Experimental part

1 Generalities

1.1 Apparatus

- Infrared spectra were recorded on a Bio-Rad FTS-135 spectrometer.
- ^{1}H NMR spectra were recorded at 200 or 300 MHz on a Varian Gemini 200, VXR 200 or Gemini 300BB in a deuterated solvent with tetramethylsilane (TMS) as internal standard. Chemical shifts are given in ppm; coupling constants are given in Hz.
- ^{13}C NMR spectra were recorded at 50 or 75 MHz on a Varian Gemini 200, VXR 200 or Gemini 300 in a deuterated solvent used as internal standard ($CDCl_3$: 77 ppm; MeOD-d_4: 49 ppm; DMSO-d_6: 39.5 ppm).
- ^{19}F NMR spectra were recorded at 288.5 MHz on a Varian Gemini 300 spectrometer with hexafluorobenzene as internal standard (-163 ppm).
- Mass spectra were recorded on a Varian MAT-44 or a FINNIGAN MAT TSQ 70 spectrometer in the laboratory of Professor de Hoffmann and Professor Habib-Jiwan.
- High resolution mass spectra (HRMS) were performed by Professor Flammang at Université de Mons-Hainaut.
- Elemental analyses were realized in the laboratory of Dr Stone at University College, London
- GC analyses were performed on a CE Instruments GC 8000^{Top} with a Merck-Hitachi D-2500 Chromato Integrator on a Cp-Sil 8 CB WCOT Fused Silica (30 m x 0.25 mm – 0.25 µm) column; chiral GC analyses were done on a CE Instruments HRGC 5300 with a Merck-Hitachi D-2500 Chromato Integrator or a Thermo Finnigan Trace GC with a Thermo Finnigan ChromCard program on a Chirasil Dex (25 m x 0.25 mm – 0.25 µm) column. Temperature programs are given as follows: (initial temperature (°C) / initial time (min) / ramp (°C/min) / final temperature (°C) / final time (min)) or (initial temperature (°C) / initial time (min) / ramp (°C/min) / intermediate temperature (°C) / ramp (°C/min) / final temperature (°C) / final time (min)).
- Optical rotations were measured on a Perkin-Elmer 241 MC Polarimeter. Concentrations are given in g/100 ml.

- Melting points were measured with a Büchi apparatus (oil bath) and are uncorrected.
- Bulb-to-bulb distillations were performed with a Büchi GKR 50 or GKR 51.

1.2 Techniques

- All reactions were realized under argon atmosphere unless otherwise stated.
- Phase-transfer reactions were performed with an Electrothermal Reacto-Station RS1000.
- For reactions at 0°C, flasks were placed in an ice bath; for reactions at -78°C, flasks were placed in a dry-ice / *iso*-propanol bath; intermediate temperatures were realized by adding the desired quantity of dry-ice to *iso*-propanol; for longer reaction times flasks were placed in an *iso*-propanol bath cooled by a Haake EK90 cryostat.
- Evaporation of solvents was performed at ±35°C with a rotary evaporator connected to a water pump (~16 mmHg) unless otherwise stated.
- Flash chromatographies were performed on silica gel "60 Merck 40-63 µm". Solvents used were of technical grade and distilled prior to use. R_f values were determined on silicagel plates Merck 60 F_{254} on aluminum support. Spots were visualized using UV light (λ = 254 mm) or revealed using an aqueous potassium permanganate solution.
- *n*-butyllithium in hexanes was titrated in dry THF using 2,5-dimethoxybenzylic alcohol or diphenylacetic acid.
- CH_2Cl_2 and benzene were dried over CaH_2 and distilled.
- THF, diethyl ether and toluene were dried over Na / benzophenone and distilled.
- Ethanol was dried over mg with a trace of iodine and distilled.
- DMSO was distilled and stored over activated molecular sieves 4Å.
- Hexamethylphosphoramide was dried over CaH_2 and distilled.
- Triethylamine was dried over CaH_2 and distilled.
- Enones, sulfonyl chlorides were distilled prior to use.
- Copper(II) triflate, zinc(II) chloride, and, when specified, potassium fluoride were dried by heating overnight at 150°C under reduced pressure.

