.

Scheme 5



The structure of (*R*)-**17b** was determined on the basis of ^{1}H- and ^{13}C-NMR, and ESI mass spectra, and the absolute configuration was unambiguously established by X-ray crystallography (*Fig. 2*). The compound in the crystal is enantiomerically pure, and the molecule has the (*R*)-configuration.

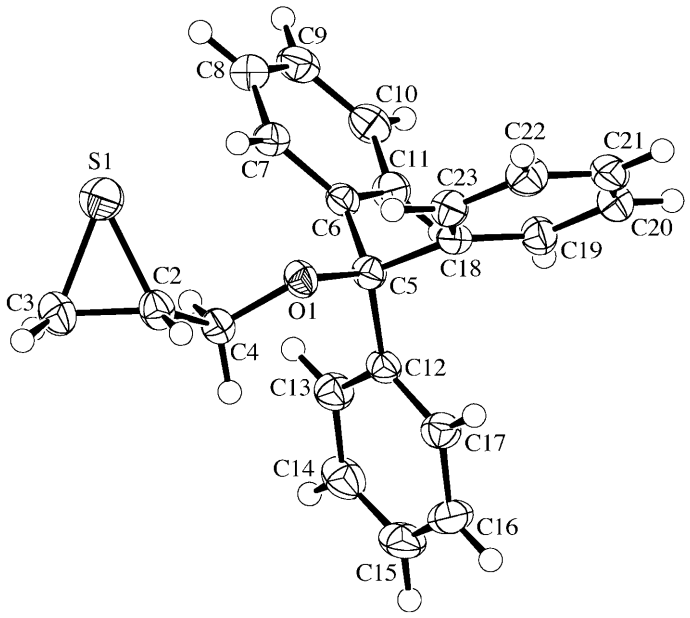
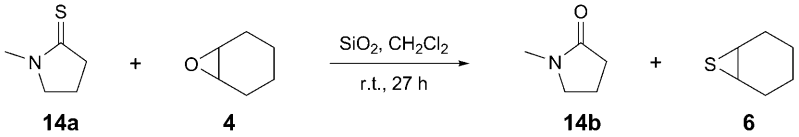


Fig. 2. *ORTEP Plot* [12] *of the molecular structure of* (R)-**17b** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability)

A reaction mechanism of the formation of (*R*)-**17b** (and (*RS*)-**17a**) is depicted in *Scheme 5*. In contrast to the reaction of **14a** and (*R*)-**11**, the S-atom of **14a** attacked preferably the less hindered C(3)-atom of (*R*)-**16b** to give the zwitterionic intermediate **D** with retention of the configuration (see also [5b][16]). Cyclization of **D** gave the spirocyclic 1,3-oxathiolane **E**, which underwent ring opening to afford **F**. The latter then decomposes to yield the product (*R*)-**17b** *via* an S_N2 mechanism, in which the anionic S-atom attacks the stereogenic C-atom with inversion of the configuration.

2.5. *Reaction of* **14a** *with 1,2-Epoxycyclohexane* (= *7-Oxabicyclo[4.1.0]heptane*; **4**). As expected, the analogous SiO_2-catalyzed reaction of **14a** with **4** (molar ratio 1.1 : 1.0) in dry CH_2Cl_2 occurred smoothly at room temperature and gave, after 27 h and purification by means of column chromatography on SiO_2 (hexane/Et_2O 23 : 1), pure 7-thiabicyclo[4.1.0]heptane (**6**) [4b] in 73.7% yield (*Scheme 6*).

Scheme 6



14a **4** **14b** **6**

3. Conclusions. – In addition to previously reported examples, the *Lewis* acid-catalyzed reaction of the oxirane (*R*)-**11** with (−)-thiofenchone (**10**) confirms the generality of the regio- and stereoselective formation of 1,3-oxathiolanes from oxiranes and thioketones ([4a] and refs. cit. therein). Whereas 2-aryl- and 2-vinyloxiranes yield 4-substituted 1,3-oxathiolanes with inversion of the configuration, the reaction with 2-alkyloxiranes lead to 5-alkyl-1,3-oxathiolanes with retention of the configuration. Analogous reactions providing 1,3-oxathiolanes occur with heterocyclic thiones such as 1,3-thiazole-5(4*H*)-thiones [18], 1,3-dithiolane-2-thiones [16], and thiolactones [5b].

