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MICROBIOLOGICAL REDUCTION OF KETO-SULFONES. APPLICATION IN A THREE-STEP SYNTHESIS OF (S)-(+)-β-ANGELICA LACTONE

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Abstract : Microbiological reductions of several keto-sulfones led to the corresponding hydroxy-sulfones in moderate to high enantiomeric excess. A three-step synthesis of (S)-(+)-β-angelica lactone from ethyl-4-oxo-3-(phenyl-sulfonyl)-pentanoate *via* the intermediate chiral alcohol is described.

Several microbiological preparations of enantiomerically enriched hydroxy-sulfones have been reported.[1-5]. (S)-1-(phenylsulfonyl)-2-propanol was obtained in high yield and high enantiomeric excess from 1-(phenylsulfonyl)-2-propanone by reduction with baker's yeast[2,3] or incubation with *Corynebacterium equi*,[4] while the enantiomeric (R)-alcohol could only be obtained in 25% yield by kinetically-controlled oxidation of a mixture of four stereoisomers of 1-(phenyl-sulfinyl)-2-propanol with *C. equi*.[4] Other keto-sulfones also led to (S)-alcohols by reduction with baker's yeast and it was noticed that minor structural changes had marked effects on the results (6-68% yield and 22-98% ee).[1]

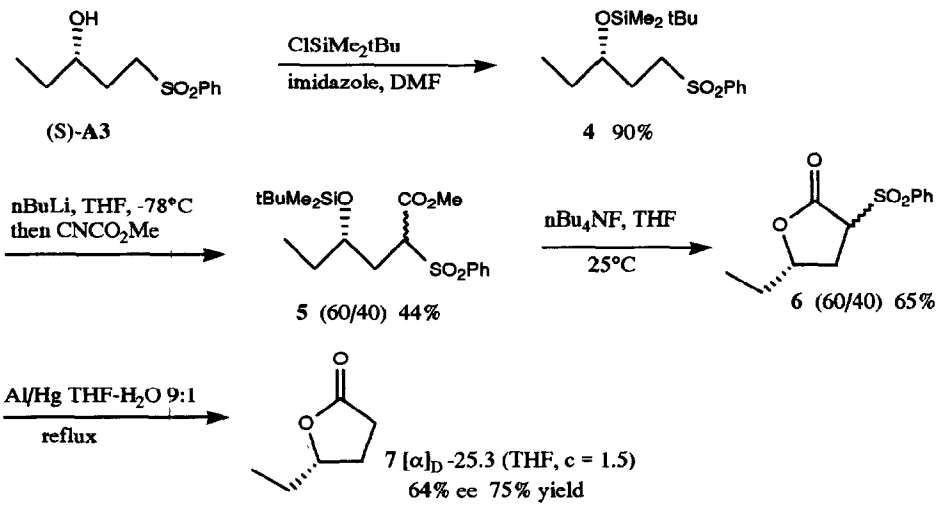
Since hydroxysulfones are versatile synthetic intermediates, especially for the synthesis of saturated and unsaturated lactones,[1,6,7,8a] we set out to prepare several of these compounds by microbiological reduction. Another aim of this work was to obtain, *via* an intermediate hydroxysulfone, β-angelica lactone, a useful synthetic intermediate in enantioselective synthesis.[8c]

The first part of this paper deals with the microbiological reduction of three keto-sulfones **1-3** in order to prepare both enantiomers of the corresponding alcohols **A1-A3** (Table I). Baker's yeast reduction of 1 led to the product already described by others for the same reaction,[2,3] namely (S)-**A1**. Enantiomeric (R)-**A1** was obtained by reduction with the fungus *Geotrichum candidum*.

