# Stereoselective synthesis of 2,4-disubstituted butanolides*

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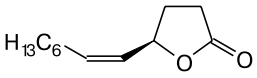
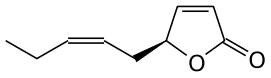
A series of 2,4-disubstituted butanolides was prepared based on the *trans*-stereoselective electrophilic cyclization of substituted *N*-(pent-4-enoyl)pyrrolidines. The butanolides may be considered as synthons for this type of natural products.

**Key words:** substituted butanolides, *N*-(pent-4-enoyl)pyrrolidines, electrophilic cyclization, substituted (tetrahydrofuran-2-ylidene)ammonium bromides.

Substances comprising a five-membered lactone ring are widely spread among natural metabolites (see Ref. 2 and references cited therein), many of them being of interest due to their perspective biological activity. The insect feromones with lactone ring **1** and **2** (see Ref. 3) as well as compounds **3** (see Ref. 4) and **4** (see Ref. 5) with cytostatic activity may be mentioned as examples.



**1**



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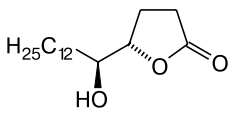

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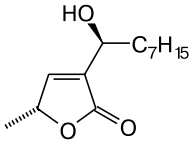
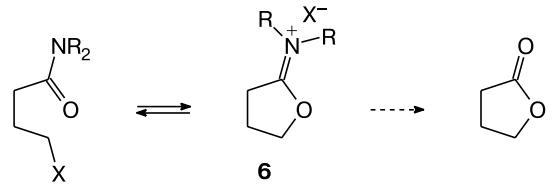


**4**

In recent years, halogenolactonization of γ,δ-unsaturated carboxylic acids and their derivatives (see, for example, Ref. 6) has been found to be the most popular among known methods for the butanolide ring construction. Earlier, we have reported[7] on a new type of ring-chain tautomerizm, consisting of reversible transformation of γ-halobutyric acid dialkylamides **5** into dialkyl(tetrahydrofuran-2-ylidene)ammonium halides **6** detected by $^1$H NMR spectroscopy (Scheme 1). Taking into account that immonium salts of type **6** were considered as possible intermediates in halogenolactonization of γ,δ-unsaturated carboxylic acid amides,[6c] it was of interest to identify them in this process as well as to investigate the possibility of their use in stereoselective synthesis of substituted butanolides.

**Scheme 1**



**5** **6**

X = Cl, Br, I

We chose *N*-(2-phenylthiopent-4-enoyl)- and *N*-(2-phenylsulfonylpent-4-enoyl)pyrrolidines (**7** and **8**) as the first subjects of investigation. Our choice was based on the suggestion (*cf.* Ref. 8) that such α-substituents might have remarkable stereocontrol over process under investigation. In addition, if we succeeded, such functionalization might turn out useful for further utilization of the thus produced substituted butanolides in synthesis of natural products of the type **1—4**.

Phenylthioacetic acid (**9**) was used as the starting material, which was transformed by standard methods into the target amide **7** *via* amide **10** in total yield 96% (Scheme 2). We investigated a new procedure of deprotonation of amide **10** with lithium diisopropylamide generated *in situ* in the system Li—$HNPr^i_2$ (~7 mol.%)—methylstyrene as an alternative. In this case, the yield of amide **7** was 75%.

Amide **12**, synthesized from phenylsulfonylacetic acid (**11**), was subjected to allylation under different conditions as well. The allylation product **8** was obtained in the highest yield under the action of NaH—AllBr, whereas $Pd^0$-catalyzed allylation of **12** with allyl acetate or diallyl carbonate turned out to be less efficient (*cf.* Ref. 9).

As it has been reported earlier,[1] bromination of allylic sulfide **7** led to the stereoselective formation of immonium

* For preliminary communication, see Ref. 1.

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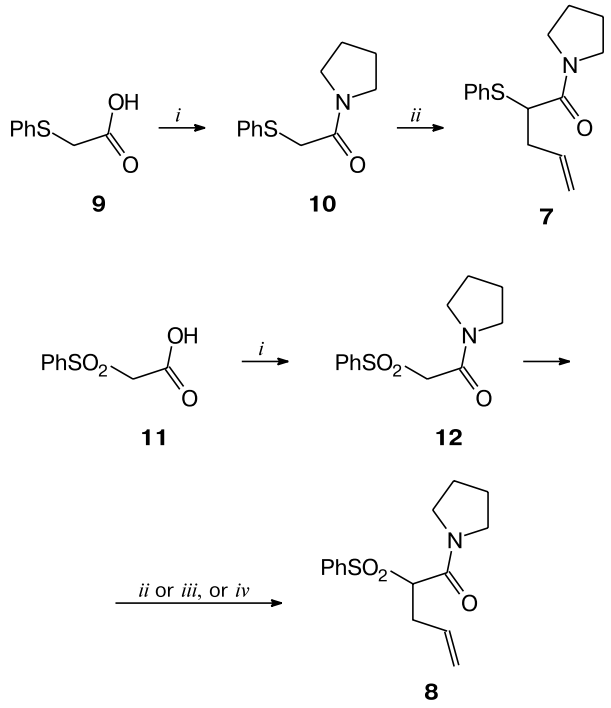
**Scheme 2**