1.3 Abbreviations and symbols

1.3.1 Reagents and solvents

AcOEt	ethyl acetate
CH_2Cl_2	dichloromethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
Et_3N	triethylamine
Et_2O	diethyl ether
EtOH	ethanol
HMPA	hexamethylphosphoramide
MeOH	methanol
n-BuLi	*n*-butyllithium
THF	tetrahydrofuran
TBDMSCl	*tert*-butyldimethylsilyl chloride
TIPSCl	tri-*iso*-propylsilyl chloride
TMS	tetramethylsilane
TMSCl	trimethylsilyl chloride

1.3.2 Abbreviations

APCI	atmospheric pressure chemical ionization
CI	chemical ionization
b.p.	boiling point
d	doublet
Δ	heating at reflux
EI	electronic impact
eq.	equivalents
Et	ethyl
FAB	fast atom bombardment
GC	capillary gas chromatography
IR	infrared
m	massif
Me	methyl
M.F.	molecular formula
m.p.	melting point
mult	multiplet
M.W.	molecular weight

NMR	nuclear magnetic resonance
Ph	phenyl
q	quartet
R_f	ratio of fronts
RT	room temperature
s	singlet
sext	sextet
TLC	thin layer chromatography
t_R	retention time

2 Synthesis of 27

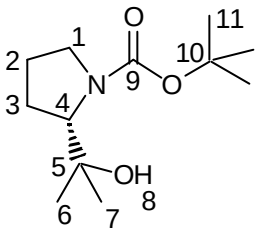
2.1 Synthesis of 2-(1-hydroxy-1-methylethyl)pyrrolidine-1-carboxylic acid *tert*-butyl ester 31

M.F.: $C_{12}H_{23}NO_3$ (**M.W.** 229.31) **RN: 155728-50-0**

Reference: Kanth, J.V.B.; Periasamy, M. *Tetrahedron*, **1993**, *49*, 5127-5132.

In a flame-dried three-necked flask equipped with an addition funnel, a reflux condenser and a mechanical stirrer, 62 g (270.4 mmol; 1eq.) of 1,1-dimethylethyl (2*S*)-2-(1-hydroxy-1-methylethyl)pyrrolidine-1-carboxylate **224** were dissolved in 314 ml of dry Et_2O. The mixture was cooled to 0°C and 213 ml (220.7 g; 676 mmol; 2.5 eq.) of methylmagnesium bromide, 3.0M in diethyl ether, were slowly added. After the addition was complete, the mixture was stirred for 3 hours. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The 2 phases were separated and the aqueous phase was extracted 2 times with Et_2O. The organic phase was washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was obtained as a white solid and was pure enough to be used without any further purification.

Yield: 59.36 g (96 %)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.07 and 1.16 (*2 s*, 6 H, 6, 7); 1.48 (*s*, 9 H, 11); 1.6-2.15 (*m*, 4 H, 2, 3); 3.16 (*m*, 1 H, 1); 3.7 (*m*, 1 H, 4); 3.87 (*m*, 1 H, 1); 5.92 (*broad s*, 1 H, 8)
^{13}C NMR ($CDCl_3$, 50 MHz): 23.9 and 28.8 (2, 3); 27.4 and 27.9 (6, 7); 28.1 (11); 28.8 (3); 48.0 (1); 67.0 (4); 73.3 (5); 80.0 (10); 152.3 (9)
IR (solid deposit, cm^{-1}): 1171; 1401; 1666 (C=O); 2975 (C-H); 3370 (O-H)
Mass (CI +Q1MS): 130 ($[M-(COO-t-Bu)]^+$, 21%); 156 ($[M-(O-t-Bu)]^+$, 38%); 174 (100%); 230 ($[M+H]^+$, 18%)
GC (100/0/10/290/15): t_R = 10.93 min

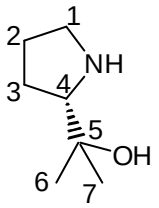
2.2 Synthesis of 2-[(2*S*)-pyrrolidin-2-yl]propan-2-ol 30

M.F.: $C_7H_{15}NO$ (**M.W.** 129.2) **RN: 92053-25-3**

Reference: Kanth, J. V. B.; Periasamy, M. *Tetrahedron* **1993**, *49*, 5127-5132.