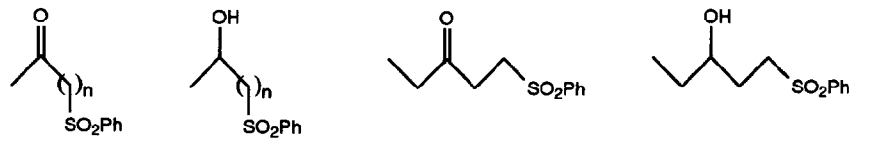
Run	Starting material	Product	Microorganism[a]	[α]	ee(%)	Yield (%)	Reaction time (h)	temperature (°C)
1[b]	**1**	(S)-**A1**	A	+15.9[c]	>95	99	24	25
2	**1**	(R)-**A1**	B	-15.5[d]	>95	80	24	27
3	**2**	(S)-**A2**	A	+20.7[c]	>95	80	192	25
4	**2**	(S)-**A2**	C	+22[d]	>95	50	28	27
5	**2**	(R)-**A2**	D	-3.7[d]	16.6	100	24	27
6	**3**	(S)-**A3**	A	+16[c]	64	27	192	25
7	**3**	(R)-**A3**	D	-13[d]	46[e]	100	24	27

[a] A Baker's yeast, B Geotrichum candidum, C Aspergillus niger, D Mortierella isabellina ; [b] same result as in ref 2 and 3 ; [c] $[\alpha]_D$ ($CHCl_3$, c = 1) (c : g/100 mL) ; [d] $[\alpha]_J$ (runs 2 : MeOH, c = 3 ; 4 and 5 : $CHCl_3$, c= 1 ; 7 : $CHCl_3$, C = 0.6) ; [e] this result was not reproducible as another experiment led to $[\alpha]_J$ = -2 and 7% ee only.

Table 1



Scheme 1



n = 1 **1** **A1** **3** **A3**
n = 2 **2** **A2**

This one-step preparation of (R)-**A1** gave the same[4] or even better[9] enantiomeric excess and a higher yield[4,9] than the *C. equi.* oxidation of 1-(phenylsulfinyl)-2-propanol[4] or the kinetic resolution of racemic alcohol with porcine pancreatic lipase.[9]

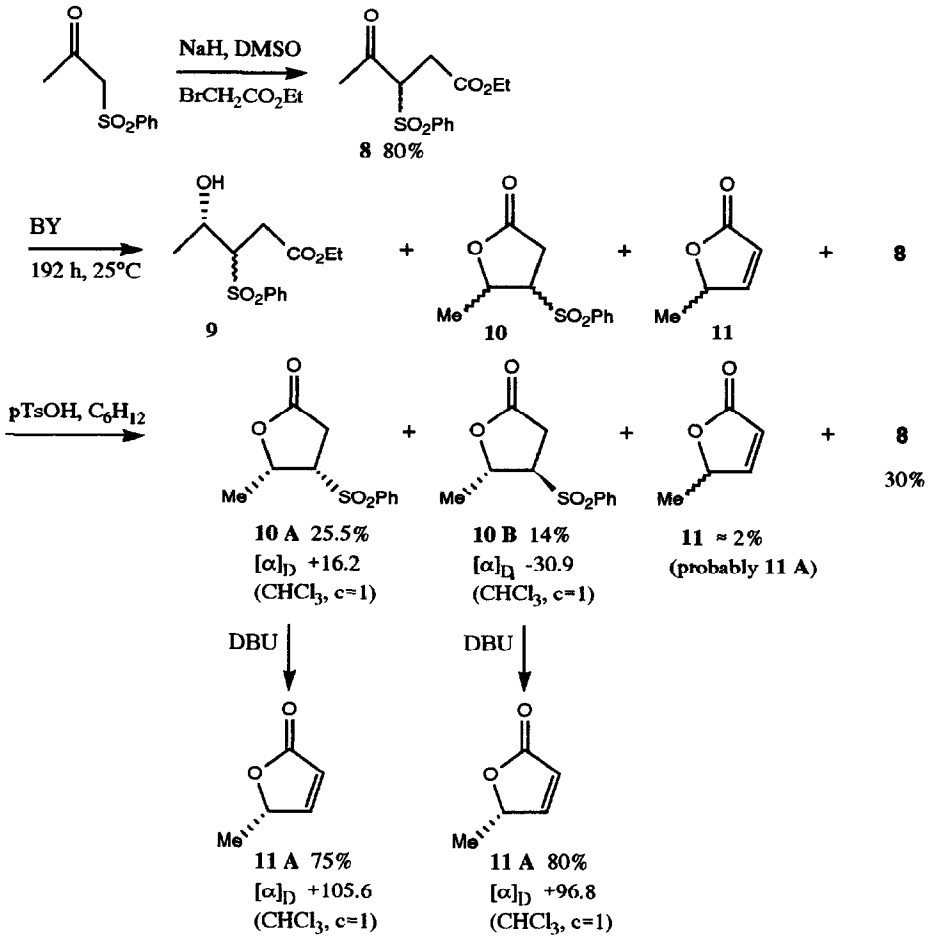
Alcohol (S)-**A2** was obtained satisfactorily by baker's yeast reduction but the reaction time was higher than for (S)-**A1** (8 days instead of 1 day). The same alcohol could also be prepared with the fungus *Aspergillus niger*, more quickly but in lower yield, and the (R)-alcohol was obtained in low enantiomeric excess with the fungus *Mortierella isabellina*.