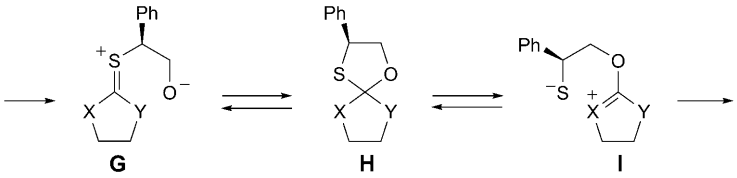
On the other hand, heterocyclic thiones containing a neighboring N-atom react with oxiranes, in general, to give thiiranes *via* a S-transfer reaction [4b][10]. This reaction also occurs with 1-methylpyrrolidine-2-thione (**14a**), which was established as a convenient and efficient S-transfer reagent and led to, in the whole, the inversion of configuration of the monosubstituted oxiranes (*R*)-**11** and (*R*)-**16b** with either aryl or alkyl substitution.

We propose that all these transformations proceed *via* an initially formed zwitterion **G**[6]), which cyclizes to give the 1,3-oxathiolane **H** (*Scheme 7*). In the cases of X, Y = C, O, S, this product is stable, whereas with X and/or Y = NR, the 1,3-oxathiolane undergoes a subsequent ring opening to give the rearranged zwitterions **I**. The latter, *via* an intramolecular S_N2 reaction, yields the thiirane and the heterocyclic oxo compound.

To the best of our knowledge, there is only one exception of this rule: (*Z*)-5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one (= 5-benzylidene-3-phenylrhoda-

[6]) This regioisomer is formed with 2-phenyl- and 2-vinyloxiranes, whereas, in the case of 2-alkyloxiranes, the zwitterion bears the residue at the alkoxy-C-atom.

Scheme 7



nine) reacts with 2-methyl- and 2-phenyloxirane, respectively, to give stable spirocyclic 1,3-oxathiolanes in a regio- and stereoselective manner [19]. This observation may be rationalized by the reduced availability of the lone electron pair of the N-atom because of its lactam nature.

We thank the analytical services of our institute for NMR and mass spectra, and elemental analyses, and *F. Hoffmann-La Roche AG*, Basel, for financial support.

Experimental Part

1. *General*. See [20]. Prep. HPLC: *Chiralcel OD*. Enantiomeric excesses (ee): anal. HPLC on a *Chiralcel OD-H* column. Optical rotations: *Perkin-Elmer-241* polarimeter ($c = 1$, in THF). IR Spectra: *Perkin-Elmer-781* FT-IR spectrophotometer; film or KBr; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker DPX-300* or *ARX-300* instruments at 300 (^1H) and 75.5 MHz (^{13}C) in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. ESI-MS: *Finnigan TSQ-700* instrument; *m/z* (rel. %). Elemental analyses were performed at the Institute of Organic Chemistry, University of Zürich.

2. *Starting Materials*. The optically active *(+)-2-phenyloxirane* ((*R*)-**11**, 97% ee, *Fluka*) and *(+)-2-[(triphenylethoxy)methyl]oxirane* ((*R*)-**16b**, 98% ee, *Aldrich*) as well as the racemic *2-[(*tert*-butoxy)-methyl]oxirane* ((*R,S*)-**16a**, *Aldrich*) were commercially available.

3. *Preparation of 1-Methylpyrrolidine-2-thione* (**14a**). To a soln. of 1-methylpyrrolidin-2-one (2.48 g, 25 mmol) in THF (250 ml) was added *Lawesson*'s reagent (5.06 g, 12.5 mmol). The mixture was stirred at 30–35° for 38 min. Then, silica gel (SiO_2; 5 g) was added to the mixture, and THF was removed. The resulting residue was subjected to CC (SiO_2; hexane/AcOEt 4:1, 2.2:1, 1.7:1, and 1.4:1) to give pure **14a**. Yield: 1.67 g (58%).