In a flask equipped with a reflux condenser, 72.59 g (1.815 mol; 7.01 eq.) of sodium hydroxide were dissolved in 294 ml of MeOH. 59.36 g (258.8 mmol; 1 eq.) of (2*S*)-2-(1-hydroxy-1-methylethyl)pyrrolidine-1-carboxylic acid *tert*-butyl ester **31** were slowly added. The mixture was then refluxed for 24 hours. After being cooled to room temperature, the solvent was evaporated. The residue was dissolved in ether and filtered. After evaporation of the solvent, a small quantity of a saturated solution of NH_4Cl was added. The aqueous phase was extracted with a large quantity of $CHCl_3$. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 32.89 g (98 %)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.12 and 1.16 (*2 s*, 6 H, 6, 7); 1.58-1.77 (*m*, 4 H, 2, 3); 2.81-3.05 (*m*, 3 H, 1, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 25.6 and 26 (6, 7); 26.1 and 26.5 (2, 3); 46.8 (1); 67.2 (4); 70.2 (5)
IR (liquid film, cm^{-1}): 1157, 1377; 2971 (C-H); 3346 (O-H)
GC (100/0/10/290/20): t_R = 7.41 min

2.3 Synthesis of 2-(1-hydroxy-1-methylethyl)pyrrolidine-1-carbaldehyde 33

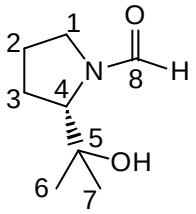
M.F.: $C_8H_{15}NO_2$ (**M.W.** 157.21) **RN: 129149-57-1**

Reference: Nakayama, K.; Thompson, W.J. *J. Am. Chem. Soc.*, **1990**, *112*, 6936-6942.

In a flame-dried flask 32.89 g (254.5 mmol; 1 eq.) of 2-pyrrolidin-2-yl-propan-2-ol **30** were dissolved in 82.22 ml (75.4 g; 1.017 mol; 3.99 eq.) of ethyl formate. The mixture

was stirred for 2 days. The volatile compounds were evaporated to obtain a viscous oil. The product was purified by bulb-to-bulb distillation under reduced pressure (125°C at $6 \cdot 10^{-3}$ mbar).

Yield: 20 g (51 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.09, 1.15, 1.18 and 1.23 (*4 s*, 6 H, 6, 7); 1.51-2.22 (*m*, 4 H, 2, 3); 3.29-3.40 (*m*, 1 H, 1); 3.65-3.81 (*m*, 2 H, 1, 4); 8.30 and 8.40 (*2 s*, 1 H, 8)
^{13}C NMR ($CDCl_3$, 75 MHz): 22.4, 23.0, 26.4 and 26.5 (6, 7); 22.9, 23.0, 26.8 and 28.4 (2, 3); 44.1 and 48.8 (1); 66.1 and 67.1 (4); 72.5 (5); 163.2 and 163.5 (8)
IR (liquid film, cm^{-1}): 1651 (C=O); 2975 (C-H); 3384 (O-H)
b.p.: 125°C at $6 \cdot 10^{-3}$ mbar

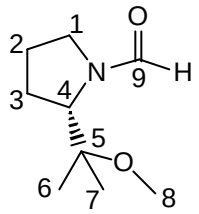
2.4 Synthesis of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine-1-carbaldehyde 34

M.F.: $C_9H_{17}NO_2$ (**M.W.** 171.23) **RN: 129173-93-9**

Reference: Nakayama, K.; Thompson, W.J. *J. Am. Chem. Soc.*, **1990**, *112*, 6936-6942.

In a flame-dried three-necked flask equipped with a reflux condenser, an addition funnel and a magnetical stirrer, 6.743 g (168.6 mmol; 1.3 eq.) of sodium hydride were put into suspension in 210 ml of dry THF. 20.39 g (129.6 mmol; 1 eq.) of 2-(1-hydroxy-1-methylethyl)pyrrolidine-1-carbaldehyde **33** in solution in 12 ml of THF were slowly added *via* the addition funnel. The mixture was stirred for 15 minutes. 18.59 ml (24.78 g; 194.5 mmol; 1.5 eq.) of dimethyl sulfate were then added through the addition funnel. Stirring was maintained for 20 hours. The mixture was then cooled to 0°C and 10 ml of water were slowly added. Solvents were evaporated and water was added to the residue. The aqueous phase was extracted 5 times with CH_2Cl_2. The organic phase was washed with water, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 28.84 g of crude product.