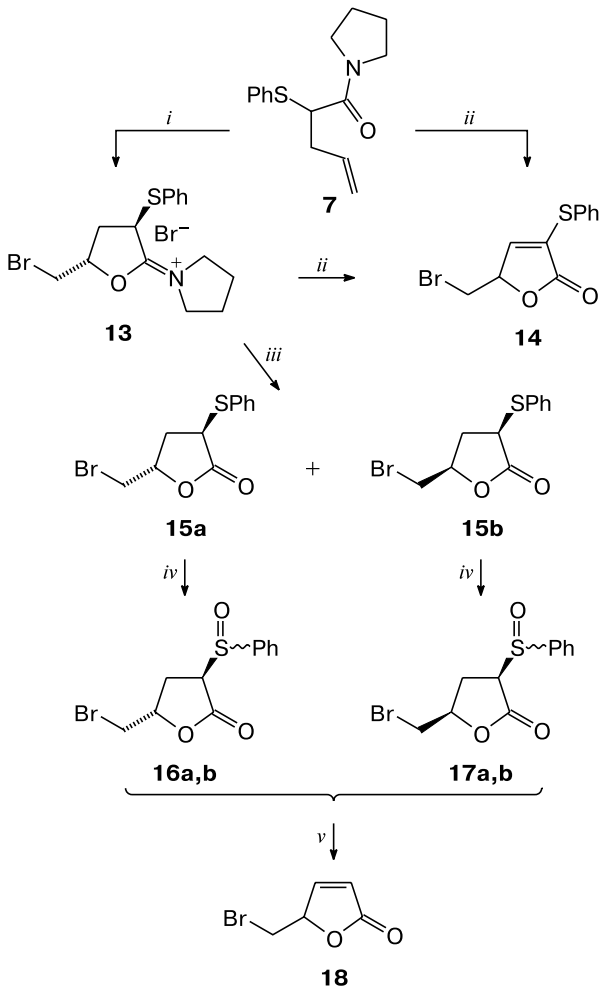

**Reagents and conditions:** *i*. $SOCl_2$, 35—40 °C, then pyrrolidine, $CH_2Cl_2$, −5 → 20 °C; *ii*. NaH, DMF, then AllBr, 20 °C or Li, methylstyrene, $HNPr^i_2$ (cat.), THF, 20 °C, then AllBr; *iii*. NaH, DMF, $Pd_2(dba)_3(CHCl_3)$ (cat., dba is dibenzylidenacetone), $Ph_3P$, AllOAc, 25 °C; *iv*. $Pd_2(dba)_3(CHCl_3)$ (cat.), $Ph_3P$, $(AllO)_2CO$, DMF, 25 °C.

salt **13** with *trans*-arrangement of substituents in the tetrahydrofuran ring. The $^1H$ NMR spectrum of the analytically pure sample of salt **13** in $CDCl_3$ contained no additional signals, which might have been evidence of its reversible transformation into the corresponding open-chain form (*cf.* Ref. 7).

Obviously, the intermediate formation of salt **13** occurred also upon treatment of amide **7** with *N*-bromosuccinimide in aqueous THF. In this case, however, full conversion of **7** required 2 equiv. of NBS. Vinyl sulfide **14** was isolated from the reaction mixture in good yield. Apparently, its formation occurred as a result of sequences of transformations, including hydrolysis of the intermediate **13** and bromination of the hydrolysis product. This suggestion was confirmed by the fact that treatment of salt **13** with equimolar amount of NBS in aqueous THF as well led to vinyl sulfide **14** (Scheme 3).

Some remarks should be made about aforementioned reaction of amide **7** with bromination agents. It is known that sulfides readily react with bromine to give the corresponding *S*,*S*-dibromides. However, a documented example[10] of such reaction for the sulfides with alkene fragments in their structure did not allow us to make a general

**Scheme 3**




**Reagents and conditions:** *i*. $Br_2$, $CHCl_3$, 0 °C; *ii*. NBS, aq. THF, 10 → 20 °C; *iii*. aq. EtOH, refluxing; *iv*. $H_2O_2$, AcOH, 20 °C; *v*. $CCl_4$, refluxing.

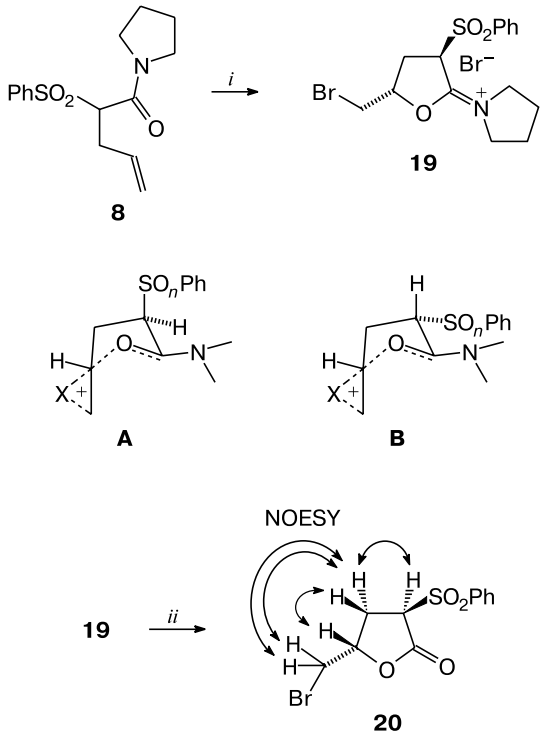
conclusion about relative reactivity of these functional groups toward bromine. In our case, the high yield of salt **13** (86%) pointed out to the fact that bromination of the double bond in unsaturated sulfide **7** is much faster than that of the phenylthio group.

Hydrolysis of salt **13** in aqueous ethanol was accompanied by partial epimerization with the formation of a mixture of lactones *trans*-**15a** and *cis*-**15b** in a ratio of ~3 : 2. Isolated by column chromatography on $SiO_2$, individual components of this mixture were further subjected to controlled oxidation with $H_2O_2$ in AcOH to the corresponding sulfoxides **16** and **17**. It turned out that formation of a new chiral center at the S-atom proceeded diastereoselectively. Indeed, oxidation of lactones **15a** and **15b** gave mixtures of two diastereomers **16a,b** and **17a,b**, respectively, in a ratio of ~2 : 3 ($^1H$ NMR data).

The structures of newly synthesized lactones **14—17** were confirmed by combination of spectroscopic methods and elemental analysis. Particularly, the assignment of tetrahydrofuran-2-ones **15** to *trans*- and *cis*-series was made based on the characteristic difference between chemical shifts of signals for α-HC(4) and β-HC(4) protons in $^1$H NMR spectrum. Thus for **15a** $\Delta\delta = 0.16$ ppm, whereas for **15b** this value is equal to 0.73 ppm, which is consistent with the particularities of the $^1$H NMR spectra recorded earlier[8] for both stereoisomers of compounds with structures similar to **15**.