Compound **3** led to (S)-**A3** with baker's yeast and to (R)-**A3** with *Mortierella isabellina*, in moderate enantiomeric excess in both cases. However run 6 showed a higher enantiomeric excess than as previously reported[1] (64% ee reproducibly instead of 22%). On the other hand we obtained poorly reproducible results from reduction with *Mortierella isabellina*. Such difficulties in reproducing bioconversion reactions have already been reported.[10,11] Interestingly, higher enantiomeric excesses for (S)-**A3** and (R)-**A3** were obtained by kinetic-resolution.[9]

The configuration of the predominant isomer obtained in run 6 was checked by chemical correlation (scheme 1). Alkylation of (S)-**A3** dianion failed to give **5** ; the reaction was thus carried out *via* silylether **4**. Compound **5** was obtained as a mixture of two diastereomers in a 60/40 ratio. Lactonisation and desulfonylation led to the known[12] lactone **7**.

We then endeavoured to reduce an already alkylated product, e.g. **8**, for the preparation of β-angelica lactone **11**. This reduction led to a complex mixture of hydroxysulfone **9**, lactones **10** and **11** and starting material **8** (scheme 2) and subsequent purification by chromatography on silica gel showed that alcohol **9** was unstable under these conditions. Accordingly, the crude reduction product was treated with paratoluenesulfonic acid and compounds **10A**, **10B**[8a] along with some unreacted starting material **8** were isolated. A small amount of lactone **11** was also obtained but could not be isolated ; the stereochemistry was thus not assigned. Lactones **10A** and **10B** both underwent elimination of sulfinic acid in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[1] giving (S)-(+)-β-angelica lactone **11A**[8] with high optical purity (litt $[\alpha]_D$ from +93.8 ($CHCl_3$, c = 0.5, 100% ee)[8c] to +117 ($CHCl_3$, c = 3.6, 96% ee)[8d]). Finally lactone **11A** was obtained in 30.3% overall yield from **8** or 43.3% allowing for the amount of **8** recovered.

It is thus now possible to prepare several chiral hydroxy-sulfones more efficiently than hitherto. These results also suggest new developments in the area of preparation of lactones from hydroxysulfones.



Scheme 2

Experimental Section

NMR spectra were obtained on either a Bruker AM 250 or a Bruker AC 200 instrument. Mass spectra were recorded on a Girdel-Nermag R10-10 mass spectrometer. Microanalyses were performed by the service de microanalyse, CNRS, ICSN, Gif-sur-Yvette. Optical rotations were measured on either a Perkin-Elmer 241 or a Perkin-Elmer 141 polarimeter. Enantiomeric excesses of compounds (R)-**A1**, (R)-**A2**, (R)-**A3**, (S)-**A1**, (S)-**A2**, (S)-**A3** and **7** were evaluated by ^{1}H NMR with (+)-Eu-(hfc)$_3$.