^{1}H NMR ($CDCl_3$, 300 MHz): 1.07, 1.13, 1.15 and 1.18 (*4 s*, 6 H, 6, 7); 1.60-2.21 (*m*, 4 H, 2, 3); 3.15-3.30 (*m*, 1 H, 1); 3.20 (*s*, 3 H, 8); 3.70-4.20 (*m*, 2 H, 1, 4); 8.30 and 8.35 (*2 s*, 1 H, 9)
^{13}C NMR ($CDCl_3$, 50 MHz): 18.5 and 21.0 (6, 7); 24.0 and 27.0 (2, 3); 44.0 (1); 48.5 (8); 64.5 (4); 77.5 (5); 163.5 (9)

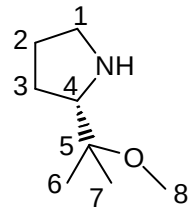
2.5 Synthesis of (2*S*)-(-)-2-(1-methoxy-1-methylethyl)pyrrolidine 27

M.F.: $C_8H_{17}NO$ (**M.W.** 143.22) **RN: 118971-00-9**

Reference: Kanth, J.V.B.; Periasamy, M. *Tetrahedron*, **1993**, *49*, 5127-5132.

In a flask equipped with a reflux condenser were put 297 ml of a 10% KOH solution. 22.2 g (129.6 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine-1-carboxaldehyde **34** were then slowly added. The mixture was refluxed for 90 minutes. Once cooled to room temperature, it was extracted 5 times with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (120°C at 15 mmHg).

Yield: 14.1 g (76 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.14 and 1.18 (*2 s*, 6 H, 6, 7); 1.66-1.75 (*m*, 4 H, 2, 3); 2.81-2.85 (*m*, 1 H, 1); 2.97-3.05 (*m*, 2 H, 1, 4); 3.22 (*s*, 3 H, 8)
^{13}C NMR ($CDCl_3$, 75 MHz): 21.3 and 21.9 (6, 7); 25.8 and 26.4 (2, 3); 47.0 (1); 49.1 (8); 66.9 (4); 76.1 (5)
IR (liquid film, cm^{-1}): 2827 (O-CH_3); 2970 (C-H); 3347 (N-H)
Mass (CI/CH_4-N_2O): 70 ($[C_4H_8N]^+$, 34%); 112 ($[M\text{-}OMe]^+$, 100%); 144 ($[M+H]^+$, 20%)
[a]$^{D}_{20}$: -24.0° (c=0.876; $CHCl_3$) [lit.: -24.5° (c=2.36; CH_3OH)]
b.p.: 120°C at 15 mmHg

3 Synthesis of sulfonyl chlorides

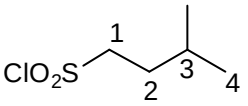
3.1 Synthesis of 3-methyl-1-butanesulfonyl chloride 35

M.F.: $C_5H_{11}ClO_2S$ (**M.W.** 170.65) **RN: 22795-37-5**

In a three-necked flask equipped with a magnetical stirrer, a thermometer, a gas inlet and a gas outlet, 1 g (1.197 ml; 9.595 mmol; 1 eq.) of 3-methylbutane-1-thiol was put into suspension in 30 ml of water. The flask was placed in an ice-bath and chlorine was then bubbled through the mixture. The temperature was kept below 10°C. When the mixture was yellowish green, the reaction was stopped. The aqueous phase was extracted with Et_2O. The organic phase was washed with a saturated solution of $NaHSO_3$ and a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was obtained sufficiently pure to be used without purification.

Yield: 1.534 g (94%)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.90 (*d*, $^3J_{4\text{-}3}$ = 6.5, 6 H, 4); 1.90 (*mult*, 1 H, 3); 1.89-1.98 (*m*, 2 H, 2); 3.66 (*mult*, 2 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 21.8 (4); 26.8 (3); 32.6 (2); 64.1 (1)
IR (liquid film, cm^{-1}): 1166 (O=S=O); 1373 (O=S=O); 2962 (C-H)
Mass (EI +Q1MS): 43 ($[(CH_3)_2CH]^+$, 100%); 55 ($[(CH_3)_2CHCH_2]^+$, 45%); 70 ($[M\text{-}SO_2Cl]^+$, 87%); 169 ($[M\text{-}H]^+$, 2%)