4. *Reaction of (−)-(1*R,*4*S*)-1,3,3-Trimethylbicyclo[2.2.1]heptane-2-thione* (**10**; (−)-thiofenchone) *with (*R*)-2-Phenyloxirane* ((*R*)-**11**, 91% ee[7])). To a stirred soln. of **10** (178 mg, 1.06 mmol) and (*R*)-**11** (0.23 ml, 2 mmol) was added a soln. of 1M $SnCl_4$ (0.5 ml, 0.5 mmol) at −60° under N_2. The color of the orange soln. disappeared after stirring at the same temp. for 1 h 40 min. Then, the reaction was quenched by addition of H_2O, and the mixture was washed with sat. aq. NaCl soln. (4×). The combined org. layers were dried ($MgSO_4$) and evaporated *in vacuo*. Separation of the residue by CC (SiO_2; hexane/CH_2Cl_2 25:1) and subsequent HPLC (*Chiralcel OD*; hexane) gave *(1*R,*2*S,*4*S,*4′*S*)-1,3,3-trimethyl-4′-phenylspiro[bicyclo[2.2.1]heptane-2,2′-[1,3]oxathiolane]* (**12**) and *(1*R,*2*R,*4*S,*4′*S*)-1,3,3-trimethyl-4′-phenylspiro-[bicyclo[2.2.1]heptane-2,2′-[1,3]oxathiolane]* (**13**), and two additional impure diastereoisomers in very small amounts.

Data of **12**. Yield: 110 mg (36%). Colorless crystals. M.p. 36.9–38.7°. $[\alpha]_D^{23} = -123.9$ ($c = 1$, THF). IR (KBr): 3059*w*, 3030*w*, 2997*m*, 2976*s*, 2962*s*, 2929*s*, 2876*s*, 1598*w*, 1579*w*, 1490*m*, 1469*s*, 1448*s*, 1383*w*, 1374*w*, 1362*w*, 1318*w*, 1296*w*, 1281*w*, 1249*w*, 1161*w*, 1151*m*, 1115*m*, 1093*s*, 1074*s*, 1050*w*, 1032*m*, 1003*w*, 992*w*, 958*w*, 942*w*, 921*w*, 906*m*, 895*m*, 866*m*, 824*m*, 812*w*, 787*m*, 722*s*, 699*s*. ^1H-NMR (300 MHz): 7.41–7.38 (*m*, H–C(2″), H–C(6″)); 7.31–7.18 (*m*, H–C(3″), H–C(4″), H–C(5″)); 4.65 (*t*-like, $J = 5.8$, H–C(4′)); 4.21–4.14 (*m*, CH_2(5′)); 2.10–2.00 (*m*, 1 H); 1.81–1.73 (*m*, 2 H); 1.52–1.08 (*m*, 5 H); 1.23,

[7]) During storage in the refrigerator, (*R*)-**11** racemized partially.

1.18, 1.05 (3*s*, 3 Me). ^{13}C-NMR (75 MHz): 140.4 (*s*, C(1″)); 128.4 (*d*, C(3″), C(5″)); 127.7 (*d*, C(2″), C(6″)); 127.2 (*d*, C(4″)); 111.7 (*s*, C(2)); 77.4 (*t*, C(5′)); 54.1 (*s*, C(1)); 52.8 (*d*, C(4′)); 49.5 (*d*, C(4)); 46.9 (*s*, C(3)); 42.7 (*t*, CH_2); 32.3 (*q*, Me); 30.2 (*t*, CH_2); 26.0 (*t*, CH_2); 22.3, 21.2 (2*q*, 2 Me). CI-MS (NH_3): 289 (17, $[M+H]^+$), 171 (7), 170 (100), 153 (9), 104 (8).

Crystals of **12** suitable for the X-ray crystal-structure determination were grown from EtOH.