Preparation of starting materials 1, 2, 3, 8

1-(Phenylsulfonyl)-2-propanone 1 was obtained according to ref 13 except that benzene was replaced by cyclohexane. **1-(Phenylsulfonyl)-3-pentanone** 3 was prepared following the same procedure in 83% yield. It was obtained as an oil without further purification. ^{1}H NMR ($CDCl_3$,

250 MHz) δ 1.05 (t, J = 9.1 Hz, 3H), 2.46 (q, J = 9.1 Hz, 2H), 2.91 (t, J = 9.1 Hz, 2H), 3.40 (t, J = 9.1 Hz, 2H), 7.50-8.00 (m, 5H) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 244 (M+18, 100), 227 (M+1, 28) ; Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.39 ; H, 6.24 ; S, 14.17. Found : C, 58.34 ; H, 6.29 ; S, 13.95. **1-(Phenylsulfonyl)-2-butanone 2** was prepared as described in ref 14 for preparation of the p-tolyl derivative. Sodium benzensulfinate was thus used instead of sodium p-toluenesulfinate and **2** was obtained in 90% yield after recrystallization (Et_2O, hexane). ^1H NMR ($CDCl_3$, 250 MHz) δ 2.20 (s, 3H), 2.95 (t, J = 7.8 Hz, 2H), 3.38 (t, J = 7.8 Hz, 2H), 7.50-8.00 (m, 5H) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 230 (M+18, 100), 213 (M+1, 17) ; Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.59 ; H, 5.70 ; S, 15.10. found : C, 56.29 ; H, 5.54 ; S, 14.98. **Ethyl 4-oxo-3-(phenylsulfonyl)-pentanoate 8** was prepared as described for related compounds.[15] 1-(Phenylsulfonyl)-2-propanone (3g, 15 mmol) in 40 mL of dry DMSO was introduced dropwise under argon and with stirring on sodium hydride (720 mg, 15 mmol ; obtained from 1.440 g of 50% mineral oil dispersion). Reaction proceeded for 2.5 h then ethyl bromoacetate (1.66 mL, 15 mmol) in DMSO (10 mL) was added dropwise. The mixture was stirred for 1 h at room temperature and poured into iced 10% aqueous HCl (110 mL). Extraction with CH_2Cl_2 (3 x 100 mL), washing of the combined organic phases with brine (150 mL), drying (Na_2SO_4) and evaporation yielded the crude product. Purification by column chromatography on silica gel (Et_2O/hexane 50/50) gave 3.4 g (80%) of **8**. Mp 50.7°C ; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.20 (t, J = 7.2 Hz, 3H), 2.53 (s, 3H), 2.83 (dd, J = 17.2, 10.Hz, 1H, H-1), 2.95 (dd, J = 17.2, 4.0 Hz, 1H, H-1'), 4.08 (q, J = 7.2 Hz, 2H), 4.63 (dd, J = 10.7, 4.0 Hz, 1H), 7.50-8.00 (m, 5H) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 302 (M+18, 84), 285 (M+1, 20) ; Anal. Calcd for $C_{13}H_{16}O_5S$: C, 54.92 ; H, 5.67 ; S, 11.18. Found : C, 54.92 ; H, 5.70 ; S, 10.62.

Reduction of ketosulfones with Baker's yeast

Baker's yeast purchased from Springer (6g for 1 mmol) was stirred for 0.5 h at 37°C with water (3 mL for 1 g) and sucrose (1 g for 1 g). Ketosulfone was added and the reaction mixture was stirred at room temperature under anaerobic conditions. Carbon dioxide formation could be monitored with a flowchecker. Sucrose was added from time to time to maintain CO_2 release. The reaction was allowed to proceed for 24 h (**1**) or 192 h (**2**,**3**,**8**), then celite was added with strong stirring. Baker's yeast and celite were removed by vacuum filtration through a sintered-glass funnel containing a small amount of celite and the filtrate was extracted continuously overnight with CH_2Cl_2 or Et_2O. The organic solution was dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography on silica gel.