In addition, based on literature data[8] for the $^1$H NMR spectra of enantiomerically pure analogs of lactones **16**, produced by oxidation of *trans*-isomer **15a**, we could make suggestions about relative configurations of their chiral centers. Thus a comparison of measured spin-spin coupling constant values for the HC(3)—$H_2$C(4) protons and the differences in chemical shifts for the $H_2$C(4) geminal protons with the literature data allowed us to assign 3*R**,S*S**,5*S**-configuration to stereoisomer **16a** and 3*R**,S*R**,5*S** to **16b**. Structure of lactones **16** and **17** was also confirmed by thermolysis of their mixture in $CCl_4$ to the known butenolide **18** in 90% yield (see Ref. 11).

**Scheme 4**




X = I (see Ref. 9), Br

**Reagents and conditions:** *i*. $Br_2$, $CHCl_3$, 0 °C; *ii*. *aq.* MeCN, 50 °C.

Bromination of amide **8** with bromine in $CHCl_3$ also led to the stereoselective formation of immonium salt **19** with *trans*-position of substituents in the tetrahydrofuran ring (Scheme 4). The high stereoselectivity in the related iodolactonization of α-substituted γ,δ-unsaturated carboxylic acids (see, for example, Ref. 8) was explained by preference of the suggested transition state **A** with pseudoaxial position of α-substituent over transition state **B** in which this substituent occupied pseudoequatorial position and was close to the dialkylamido group.

The given structure of the immonium salt **19**, which was characterized by spectral and analytical data, was confirmed by its hydrolysis into *trans*-lactone **20**. This process, in contrast to hydrolysis of phenyl sulfide analog **13**, proceeded almost without epimerization at the C(3) center. In turn, the relative configuration of substituents in molecule **20** was confirmed by NOESY experiment (500.13 MHz), which showed spatial proximity of α-HC(4) proton with protons in $CH_2Br$ fragment and revealed other informative cross-peaks (see Scheme 4).

## Experimental

IR spectra were recorded on a Specord M-80 instrument. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker AC-200 spectrometer with the signal of the solvent as the reference ($CDCl_3$, $\delta_H$ 7.27 and $\delta_C$ 77.0, respectively). Mass-spectra (EI, 70 eV) were recorded on a Finnigan MAT ITD-700 instrument. $R_f$ values were determined on Silufol precoated plates with Silica gel. Melting points were determined with the Kofler apparatus. Column chromatography was performed on Silica gel 60 (0.04-0.06 mm, Fluka).

Solvents used were purified and dried by standard methods. $Br_2$ was distilled over $P_2O_5$. Chemicals such as $Pd_2(dba)_3(CHCl_3)$, $SOCl_2$, pyrrolidine, NaH, $HNPr^i_2$, methylstyrene, and allylbromide were commercially available from Aldrich.

(Phenylthio)acetic acid (**9**)[12] and (phenylsulfonyl)acetic acid (**11**)[13] were obtained by known procedures.

***N*-[(Phenylthio)acetyl]pyrrolidine (10).** To a stirred mixture of $SOCl_2$ (30 mL) and DMF (0.5 mL) at 35—40 °C (Ar), acid **9** (7.56 g, 45.0 mmol) was added over a period of 15 min. After 1 h at this temperature, the excess of $SOCl_2$ was removed *in vacuo* (30 Torr, 40 °C, water bath). The oily residue was dissolved in $CH_2Cl_2$ (40 mL) and a solution of pyrrolidine (7.11 g, 100 mmol) in $CH_2Cl_2$ (30 mL) was added to the stirred (Ar) solution at −5—0 °C over a period of 30 min. The reaction mixture was heated up to 20 °C and stirred for 2 h, then it was quenched with water (20 mL). The organic layer was separated, washed with water (2×10 mL) and brine (3×10 mL), dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue (11.5 g) on $SiO_2$ with $Bu^tOMe$ as the eluent gave 8.45 g (85%) of amide **10** as colorless crystals, m.p. 78—79 °C (from hexane—$Bu^tOMe$). IR (KBr), ν/cm$^{-1}$: 684, 728, 812, 912, 1028, 1068, 1164, 1192, 1228, 1252, 1344, 1416, 1436, 1484, 1572, 1588, 1620, 1636, 2872, 2948, 2968, 3060. MS, *m*/*z* ($I_{rel}$ (%)): 222 $[M + 1]^+$ (5), 221 $[M]^+$ (43), 189 (8), 151 (3), 124 (14), 113 (37), 112 (12), 110 (16), 100 (9), 98 (100), 92 (6), 84 (11), 83 (18), 78 (11), 77 (14),

70 (26), 69 (15), 65 (12), 56 (31), 55 (70). $^1$H NMR, δ: 1.90 (m, 4 H, 2 $CH_2$); 3.45 (m, 4 H, 2 $CH_2N$); 3.64 (s, 2 H, $CH_2S$); 7.25, 7.45 (both m, 5 H, $H_{arom}$) (*cf.* Ref. 1).

**(±)-*N*-(2-Phenylthiopent-4-enoyl)pyrrolidine (7).** ***A.*** A 55% suspension of NaH in mineral oil (0.47 g, 11.0 mmol of NaH) was added to a stirred solution of amide **10** (2.21 g, 10.0 mmol) in DMF (10 mL) at 20 °C (Ar) and after 30 min allyl bromide (1.45 g, 12.0 mmol) was added. The reaction mixture was stirred at this temperature for 1 h, then it was quenched with water (30 mL) and extracted with Bu$^t$OMe. The organic layer was separated, washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue (2.8 g) on $SiO_2$ with Bu$^t$OMe as the eluent gave 2.50 g (96%) of amide **7** as colorless crystals, m.p. 46—47 °C (from light petroleum, b.p. 40—70 °C, which was used hereinafter). $^1$H NMR, δ: 1.80 (m, 4 H, 2 $CH_2$); 2.45, 2.76 (both m, 2 H, $H_2C(3)$); 3.40 (m, 4 H, 2 $CH_2N$); 3.70 (dd, 1 H, CHS, $J$ = 11 Hz, $J$ = 6 Hz); 5.10 (m, 2 H, $H_2C$=), 5.80 (m, 1 H, HC=); 7.30, 7.50 (both m, 5 H, $H_{arom}$) (*cf.* Ref. 1).