Data of **13**. Yield: 47 mg (15%). Purity 91% on the basis of ^{1}H-NMR spectra. $[\alpha]_D^{23} = -2.6$ ($c = 1$, THF). IR: 3085*w*, 3063*w*, 3028*w*, 2958*s*, 2874*s*, 1602*m*, 1494*m*, 1468*s*, 1455*s*, 1385*m*, 1373*m*, 1364*m*, 1289*w*, 1278*w*, 1241*w*, 1201*w*, 1148*w*, 1113*m*, 1093*s*, 1070*s*, 1032*m*, 999*m*, 956*w*, 908*m*, 887*m*, 865*m*, 819*w*, 759*m*, 698*s*. ^{1}H-NMR (300 MHz): 7.44–7.40 (*m*, H–C(2″), H–C(6″)); 7.34–7.22 (*m*, H–C(3″), H–C(4″), H–C(5″)); 4.45–4.37 (*m*, H–C(4′), 1 H–C(5′)); 3.80–3.71 (*m*, 1 H–C(5′)); 1.90–1.22 (*m*, 7 H); 1.16, 1.13, 1.08 (3*s*, 3 Me). ^{13}C-NMR (75 MHz): 137.2 (*s*, C(1″)); 128.5 (*d*, C(3″), C(5″)); 128.1 (*d*, C(2″), C(6″)); 127.6 (*d*, C(4″)); 111.7 (*s*, C(2)); 79.5 (*t*, C(5′)); 54.8 (*s*, C(1)); 53.0 (*d*, C(4′)); 48.9 (*d*, C(4)); 47.1 (*s*, C(3)); 40.5 (*t*, CH_2(7)); 33.4 (*t*, CH_2); 28.5 (*q*, Me); 25.6 (*t*, CH_2); 24.0, 16.6 (2*q*, 2 Me). CI-MS (NH_3): 291 (6), 290 (20), 289 (100, $[M+H]^+$), 171 (9), 170 (82), 153 (6), 104 (9).

5. *Reactions of* **14a**. 5.1. *With (*R*)-2-Phenyloxirane* ((*R*)-**11**) *in the Absence of SiO_2.* When (*R*)-**11** (0.24 g, 2.0 mmol, 91% ee) was added to **14a** (0.29 g, 2.5 mmol) at r.t., the mixture became warm. Then, dry CH_2Cl_2 (20 ml) was added under stirring, and TLC showed complete conversion of (*R*)-**11**. After stirring the mixture at r.t. for 1 h 15 min, CH_2Cl_2 was evaporated *in vacuo*. *(*S*)-2-Phenylthiirane* ((*S*)-**15**) [14][3]) was separated by CC (SiO_2; hexane/Et_2O 200:1, 40:1, and 25:1) in 55% yield (150 mg) with 92.5% ee (HPLC, *Chiralcel OD-H*; t_R(*R*) 19.6 min, t_R(*S*) 20.73 min; eluent, hexane; flow rate, 0.5 ml/min; 19 atm; 202 nm; $[\alpha]_D^{23} = +28.5$ ($c = 1.0$, heptane)) as a colorless oil[8]).

5.2. *With* (*R*)-**11** *in the Presence of SiO_2.* To a soln. of **14a** (0.24 g, 2.1 mmol) in dry CH_2Cl_2 (3 ml) was added (*R*)-**11** (0.24 g, 2.0 mmol) at 0°. The mixture was stirred at 0° for 1 h and then left to warm to r.t. After stirring overnight at r.t., (*R*)-**11** was not completely converted (TLC). Then, CH_2Cl_2 (3 ml) and SiO_2 (2 g) were added to the mixture, and the reaction was continued at r.t. After 30 h, no (*R*)-**11** could be detected by TLC, the mixture was filtered, and the residue was washed with Et_2O (4×). Then, the combined filtrate was evaporated *in vacuo*, and (*S*)-**15** was separated by CC (SiO_2; hexane/Et_2O): 148 mg (56%), 87.6% ee (*Chiralcel OD-H*; t_R(*R*) 20.5 min, t_R(*S*) 21.8 min; eluent, hexane; flow rate, 0.5 ml/min; 19 atm; 202 nm; $[\alpha]_D^{23} = +26.5$ ($c = 1.0$, heptane)).