3.2 Synthesis of 6-chloro-1-hexanesulfonyl chloride 37

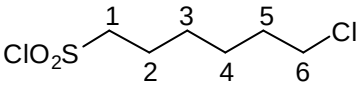
M.F.: $C_6H_{12}Cl_2O_2S$ (**M.W.** 219.12) **RN: 1633-80-3**

In a three-necked flask equipped with a magnetical stirrer, a thermometer, a gas inlet and a gas outlet, 1 g (7.449 mmol; 1 eq.) of 6-mercapto-1-hexanol was put into suspension in 9.4 ml of water. The flask was placed in an ice-bath and chlorine was then bubbled through the mixture. The temperature was kept below 10°C. When the mixture was yellowish green the reaction was stopped. The aqueous phase was

extracted with Et_2O. The organic phase was washed with a saturated solution of $NaHSO_3$ and a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was obtained sufficiently pure to be used without purification. It could be purified by bulb-to-bulb distillation (125°C at $6{\cdot}10^{-2}$ mbar) but it degradated upon heating.

Yield: 1.258 g (77%)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.44-1.65 (m, 4 H, 3, 4); 1.74-1.86 (m, 2 H, 5); 2.01-2.16 (m, 2 H, 2); 3.55 (t, $^3J_{6\text{-}5}$ = 6.3, 2 H, 6); 3.68 (mult, 2 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 24.2 (2); 26.2 (4); 27.4 (3); 32.1 (5); 44.5 (6); 65.4 (1)
IR (liquid film, cm^{-1}): 1165 (O=S=O); 1373 (O=S=O); 2864; 2940 (C-H)
Mass (CI/CH_4-N_2O): 83 (100%); 119 ($[M\text{-}SO_2Cl]^+$ (^{35}Cl), 18%); 121 ($[M\text{-}SO_2Cl]^+$ (^{37}Cl), 6%); 183 ($[M\text{-}Cl]^+$ (^{35}Cl), 23%); 185 ($[M\text{-}Cl]^+$ (^{37}Cl), 9%); 219 ($[M+H]^+$ (2 x ^{35}Cl), 31%); 221 ($[M+H]^+$ (^{35}Cl + ^{37}Cl), 22%); 223 ($[M+H]^+$ (2 x ^{37}Cl), 5%)
b.p.: 125°C at $6{\cdot}10^{-3}$ mbar

4 Synthesis of sulfonamides

4.1 General procedure

In a flame-dried two-necked flask equipped with a magnetical stirrer, 1 eq. of amine and 1 eq. of Et_3N were dissolved in Et_2O or CH_2Cl_2. The solution was stirred and 1 eq. of sulfonyl chloride was slowly added. The stirring was maintained for 4 hours. After that time the reaction mixture was filtered and the solvent evaporated.
The product was purified by flash chromatography.

4.2 Synthesis of sulfonamides containing no other function

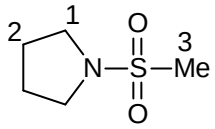
*4.2.1 Synthesis of 1-methylsulfonylpyrrolidine **11***

M.F.: $C_5H_{11}NO_2S$ (**M.W.** 149.2) **RN: 51599-68-9**

Following the general procedure described in 4.1 with:

2.8 ml (33.51 mmol, 1 eq.) of pyrrolidine
4.66 ml (33.51 mmol, 1 eq.) of Et_3N
2.59 ml (33.51 mmol, 1 eq.) of methanesulfonyl chloride
34 ml of ether
Flash chromatography: CH_2Cl_2 100 %

Yield: 2.2 g (44%)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.95 (*m*, 4 H, 2); 2.82 (*s*, 3 H, 3); 3.33 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 25.1 (2); 33.5 (3); 47.3 (1)
IR (liquid film, cm^{-1}): 1147 (NSO_2); 1328 (NSO_2); 2984 (C-H)
Mass (CI/CH_4-N_2O): 150 ($[M+H]^+$, 100%)
m.p.: 69-70°C

*4.2.2 Synthesis of (2S)-1-methylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **14***

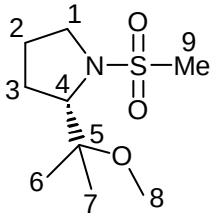
M.F.: $C_9H_{19}NO_3S$ (**M.W.** 221.31)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

Following the general procedure described in 4.1 with:
5.978 g (41.7 mmol, 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27**
5.8 ml (41.7 mmol, 1 eq.) of Et_3N
3.23 ml (41.7 mmol, 1 eq.) methanesulfonyl chloride
60 ml of Et_2O
Flash chromatography (ether : petroleum ether 90 : 10).