Reduction of ketosulfones with Geotrichum candidum, Aspergillus niger or Mortierella isabellina[11]

Microorganisms were grown in 500 mL conical flasks containing 100 mL of culture medium or in a 2 L fermentor. The culture medium for *G. candidum* was : glucose (50 g), yeast extract (10 g), peptone (10 g), H_2O (1 L), pH = 7.1 ; for *A. niger* : glucose (20 g), soyoptim (5 g), yeast extract (5 g), NaCl (5 g), KH_2PO_4 (5 g), H_2O (1 L), pH = 5.8 ; for *M. isabellina* : the same as above, except glucose 40 g. After cultivation wet cells were separated, washed throughly with saline (NaCl 8 g/L) and pressed into a wet cake. Bioconversions were run in conical flasks containing 50 mL of distilled water per 5 g of wet cells and 50 mg of ketosulfone. After 24 or 28 h (Table 1) of incubation at 27°C on a rotary shaker (200 rpm), the mixture was filtered or centrifuged and the filtrate extracted continuously overnight with Et_2O. The organic phase was dried ($MgSO_4$) and evaporated and the crude product was purified by column chromatography on silica gel.

1-(Phenylsulfonyl)-2-propanol A1

The chromatography eluent was the mixture Et_2O/hexane 50/50. (S)-Isomer was obtained by baker's yeast reduction and (R)-isomer *via G. candidum*. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.25 (d, J = 6.8 Hz, 3H), 3.14-3.34 (m, J = 14.3, 8.4, 3 Hz, 2H), 3.40-3.50 (m, 1H, H-2), 4.24-4.39 (m, 1H, OH), 7.50-8.01 (m, 5H) ; Anal. Calcd for $C_9H_{12}O_3S$: C, 53,98 ; H, 6.04 ; S, 16.01. Found : C, 53,80 ; H, 5.87 ; S, 16.07. (S)-Isomer : $[\alpha]_D^{25°C}$ = +15.9 ($CHCl_3$, c = 1), ee>95% ; (R)-isomer : $[\alpha]_J^{25°C}$ = -15.5 (MeOH, c = 3), ee>95%.

1-(Phenylsulfonyl)-3-butanol A2

The chromatography eluent was the mixture Et_2O/hexane 50/50. (S)-Isomer was obtained by baker's yeast or *A. niger* reduction and (R)-isomer *via M. isabellina*. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.21 (d, J = 6.0 Hz, 3H, H-4), 1.68-2.02 (m, 3H, H-2, OH), 3.13-3.38 (m, J gem = 13.9 Hz, 2H, H-1), 3.90 (dtd, J = 8.3, 6.0, 3.9 Hz, 1H, H-3), 7.50-8.00 (m, 5H, Ph) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 232 (M+18, 100), 215 (M+1, 72) ; Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56,05 ; H, 6.59 ; S, 14.96. Found : C, 56.01 ; H, 6.46 ; S, 14.70. (S)-Isomer from baker's yeast : $[\alpha]_D^{25°C}$ = +20.7 ($CHCl_3$, c = 1), ee>95% ; (S)-isomer from *A. niger* : $[\alpha]_J^{25°C}$ = +22 ($CHCl_3$, c = 1), ee>95% ; (R)-isomer from *M. isabellina* : $[\alpha]_J^{25°C}$ = -3.7 ($CHCl_3$, c = 1), ee = 16.6%.