5.3. *With (*RS*)-2-[(*tert*-Butoxy)methyl]oxirane* ((*RS*)-**16a**). The reaction of **14a** (135 mg, 1.1 mmol) with (*RS*)-**16a** (129 mg, 1.0 mmol) in anh. CH_2Cl_2 (15 ml) and SiO_2 (4.5 g) for 3.5 h at r.t., yielded, after purification by CC (SiO_2, hexane/Et_2O 13:1 and 10:1), 91 mg (62.8%) of pure *2-[(*tert*-butoxy)methyl]thiirane* ((*RS*)-**17a**). ^{1}H-NMR (300 MHz, $CDCl_3$): 3.66 (*dd*, $J \approx 10.0, 5.5$, 1 H–C(1′)); 3.23 (*dd*, $J \approx 10.0, 6.5$, 1 H–C(1′)); 3.07–2.98 (*m*, H–C(2)); 2.52 (*d*-like, $J \approx 6.1$, 1 H–C(3)); 2.20 (*d*, *d*-like, $J \approx 5.3, 1.1$, 1 H–C(3)); 1.20 (*s*, Me_3C).

5.4. *With (*R*)-2-[(Triphenylmethoxy)methyl]oxirane* ((*R*)-**16b**). The reaction of **14a** (69 mg, 0.6 mmol) with (*R*)-**16b** (158 mg, 0.5 mmol) in anh. CH_2Cl_2 (15 ml) and SiO_2 (4.5 g) for 1 d at r.t., yielded, after purification by CC (SiO_2, hexane/Et_2O 4:3) 145 mg (87.3%) of pure *(*R*)-2-[(triphenylmethoxy)methyl]thiirane* ((*R*)-**17b**) [17][5]). $[\alpha]_D^{21} = +4.2$ ($c = 1.0$, CH_2Cl_2). $[\alpha]_D^{21} = +6.1$ ($c = 1.0$, THF). Colorless crystals. M.p. 108.6–109.6°. IR (KBr): 3084*w*, 3057*m*, 3032*w*, 3021*w*, 2925*w*, 2913*w*, 2864*w*, 1595*w*, 1490*s*, 1447*s*, 1395*w*, 1320*w*, 1214*m*, 1178*w*, 1154*m*, 1091*s*, 1076*s* (sh), 1031*m*, 1001*w*, 988*m*, 900*m*, 777*m*, 765*s*, 744*m*, 710*s*, 701*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.47–7.43 (*m*, 6 arom. H); 7.31–7.19 (*m*, 9 arom. H); 3.37 (*dd*, $J = 9.9, 5.4$, 1 H–C(1′)); 3.12 (*dd*, $J = 10.0, 6.5$, 1 H–C(1′)); 3.06–2.98 (*m*, H–C(2)); 2.46 (*d*-like, $J \approx 6.1$, 1 H–C(3)); 2.10 (*dd*, $J \approx 5.3, 1.1$, 1 H–C(3)). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 143.9 (*s*, 3 arom. C); 128.6 (*d*, 6 arom. CH); 127.8 (*d*, 6 arom. CH); 127.0 (*d*, 3 arom. CH); 86.8 (*s*, Ph_3C); 68.3 (*t*, CH_2(1′)); 32.8 (*d*, CH(2)); 23.7 (*t*, CH_2(3)). ESI-MS (MeOH/CH_2Cl_2): 355 (17, $[M+Na]^+$), 304 (8), 282 (7), 243 (100, Ph_3C^+). Anal. calc. for $C_{22}H_{20}OS$ (332.47): C 79.48, H 6.06, S 9.64; found: C 79.34, H 5.93, S 9.64.

Crystals of (*R*)-**17b** suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane.