***B.*** To a stirred suspension of finely cut Li (21 mg, 3 mmol) in THF (5 mL), amide **10** (0.62 g, 2.8 mmol), methylstyrene (0.19 g, 1.6 mmol), and $HNPr^i_2$ (20 mg, 0.20 mmol) were added at 20 °C (Ar). The reaction mixture was stirred at this temperature for 2.5 h (until Li was almost completely dissolved), and then 0.40 g (3.31 mmol) of allyl bromide was added. After 1 h, the reaction mixture was quenched with saturated $NH_4Cl$ solution and extracted with Bu$^t$OMe. The extract was washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue (0.8 g) on $SiO_2$ with a mixture of light petroleum—Bu$^t$OMe as the eluent gave 0.55 g (75%) of amide **7**, practically identical (m.p., $^1$H NMR spectrum) with the sample of this compound described earlier.

***N*,*N*-(Butan-1,4-diyl)-*N*-(5*S**-bromomethyl-3*R**-phenylthiotetrahydrofuran-2-ylidene)ammonium bromide (13).** To a stirred solution of amide **7** (1.30 g, 5.0 mmol) in $CHCl_3$ (15 mL), a solution of $Br_2$ (0.85 g, 5.3 mmol) in $CHCl_3$ (15 mL) was added over a period of 20 min at 0 °C (Ar). The reaction mixture was kept at this temperature for 15 min, then concentrated *in vacuo*, and the residue was crystallized from MeCN to give 1.81 g (86%) of salt **13** as colorless crystals, m.p. 131—136 °C. Found (%): C, 43.16; H, 4.60; Br, 37.48; N, 3.40; S, 7.48. $C_{15}H_{19}Br_2NOS$. Calculated (%): C, 42.77; H, 4.55; Br, 37.94; N, 3.33; S, 7.61. IR (KBr), ν/cm$^{-1}$: 508, 656, 708, 780, 800, 852, 976, 1060, 1128, 1152, 1208, 1248, 1300, 1344, 1404, 1420, 1452, 1692, 2840, 2876, 2948, 3012. MS, *m*/*z* ($I_{rel}$ (%)): 421 $[M]^+$ (3), 342 (12), 341 (25), 339 (8), 323 (4), 312 (9), 308 (15), 306 (17), 260 (9), 232 (5), 228 (14), 192 (15), 189 (7), 163 (32), 161 (34), 152 (18), 151 (100), 149 (10), 136 (10), 135 (38), 129 (28), 128 (34), 110 (43), 109 (45), 99 (19), 98 (100), 85 (22), 81 (31), 72 (16), 70 (53), 56 (47), 55 (79). $^1$H NMR, δ: 1.90—2.35 (m, 4 H, 2 $CH_2$); 2.58 (ddd, 1 H, α-HC(4), $J$ = 1.0 Hz, $J$ = 6.4 Hz, $J$ = 13.9 Hz); 3.44 (ddd, 1 H, β-HC(4), $J$ = 8.5 Hz, $J$ = 9.8 Hz, $J$ = 13.9 Hz); 3.50—3.70 (m, 2 H, $CH_2N$); 3.69 (dd, 1 H, HCBr, $J$ = 6.3 Hz, $J$ = 10.8 Hz); 3.86 (dd, 1 H, HCBr, $J$ = 7.1 Hz, $J$ = 10.8 Hz); 3.90—4.00 (m, 1 H, HCN); 4.19—4.32 (m, 1 H, HCN); 4.68 (dddd, 1 H, HC(5), $J$ = 6.3 Hz, $J$ = 6.4 Hz, $J$ = 7.1 Hz, $J$ = 9.8 Hz); 5.11 (dd, 1 H, HC(3), $J$ = 1.0 Hz, $J$ = 8.5 Hz); 7.37—7.54 (m, 5 H, $H_{arom}$).

**5-Bromomethyl-3-phenylthiofuran-2(5*H*)-one (14).** ***A.*** To a stirred solution of amide **7** (0.26 g, 1.0 mmol) in a mixture of THF (2 mL) and water (0.5 mL), NBS (0.36 g, 2.0 mmol) was added portionwise over a period of 20 min at 10 °C. The reaction mixture was stirred at 20 °C for 1 h, diluted with 3 mL of water, and extracted with MeOBu$^t$. The organic layer was washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue on $SiO_2$ with a mixture light petroleum—Bu$^t$OMe (10 : 1) as the eluent gave 0.2 g (70%) of lactone **14** as colorless crystals, m.p. 81—83 °C (from light petroleum—MeOBu$^t$). Found (%): C, 46.33; H, 3.18; Br, 28.02, S, 11.24. $C_{11}H_9BrO_2S$. Calculated (%): C, 46.44; H, 3.34; Br, 27.83, S, 11.17. IR (KBr), ν/cm$^{-1}$: 496, 540, 576, 616, 692, 704, 752, 772, 792, 852, 872, 904, 1004, 1024, 1056, 1160, 1240, 1268, 1316, 1328, 1424, 1476, 1580, 1600, 1760, 2852, 2924, 3024. 3088. The $^1$H NMR spectral data are given in Table 1.

***B.*** To a stirred solution of salt **13** (0.18 g, 0.43 mmol) in a mixture of THF (2 mL) and water (1.0 mL), NBS (0.1 g, 0.56 mmol) was added at 10 °C. The reaction mixture was stirred for 2 h at 20 °C and worked up similarly to the previous procedure to give 0.08 g (65%) of lactone **14**, practically identical (m.p., $^1$H NMR spectrum) with the sample of this compound described earlier.