1-(Phenylsulfonyl)-3-pentanol A3

The chromatography eluent was the mixture Et_2O/hexane 50/50. (S)-Isomer was obtained by baker's yeast reduction and (R)-isomer *via M. isabellina*. ^1H NMR δ 0.92 (t, J = 6.7 Hz, 3H, H-5), 1.37-1.57 (m, $J_{H-4\ H-3}$ = 4.0 Hz, 2H, H-4), 1.61-1.86 (m, J = 14.0, 9.1, 4.8, 2.7 Hz, 2H, H-2, OH), 1.86-2.10 (m, J = 8.9, 6.6, 5.7 Hz, 1H, H-2'), 3.10-3.45 (m, J = 13.4, 9.1, 8.9, 5.7, 4.8 Hz, 2H, H-1), 3.62 (dtd, J = 6.6, 4.0, 2.7 Hz, 1H, H-3), 7.50-8.00 (m, 5H, Ph) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 246 (M+18, 100), 229 (M+1, 61) ; Anal. Calcd for $C_{11}H_{16}O_3S$: C, 57.87 ; H, 7.06 ; S, 14.04. Found : C, 57.46 ; H, 7.00 ; S, 13.87. (S)-Isomer : $[\alpha]_D^{25°C}$ = +16 ($CHCl_3$, c = 1), ee = 64% ; (R)-isomer : $[\alpha]_J^{25°C}$ = -13 ($CHCl_3$, c = 0.6), ee = 46%.

(+)-(3S)-(tert-Butyldimethylsiloxy)-1-(phenylsulfonyl)-pentane 4

Dimethyl-tert-butyl-chlorosilane (5.42 g, 36 mmol) and imidazole (3.40 g, 50 mmol) were added to a solution of hydroxysulfone (S)-**A3** (4.56 g, 20 mmol) in dry DMF (25 mL). This mixture was stirred overnight at room temperature and then water (60 mL) was added. Extraction with Et_2O (5 x 80 mL), drying of the combined organic phases (Na_2SO_4) and evaporation gave an oil. The crude product was purified by removing DMF under reduced pressure (0.1 Tor) followed by column chromatography on silica gel (Et_2O/hexane 50/50). Compound **4** was obtained as an oil (6.84 g, 90%). ^1H NMR ($CDCl_3$, 250 MHz) δ -0.06 (s, 3H), 0.00 (s, 3H), 0.75-0.90 (m, 12H, tBu, H-5), 1.35-1.55 (m, 2H, H-2), 1.65-1.97 (m, 2H, H-4), 3.17 (t, J = 8.0 Hz, 2H, H-1), 3.67 (tt, J = 5.7 Hz (H-3 H-4), 4.9 Hz (H-3 H-2), 1H, H-3), 7.50-8.00 (m, 5H, Ph) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 360 (M+18, 4), 343 (M+1, 100), 285 (M-57, 27), $[\alpha]_D^{25°C}$ = +15.9 ($CHCl_3$, c = 1.27).

Methyl(2S,4S)-(tert-butyldimethylsilyloxy)-2-(phenylsulfonyl)-hexanoate and methyl (2R,4S)-(tert-butyldimethylsilyloxy)-2-(phenylsulfonyl)hexanoate diastereomeric mixture 5

Butyllithium (3.6 mL of 0.1 M solution in hexane, 3.6 mmol) was added at -78°C under argon and with stirring to a solution of **4** (1.026 g, 3 mmol) in THF (6 mL). The reaction mixture was allowed to warm up to 0°C, stirred 1 h at 0°C and cooled again to -78°C. HMPA (525 µL,

3 mmol) and methyl cyanoformate (265 µL, 3.3 mmol) were added at this temperature. The reaction mixture was allowed to warm up slowly to room temperature and stand at this temperature overnight. Hydrolysis with water (10 mL), extraction of the aqueous phase with Et_2O (3 x 20 mL), drying of the combined organic phases (Na_2SO_4), evaporation and column chromatography on silica gel (Et_2O/hexane 25/75) led to **5** as an oil (0.528 g, 44%). ^1H NMR (mixture of diastereomers) ($CDCl_3$, 250 MHz) δ -0.1-0.1 (m, 6H), 0.70-0.95 (m, 12H, tBu, H-6), 1.15-1.70 (m, 2H, H-5), 2.00-2.35 (m, 2H, H-3), 3.50-3.68 (m, 3.5 H, $CO_2\underline{Me}$, 0.5 H-4), 3.68-3.80 (m, 0.5H, 0.5 H-4), 4.14 (dd, J = 8.5, 3.6 Hz, 0.5H, 0.5 H-2), 4.21 (dd, J = 10.4, 2.4 Hz, 0.5H, 0.5 H-2), 7.50-8.00 (m, 5H, Ph) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 418 (M+18, 100), 401 (M+1, 67), 343 (M-57, 23) ; Anal. Calcd for $C_{19}H_{32}O_5SSi$: C,56.97 ; H, 8.05 ; S, 8.00. Found : C, 57.24 ; H, 7.95 ; S, 7.97.