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[8]) In [14b], it was claimed that (*S*)-**15** was obtained with $[\alpha]_D = +39.3$ (heptane), which was correlated with an ee of 90%.

5.5. *With 1,2-Epoxycyclohexane* (= *7-Oxabicyclo[4.1.0]heptane*; **4**). The reaction of **4** (190 mg, 1.65 mmol) with **14a** (147 mg, 1.5 mmol) in anh. CH_2Cl_2 (15 ml) and SiO_2 (4.0 g) for 27 h at r.t., yielded, after purification by CC (SiO_2; hexane/Et_2O 23 : 1), 126 mg (73.7%) of pure *7-thiabicyclo[4.1.0]heptane* (**6**) [4b].

6. *X-Ray Crystal-Structure Determination of* **12** *and (*R*)-***17b*** (*Table* and *Figs. 1* and *2*)*[9]). All measurements were performed on a *Nonius KappaCCD* area-detector diffractometer [21] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700*

Table. *Crystallographic Data of Compounds* **12** *and (*R*)-***17b***

	12	(*R*)-**17b**
Crystallized from	EtOH	Et_2O/hexane
Empirical formula	$C_{18}H_{24}OS$	$C_{22}H_{20}OS$
Formula weight [g mol^{-1}]	288.45	332.46
Crystal color, habit	colorless, plate	colorless, prism
Crystal dimensions [mm]	$0.05 \times 0.17 \times 0.30$	$0.15 \times 0.22 \times 0.28$
Temp. [K]	160(1)	160(1)
Crystal system	monoclinic	monoclinic
Space group	$P2_1$	$P2_1$
Z	2	2
Reflections for cell determination	36425	16937
2θ Range for cell determination [°]	4–55	4–55
Unit cell parameters:		
a [Å]	7.2196(2)	8.7354(3)
b [Å]	6.3380(2)	10.6394(3)
c [Å]	16.6427(6)	9.5620(2)
β [°]	91.161(2)	98.159(2)
V [Å^3]	761.38(4)	879.69(4)
D_X [g cm^{-3}]	1.258	1.255
μ(MoK_α) [mm^{-1}]	0.207	0.189
Scan type	ϕ and ω	ϕ and ω
$2\theta_{(max)}$ [°]	55	55
Transmission factors (min; max)	0.912; 0.991	0.906; 0.973
Total reflections measured	16865	19556
Symmetry-independent reflections	3432	4039
Reflections with $I > 2\sigma(I)$	2740	3466
Reflections used in refinement	3432	4038
Parameters refined; restraints	185; 1	218; 1
Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0414	0.0431
$wR(F^2)$ (all data)	0.0873	0.1016
Weighting parameters [a; b][a])	0.0360; 0.1237	0.0589; 0.0238
Goodness-of-fit	1.033	1.099
Secondary extinction coefficient	0.025(4)	0.36(2)
Final Δ_{max}/σ	0.002	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.26; −0.34	0.27; −0.29

[a]) $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$.

[9]) CCDC-809596 and 809597 contain the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

cooler. The data collection and refinement parameters are given in the *Table*, and views of the molecules are shown in *Figs. 1* and *2*. Data reduction was performed with HKL Denzo and Scalepack [22]. The intensities were corrected for *Lorentz* and polarization effects, and absorption corrections based on the multi-scan method [23] were applied. The structures were solved by direct methods using SIR92 [24], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where 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 Me groups in **12**). The refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in both cases. In (*R*)-**17b**, one reflection, whose intensity was considered to be an extreme outlier, was omitted from the final refinement. Refinement of the absolute structure parameters [25] yielded a value of 0.01(7) and 0.00(7), resp., which confidently confirmed that the refined models correspond with the true enantiomorphs. Neutral atom scattering factors for non-H-atoms were taken from [26a], and the scattering factors for H-atoms were taken from [27]. Anomalous dispersion effects were included in F_c [28]; the values for f' and f'' were those of [26b]. The values of the mass attenuation coefficients are those of [26c]. All calculations were performed using the SHELXL97 [29] program.

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