**5*S**-Bromomethyl-3*R**-phenylthiotetrahydrofuran-2-one (15a) and 5*R**-bromomethyl-3*R**-phenylthiotetrahydrofuran-2-one (15b).** A solution of salt **13** (1.05 g, 2.5 mmol) in 10 mL of ~95% EtOH was refluxed for 1 h, concentrated *in vacuo*, diluted with 10 mL of water and extracted with 50 mL of Bu$^t$OMe. The organic layer was separated, washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue (0.72 g) on $SiO_2$ with a mixture of light petroleum—Bu$^t$OMe (3 : 2) as the eluent gave 0.43 g (60%) of lactone **15a** and 0.27 g (37%) of **15b** in the order of elution.

*trans*-Isomer **15a**: colorless oil, $R_f$ 0.65 (hexane—MeOBu$^t$, 2 : 3). Found (%): C, 45.95; H, 3.96; Br, 27.50; S, 10.87. $C_{11}H_{11}BrO_2S$. Calculated (%): C, 46.00; H, 3.86; Br, 27.83; S, 11.16. IR ($CHCl_3$), ν/cm$^{-1}$: 664, 692, 728, 924, 1012, 1024, 1068, 1092, 1172, 1228, 1296, 1336, 1444, 1480, 1584, 1784, 3016, 3024. MS, *m*/*z* ($I_{rel}$ (%)): 288 $[M + 1]^+$ (42), 287 $[M]^+$ (7), 286 (43), 208 (2), 207 (11), 206 (4), 193 (5), 179 (15), 165 (15), 164 (11), 163 (100), 161 (6), 148 (7), 147 (4), 137 (29), 136 (15), 135 (87), 130 (39), 129 (11), 123 (19), 121 (6), 116 (6), 110 (29), 109 (73), 91 (11), 84 (14), 76 (11), 69 (7), 65 (21). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR, δ: 33.71, 34.10, 44.79, 76.04, 128.97, 129.35, 130.51, 133.72, 173.80.

*cis*-Isomer **15b**: colorless oil, $R_f$ 0.56 (hexane—MeOBu$^t$, 2 : 3). Found (%): C, 45.99; H, 3.76; Br, 27.48; S, 10.97. $C_{11}H_{11}BrO_2S$. Calculated (%): C, 46.00; H, 3.86; Br, 27.83; S, 11.16. IR ($CHCl_3$), ν/cm$^{-1}$: 664, 692, 728, 936, 1020, 1092, 1160, 1224, 1340, 1424, 1444, 1584, 1636, 1784, 3016, 3024. MS, *m*/*z* ($I_{rel}$ (%)): 288 $[M + 1]^+$ (44), 287 $[M]^+$ (6), 286 (44), 208 (4), 207 (24), 193 (7), 165 (16), 164 (8), 163 (67), 148 (7), 137 (18), 136 (10), 135 (58), 130 (39), 129 (11), 121 (6), 116 (6), 110 (23), 109 (100), 91 (12), 84 (20), 77 (14), 69 (7), 66 (11), 65 (30). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR, δ: 32.48, 33.78, 46.12, 75.86, 128.85, 129.31, 131.48, 133.84, 173.90.

**(3*R**,S*S**5*S**)- (16a) and (3*R**,S*R**5*S**)-5-Bromomethyl-3-phenylsulfinyltetrahydrofuran-2-ones (16b).** To a stirred solution of sulfide **15a** (0.35 g, 1.2 mmol) in AcOH (3 mL), a 30% $H_2O_2$ solution (1.36 g, 12 mmol) was added at 20 °C. The reaction mixture was stirred for 3 h, diluted with 15 mL of water, and extracted with 50 mL of $CHCl_3$. The organic layer was sepa-

**Table 1.** $^1$H NMR spectra of compounds **14—18** and **20**

| Compound | δ (*J*/Hz) | | | | |
|---|---|---|---|---|---|
| | HC(3) (dd, 1 H) | HC(4) (ddd, 1 H) | HC(5) (dddd, 1 H) | HCBr (dd, 1 H) | $H_{arom}$ (m, 5 H) |
| **14** | — | 6.53 (d, *J* = 1.8) | 5.14 (ddd, *J* = 1.8, *J* = 4.7, *J* = 6.2) | 3.46 (*J* = 6.2, *J* = 10.8); 3.56 (*J* = 4.7, *J* = 10.8) | 7.44—7.58 |
| **15a** | 4.00 (*J* = 4.8, *J* = 8.9) | 2.41 (*J* = 4.8, *J* = 7.1, *J* = 14.0); 2.57 (*J* = 7.0, *J* = 8.9, *J* = 14.0) | 4.58 (*J* = 4.9, *J* = 4.9, *J* = 7.0, *J* = 7.1) | 3.43, 3.44 (both d, 1 H each, *J* = 4.9) | 7.27—7.64 |
| **15b** | 3.96 (*J* = 9.5, *J* = 9.5) | 2.10 (*J* = 8.0, *J* = 9.5, *J* = 13.7); 2.83 (*J* = 6.7, *J* = 9.5, *J* = 13.7) | 4.57 (m) | 3.25 (*J* = 7.2, *J* = 10.7); 3.46 (*J* = 4.8, *J* = 10.7) | 7.27—7.60 |
| **16a** | 4.24 (*J* = 3.4, *J* = 10.2) | 2.44 (*J* = 7.3, *J* = 10.2, *J* = 15.1); 2.89 (*J* = 3.4, *J* = 7.7, *J* = 15.1) | 3.94 (*J* = 4.2, *J* = 4.9, *J* = 7.3, *J* = 7.7) | 3.40 (*J* = 4.2, *J* = 11.1); 3.46 (*J* = 4.9, *J* = 11.1) | 7.56—7.73 |
| **16b** | 3.86 (*J* = 6.5, *J* = 10.2) | 2.01 (*J* = 4.7, *J* = 10.2, *J* = 14.6); 2.94 (*J* = 6.5, *J* = 8.4, *J* = 14.6) | 4.89 (*J* = 3.2, *J* = 4.7, *J* = 4.7, *J* = 8.4) | 3.51 (*J* = 3.2, *J* = 11.3); 3.63 (*J* = 4.7, *J* = 11.3) | 7.54—7.72 |
| **17a** | 3.81 (*J* = 8.4, *J* = 10.2) | 2.22 (*J* = 7.3, *J* = 10.2, *J* = 14.2); 2.60 (*J* = 7.0, *J* = 8.4, *J* = 14.2) | 4.71 (*J* = 5.3, *J* = 7.0, *J* = 7.3, *J* = 8.0) | 3.53 (*J* = 8.0, *J* = 10.3); 3.63 (*J* = 5.3, *J* = 10.3) | 7.52—7.70 |
| **17b** | 4.37 (*J* = 7.1, *J* = 10.5) | 2.37 (*J* = 6.2, *J* = 7.1, *J* = 14.7); 2.73 (*J* = 8.1, *J* = 10.5, *J* = 14.7) | 4.65 (*J* = 5.0, *J* = 6.2, *J* = 7.9, *J* = 8.1) | 2.62 (*J* = 7.9, *J* = 10.5); 3.08 (*J* = 5.0, *J* = 10.5) | 7.54—7.73 |
| **18** | 6.27 (*J* = 1.8, *J* = 5.7) | 7.56 (dd, *J* = 1.7, *J* = 5.7) | 5.25 (*J* = 1.7, *J* = 1.8, *J* = 4.6, *J* = 7.3) | 3.45 (*J* = 7.3, *J* = 10.6); 3.68 (*J* = 4.6, *J* = 10.6) | — |
| **20** | 4.22 (*J* = 4.1, *J* = 10.4) | 2.62 (*J* = 7.3, *J* = 10.4, *J* = 14.9); 3.19 (*J* = 4.1, *J* = 7.4, *J* = 14.9) | 4.98 (*J* = 3.5, *J* = 5.2, *J* = 7.3, *J* = 7.4) | 3.58 (*J* = 3.5, *J* =11.3); 3.65 (*J* = 5.2, *J* = 11.3) | 7.58—8.02 |