(2S,5S)-5-Ethyl-3-(phenylsulfonyl)-tetrahydro-2-furanone and (2R,5S)-5-ethyl-3-(phenylsulfonyl)-tetrahydro-2-furanone diastereomeric mixture 6

Tetrabutylammonium fluoride (2.3 mL of solution 1M in THF, 2.3 mmol) was added to compound **5** (0.440 g, 1.1 mmol) dissolved in THF (5 mL) at 0°C. The reaction mixture was then stirred at room temperature until **5** disappeared, as verified by TLC monitoring. Evaporation of THF, stirring with Et_2O (10 mL), washing of the organic phase with brine (3 mL), drying (Na_2SO_4) and evaporation led to the crude product **6** which was purified by column chromatography on silica gel (Et_2O/hexane 40/60) (0.182 g, 65%). ^1H NMR (mixture of diastereomers) ($CDCl_3$, 250 MHz) δ 0.95-1.10 (m, 3H, $C\underline{H}_3$-CH_2), 1.50-2.00 (m, 2H, CH_3-$C\underline{H}_2$), 2.20-2.40 (m, J = 14.6, 8.8, 2.9 Hz, 0.6 H, H-4 (trans is.)), 2.48-2.65 (m, 0.4 H, H-4 (cis is.)), 2.76-2.88 (m, 0.4H, H-4' (cis is.)), 3.05-3.20 (m, J = 14.6, 10.0, 6.6 Hz, 0.6 H, H-4' (trans is.)), 4.07 (dd, J = 10.0, 2.9 Hz, 0.6H, H-3 (trans is.)), 4.25 (t, J = 9.8 Hz, 0.4H, H-3 (cis is.)), 4.32-4.48 (m, 0.4H, H-5 (cis is.)), 4.64 (m, 0.6H, H-5 (trans is.)), 7.50-8.00 (m, 5H, Ph) ; MS (chem. ioniz., NH_3) m/e (rel. int.) 272 (M+18, 100) ; Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68 ; H, 5.55 ; S, 12.61. Found : C, 56.75 ; H, 5.47 ; S, 12.42.

(5S)-(-)-5-Ethyl-tetrahydro-2-furanone 7

Aluminium amalgam[16] (600 mg) was added to a solution of compound **6** (0.100 g, 0.39 mmol) in the mixture THF/H_2O 90/10 (20 mL). Reaction mixture was heated to reflux for 1 h. Cooling, filtration, washing (CH_2Cl_2, 20 mL), drying (Na_2SO_4), evaporation and column chromatography on silica gel (eluent : Et_2O/hexane 50/50) led to compound **7**[12] (33.3 mg, 75%) : ^1H NMR ($CDCl_3$, 250 MHz) δ 0.96 (t, J = 7.3 Hz, 3H, $C\underline{H}_3$-CH_2), 1.50-1.95 (m, 3H, CH_3-$C\underline{H}_2$, H-4), 2.20-2.40 (m, 1H, H-4'), 2.44-2.68 (m, 2H, H-3), 4.41 (m, 1H, H-5). $[\alpha]_D^{25°C}$ = -25.3 (THF, c = 1.5), ee = 64%.