rated, washed with water and brine, dried with $Na_2SO_4$, concentrated *in vacuo*, and additionally kept under vacuum (2 Torr) for 1 h at 40 °C. A mixture of diastereomers **16a** and **16b** (~1 : 1.5, $^1$H NMR data) (0.36 g, ~100%) was obtained. Double crystallization of the obtained product from $CHCl_3$—$Et_2O$ (1 : 1) afforded isomer **16a** as colorless crystals, m.p. 133—135 °C. The mother liquor was concentrated *in vacuo*, and triple crystallization of the residue from $Et_2O$ afforded isomer **16b** as colorless crystals, m.p. 101—103 °C.

Sulfoxide **16a**. Found (%): C, 43.85; H, 3.70; Br, 26.34; S, 10.57. $C_{11}H_{11}BrO_3S$. Calculated (%): C, 43.58; H, 3.66; Br, 26.36; S, 10.57. IR (KBr), ν/cm$^{-1}$: 648, 684, 740, 928, 1020, 1056, 1072, 1104, 1220, 1368, 1456, 1772, 2872-3076. MS, *m/z* ($I_{rel}$ (%)): 304 [M + 1]$^+$ (9), 302 (9), 288 (2), 179 (20), 177 (22), 163 (4), 148 (35), 146 (30), 135 (10), 127 (24), 126 (80), 125 (100), 110 (41), 109 (59), 97 (77), 83 (98), 78 (97), 77 (72), 69 (42), 65 (44), 57 (20), 55 (69), 51 (60). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR, δ: 26.41, 34.13, 63.35, 76.97, 124.82, 129.34, 132.30, 139.18, 168.50.

Sulfoxide **16b**. Found (%): C, 43.89; H, 3.91; Br, 26.28; S, 10.54. $C_{11}H_{11}BrO_3S$. Calculated (%): C, 43.58; H, 3.66; Br, 26.36; S, 10.57. IR (KBr), ν/cm$^{-1}$: 656, 688, 744, 876, 972, 1000, 1044, 1088, 1160, 1188, 1216, 1268, 1304, 1340, 1444, 1480, 1780, 2856—3064. MS, *m/z* ($I_{rel}$ (%)): 304 [M + 1]$^+$ (4), 302 (4), 179 (15), 177 (15), 148 (16), 146 (14), 126 (62), 125 (100), 110 (30), 109 (30), 97 (57), 83 (84), 78 (93), 77 (65), 69 (31), 65 (36), 55 (77), 51 (62). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR, δ: 22.65, 35.21, 64.61, 77.04, 123.84, 129.62, 131.75, 141.38, 170.88.

**5*R**-Bromomethyl-3*R**-phenylsulfinyltetrahydrofuran-2-ones* 17a и 17b.** Similarly, a mixture of isomeric sulfoxides **17a** and **17b** (~1.5 : 1, $^1$H NMR data) (0.21 g, ~100%) was obtained from sulfide **15b** (0.2 g, 0.70 mmol). Crystallization of the thus obtained product from $CHCl_3$—$Et_2O$ (1 : 1) afforded isomer **17a** as colorless crystals, m.p. 147—150 °C. The mother liquor was concentrated *in vacuo*, and the isomer **17b** was obtained as colorless crystals, m.p. 123—126 °C, by double crystallization of the residue from $Et_2O$.

Sulfoxide **17a**. Found (%): C, 43.78; H, 3.54; Br, 26.46; S, 10.81. $C_{11}H_{11}BrO_3S$. Calculated (%): C, 43.58; H, 3.66; Br, 26.36; S, 10.57. IR (KBr), ν/cm$^{-1}$: 644, 684, 740, 828, 928, 1036, 1064, 1104, 1184, 1228, 1292, 1368, 1464, 1496, 1780, 2944, 3048. MS, *m/z* ($I_{rel}$ (%)): 304 [M + 1]$^+$ (3), 302 (3), 179 (10), 177 (8), 148 (17), 146 (18), 135 (5), 127 (13), 126 (70), 125 (100), 110 (20), 109 (38), 97 (55), 83 (75), 78 (85), 77 (64), 69 (32), 65 (28), 55 (90), 51 (55). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR ($(CD_3)_2SO$), δ: 22.22, 34.26, 64.07, 77.27, 124.07, 129.64, 131.51, 141.23, 171.07.

Sulfoxide **17b**. Found (%): C, 43.88; H, 3.73; Br, 26.23; S, 10.72. $C_{11}H_{11}BrO_3S$. Calculated (%): C, 43.58; H, 3.66; Br, 26.36; S, 10.57. IR (KBr), ν/cm$^{-1}$: 644, 692, 756, 984, 1040, 1084, 1160, 1180, 1216, 1332, 1380, 1452, 1480, 1760, 2956—3060. MS, *m/z* ($I_{rel}$ (%)): 304 [M + 1]$^+$ (3), 302 (3), 179 (7), 177 (11), 163 (4), 148 (18), 146 (15), 127 (9), 126 (56), 125 (100), 110 (22), 109 (32), 97 (40), 83 (87), 78 (82), 77 (56), 69 (23), 65 (25), 55 (77), 51 (55). The $^1$H NMR spectral data are given in Table 1. $^{13}$C NMR, δ: 25.34, 31.41, 62.78, 76.75, 125.37, 129.40, 132.33, 138.84, 168.73.

**5-Bromomethylfuran-2(5*H*)-one (18).** A suspended mixture of isomeric sulfoxides **16** and **17** (1.51 g, 5 mmol) (obtained by oxidation of a mixture of sulfides **15a,b** similarly to the procedure described above for individual stereoisomers) in $CCl_4$ (25 mL) was refluxed for 6 h. The reaction mixture was concentrated *in vacuo*, and the residue was chromatographed on $SiO_2$. Elution with $CH_2Cl_2$ gave 0.8 g (90%) of lactone **18** as colorless oil, $R_f$ 0.35 ($CH_2Cl_2$). The $^1$H NMR spectral data are given in Table 1 (*cf.* Ref. 11).

* The relative configurations at SOPh asymmetrical centers of stereoisomers **17a,b** have not been established.

***N*-[(Phenylsulfonyl)acetyl]pyrrolidine (12).** To a stirred mixture of $SOCl_2$ (15 mL) and DMF (0.3 mL), acid **11** (3.21 g, 16.0 mmol) was added over a period of 20 min at 50 °C (Ar). After 2 h at this temperature, the excess of $SOCl_2$ was removed *in vacuo* (30 Torr, 40 °C, water bath). The oily residue was dissolved in $CH_2Cl_2$ (15 mL), and a solution of pyrrolidine (2.49 g, 35 mmol) in $CH_2Cl_2$ (10 mL) was added to the solution under stirring (Ar) over a period of 30 min at −5—0 °C. The reaction mixture was heated up to 20 °C and stirred for 12 h, then it was diluted with $CH_2Cl_2$ (45 mL), washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue on $SiO_2$ with EtOAc as the eluent gave 2.55 g (63%) of amide **12** as colorless crystals, m.p. 119—121 °C (EtOAc). $^1$H NMR, δ: 1.78—2.05 (m, 4 H, 2 $CH_2$); 3.41, 3.61 (both t, 4 H, 2 $CH_2N$, $J$ = 6.7 Hz); 4.12 (s, 2 H, $CH_2S$); 7.60, 7.92 (both m, 5 H, $HC_{arom}$) (*cf.* Ref. 11).

**(±)-*N*-(2-Phenylsulfonylpent-4-enoyl)pyrrolidine (8).** ***A.*** To a stirred solution of amide **12** (1.92 g, 7.6 mmol) in DMF (10 mL), a 55% suspension of NaH in mineral oil (0.36 g, 8.3 mmol of NaH) was added at 10 °C (Ar), and after 30 min, allyl bromide (1.0 g, 8.3 mmol) was added as well. The reaction mixture was heated up to 20 °C and stirred at this temperature for 1 h, then it was quenched with 30 mL of water and extracted with $CHCl_3$. The organic layer was washed with water and brine, dried with $Na_2SO_4$, and concentrated *in vacuo*. Chromatography of the residue (2.5 g) on $SiO_2$ with EtOAc as the eluent gave 1.94 g (87%) of amide **8** as colorless crystals, m.p. 102—104 °C (from light petroleum—EtOAc). $^1$H NMR, δ: 1.80—2.04 (m, 4 H, 2 $CH_2$); 2.60—2.72 (m, 2 H, HC(3)); 3.40, 3.73 (both m, 2 H, $CH_2N$); 3.47 (t, 2 H, $CH_2N$, $J$ = 6.7 Hz); 4.16 (dd, 1 H, CHS, $J$ = 5.4 Hz, $J$ = 9.3 Hz); 5.05 (ddd, 1 H, $H_2C$=C, $J$ = 1.3 Hz, $J$ = 2.5 Hz, $J$ = 10.0 Hz); 5.10 (ddd, 1 H, $H_2C$=C, $J$ = 1.5 Hz, $J$ = 2.5 Hz, $J$ = 17.0 Hz); 5.64 (dddd, 1 H, HC=C, $J$ = 6.9 Hz, $J$ = 6.9 Hz, $J$ = 10.0 Hz, $J$ = 17.0 Hz); 7.50—7.95 (m, 5 H, $H_{arom}$) (*cf.* Ref. 9).

***B.*** To a stirred suspension of $Pd_2(dba)_3(CHCl_3)$ (27 mg, 0.025 mmol) in DMF (1 mL), $Ph_3P$ (68 mg, 0.26 mmol) was added at 25 °C (Ar), after 30 min, AllOAc (0.2 g, 2 mmol) was added, and after another 10 min, the solution was diluted with DMF (6 mL), and a solution of the sodium derivative of sulfone **12** (prepared from **12** (0.51 g, 2 mmol) and 55% suspension of NaH in mineral oil (87 mg, 2 mmol of NaH) at 25 °C) in DMF (3 mL) was added in one portion. The reaction mixture was stirred for 6 h at 25 °C and worked up as described above to give 0.36 g (60%) of amide **8** as colorless crystals, m.p. 101—103 °C (from light petroleum—EtOAc).