(S)-(+)-5-Methyl-2(5H)-furanone ((S)-(+)-β-angelica lactone) 11 A

Baker's yeast (68 g) was stirred for 0.5 h at 37°C with water (200 mL) and sucrose (68 g). Compound **8** (3.22 g, 11.3 mmol) was added and the reaction mixture was stirred at room temperature under anaerobic conditions. the reaction was allowed to proceed for 192 h and several additions (~ 10) of 20 g of sucrose were necessary to maintain CO_2 release. The crude product was obtained as it is indicated in the general method. It was dissolved in cyclohexane (50 mL), p-TsOH was added (~ 10 mg) and the mixture refluxed for 1 h. Cooling, several washings of the organic solution with water until neutralization, drying (Na_2SO_4), evaporation and column chromatography on silica gel (eluent : Et_2O/hexane 75/25) led to 958 mg of the starting material **8** (30%), 698 mg of (4S,5S)-5-ethyl-4-(phenylsulfonyl)- tetrahydro-2-furanone **10 A**[8a] (25.5%) and 382 mg of (4R,5S)-5-methyl-4-(phenylsulfonyl)-tetrahydro-2-furanone **10 B**[8a] (14%). ^1H NMR showed that the

microbiological reduction led directly to ~ 2% of β-angelica lactone **11** which was not isolated. ^{1}H NMR of **10A** ($CDCl_3$, 250 MHz) δ 1.77 (d, J = 6.8 Hz, 3H, CH_3), 2.60 (dd, J = 17.7, 8.7 Hz, 1H, H-3), 3.04 (dd, J = 17.7, 8.9 Hz, 1H, H-3'), 4.03 (m, J = 8.9, 8.7, 7.3 Hz, 1H, H-4), 5.01 (d, J = 7.3, 6.8 Hz, 1H, H-5), 7.50-8.00 (m, 5H, Ph) ; MS of **10A** (chem. ioniz., NH_3) m/e (rel. int.) 258 (M+18, 100) ; $[\alpha]_D^{25°C}$ of **10A** : +16.2 ($CHCl_3$, c = 1). ^{1}H NMR of **10B** ($CDCl_3$, 250 MHz) δ 1.43 (d, J = 6.3 Hz, 3H, CH_3), 2.78 (dd, J = 18.3, 9.5 Hz, 1H, H-3), 3.04 (dd, J = 18.3, 7.7 Hz, 1H, H-3'), 3.64 (m, J = 9.5, 7.7, 6.1 Hz, 1H, H-4), 5.00 (m, J = 6.3, 6.1 Hz, 1H, H-5), 7.55-8.00 (m, 5H, Ph) ; MS of **10B** (chem. ioniz., NH_3) m/e (rel. int.) 258 (M+18, 100), 241 (M+1, 57) ; $[\alpha]_D^{25°C}$ of **10B** : -30.9 ($CHCl_3$, c = 1). Anal. calcd for $C_{11}H_{12}O_4S$ (mixture of **10A** and **10B** : C, 54.99 ; H, 5.03 ; S, 13.34. Found : C, 54.74 ; H, 4.87, S, 13.39. A solution of lactone **10A** or **10B** (96 mg, 0.4 mmol) in CH_2Cl_2 (5 mL) was prepared and then DBU (60 µL, 0.4 mmol) was added with stirring, at room temperature. The reaction was allowed to proceed for 15 min and then 10% aqueous HCl (3 mL) was added. Extraction (CH_2Cl_2, 5 mL), drying of the combined organic phases (Na_2SO_4), evaporation and column chromatography on silica gel (eluent Et_2O/hexane 50/50) led to lactone **11A**[8] (30 mg, 75% from **10A** ; 32 mg, 80% from **10B**). ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.44 (d, J = 6.9 Hz, 3H, CH_3), 5.12 (m, 1H, H-5), 6.07 (dd, J = 5.5, 1.8 Hz, 1H, H-3), 7.41 (dd, J = 5.5, 1.9Hz, 1H, H-4) ; $[\alpha]_D^{25°C}$ = +105.6 ($CHCl_3$, c = 1) from **10A** and +96.8 ($CHCl_3$, c = 1) from **10B**.

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