***C.*** To a solution of catalyst, prepared as described above from $Pd_2(dba)_3(CHCl_3)$ (27 mg, 0.025 mmol) and $Ph_3P$ (68 mg, 0.26 mmol) in DMF (1 mL) for 5 min at 25 °C, a solution of sulfone **12** (0.51 g, 2 mmol) and diallyl carbonate (0.35 g, 2.46 mmol) in DMF (3 mL) was added. After stirring for 2 h another 0.2 g (1.4 mmol) of diallyl carbonate was added to the reaction mixture, and after additional 2 h of stirring the reaction mixture was worked up as described in the preceding experiments. Amide **8** (0.3 g, 52%) was obtained, practically identical (m.p., $^1$H NMR spectrum) to the samples of this compound described above.

***N*,*N*-(Butan-1,4-diyl)-*N*-(5*S**-bromomethyl-3*R**-phenylsulfonyltetrahydrofuran-2-ylidene)ammonium bromide (19).** To a stirred solution of amide **8** (1.08 g, 3.7 mmol) in $CHCl_3$ (15 mL), a solution of $Br_2$ (0.64 g, 4.0 mmol) in $CHCl_3$ (10 mL) was added over a period of 20 min at 0 °C (Ar). The reaction mixture was kept at this temperature for 15 min and concentrated *in vacuo*. The residue was crystallized from $CHCl_3$—$MeOBu^t$ mixture to give 1.17 g (70%) of salt **19** as colorless crystals, m.p.. 143—148 °C. Found (%): C, 39.76; H, 4.39; Br, 34.88; N, 3.39; S, 6.85. $C_{15}H_{19}Br_2NO_3S$. Calculated (%): C, 39.75; H, 4.23; Br, 35.26; N, 3.09; S, 7.08. IR (KBr), ν/cm$^{-1}$: 448, 532, 554, 640, 668, 692, 728, 748, 768, 800, 848, 876, 996, 1060, 1084, 1152, 1224, 1248, 1316, 1328, 1408, 1448, 1580, 1692, 1700, 2840, 2980. $^1$H NMR, δ: 1.90—2.40 (m, 4 H, 2 $CH_2$); 2.63 (dd, 1 H, α-HC(4), $J$ = 6.2 Hz, $J$ = 14.4 Hz); 3.36 (ddd, 1 H, β-HC(4), $J$ = 8.6 Hz, $J$ = 9.9 Hz, $J$ = 14.4 Hz); 3.80, 3.95, 4.21, 4.57 (all m, 4 H, 2 $CH_2N$); 3.78 (dd, 1 H, HCBr, $J$ = 6.5 Hz, $J$ = 10.9 Hz); 3.92 (dd, 1 H, HCBr, $J$ = 7.0 Hz, $J$ = 10.9 Hz); 5.51 (dddd, 1 H, HC(5), $J$ = 6.2 Hz, $J$ = 6.5 Hz, $J$ = 7.0 Hz, $J$ = 9.9 Hz); 5.60 (d, 1 H, HC(3), $J$ = 8.6 Hz); 7.63—8.05 (m, 5 H, $H_{arom}$).

**5*S**-Bromomethyl-3*R**-phenylsulfonyltetrahydrofuran-2-one (20).** A solution of salt **19** (2.6 g, 6.2 mmol) in a mixture of MeCN (50 mL) and $H_2O$ (10 mL) was stirred at 50 °C for 5 h, then was concentrated *in vacuo*, and the residue was extracted with $MeOBu^t$. The extract was washed with water and brine, dried with $Na_2SO_4$ and concentrated *in vacuo*. Crystallization of the residue from the EtOAc—light petroleum mixture gave 1.24 g of lactone **20** as colorless crystals, m.p. of 83—85 °C. By concentration *in vacuo* of the mother liquor and chromatography of the residue on $SiO_2$ with the mixture of light petroleum—EtOAc (20%) as the eluent gave additionally 0.41 g of lactone **20** (m.p. 82—84 °C), total yield 84%. Another fraction (0.2 g) was also isolated, which according to $^1$H NMR data turned out to be a ~2 : 1 mixture of lactone **20** and its *cis*-isomer (~5%), The latter had signals unoverlapped with the spectrum of the main isomer **20** at δ 2.77 (ddd 1 H, HC(4), $J$ = 6.5 Hz, $J$ = 8.1 Hz, $J$ = 14.6 Hz); 2.89 (ddd 1 H, HC(4), $J$ = 7.6 Hz, $J$ = 10.5 Hz, $J$ = 14.6 Hz); 4.31 (dd 1 H, HCS, $J$ = 8.1 Hz, $J$ = 10.4 Hz); 4.71 (m, 1 H, HC(5)).

Lactone **20**. Found (%): C, 41.55; H, 3.39; Br, 24.81; S, 9.96. $C_{11}H_{11}BrNO_4S$. Calculated (%): C, 41.40; H, 3.47; Br, 25.03; S, 10.04. IR (KBr), ν/cm$^{-1}$: 428, 496, 568, 576, 628, 644, 692, 716, 736, 764, 780, 836, 880, 928, 980, 1004, 1044, 1088, 1152, 1176, 1196, 1236, 1316, 1424, 1452, 1484, 1588, 1656, 1772. MS, $m/z$ ($I_{rel}$ (%)): 319 $[M]^+$ (2), 257 (3), 256 (37), 258 (34), 239 (8), 225 (6), 179 (9), 163 (6), 161 (8), 149 (3), 143 (18), 142 (25), 141 (83), 133 (9), 126 (8), 125 (64), 118 (9), 109 (3), 98 (4), 97 (32), 82 (19), 81 (16), 80 (77), 77 (47), 76 (100), 69 (5), 65 (10), 56 (5), 55 (72). The $^1$H NMR spectral data are given in Table 1.

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