Yield*:* 8.159 g (88 %)

Aspect: colorless oil
TLC: R_f = 0.36 (ether : petroleum ether 90 : 10)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.16 and 1.19 (2 *s*, 6 H, 6, 7); 1.71-2.93 (*m*, 4 H, 2, 3); 2.91 (*s*, 3 H, 9); 3.09-3.28 (*m*, 1 H, 1); 3.18 (*s*, 3 H, 8); 3.67-3.81 (*m*, 1 H, 1); 3.91-4.01 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 21.5 (6, 7); 25.7 and 26.8 (2, 3); 38.4 (9); 49.2 (8); 49.6 (1); 66.5 (4); 77.7 (5)
IR (liquid film, cm^{-1}): 1151 (NSO_2); 1332 (NSO_2); 2831 (O-CH_3); 2979 (C-H)
Mass (CI/CH_4-N_2O): 190 ($[M\text{-}OMe]^+$, 100); 222 ($[M+H]^+$, 5%)
$[\alpha]_{20}^{D}$: -32.5° (c=0.553; $CHCl_3$) [lit.: -31.4° (c=1.65; $CHCl_3$)]

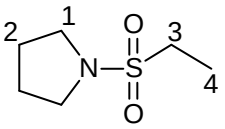
*4.2.3 Synthesis of 1-ethylsulfonylpyrrolidine **38***

M.F.: $C_6H_{13}NO_2S$ (**M.W.** 163.23) **RN: 73343-03-0**

Following the general procedure described in 4.1 with:
2 ml (1.704 g; 23.95 mmol; 1 eq.) of pyrrolidine
3.33 ml (2.424 g; 23.95 mmol; 1 eq.) of Et_3N
2.27 ml (3.08 g; 23.95 mmol; 1 eq.) of ethanesulfonyl chloride
34.31 ml of ether
Flash chromatography: ether : petroleum ether 80 : 20

Yield: 3.55 g (91 %)

Aspect: colorless oil
TLC: R_f = 0.6 (ether : petroleum ether 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.38 (*t*, $^3J_{4\text{-}3}$ = 7, 3 H, 4); 1.90-2.00 (*m*, 4 H, 1); 3.01 (*q*, $^3J_{3\text{-}4}$ = 7.3, 2 H, 3); 3.30-3.40 (*m*, 4 H, 2)
^{13}C NMR ($CDCl_3$, 50 MHz): 7.4 (4); 25.3 (2); 43.5 (1); 47.2 (3)
IR (liquid film, cm^{-1}): 1148 (NSO_2); 1328 (NSO_2); 2960 (C-H)
Mass (CI/CH_4-N_2O): 70 ($[C_4H_8N]^+$, 32%); 162 (36%); 164 ($[M+H]^+$, 100%); 166 (60%); 327 ($[2M+H]^+$, 26%)

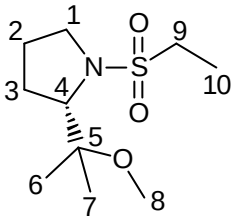
*4.2.4 Synthesis of (2S)-1-ethylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **43***

M.F.: $C_{10}H_{21}NO_3S$ (**M.W.** 235.34)

Following the general procedure described in 4.1 with:
2.073 g (14.473 mmol, 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27**
2 ml (14.473 mmol, 1 eq.) of Et_3N
1.37 ml (14.473 mmol, 1 eq.) of ethanesulfonyl chloride
21 ml of Et_2O
Flash chromatography: ether : petroleum ether 90 : 10

Yield: 3.073 g (90 %)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.14 and 1.17 (*s*, 6 H, 6, 7); 1.37 (*t*, $^3J_{10\text{-}9}$ = 3.3, 3 H, 10); 1.70-2.10 (*m*, 4 H, 2, 3); 3.02-3.19 (*m*, 1 H, 1); 3.14 (*mult*, 2 H, 9); 3.21 (*s*, 3 H, 8); 3.78-3.82 (*m*, 1 H, 1); 4.08-4.13 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 9.2 (10); 21.3 and 21.5 (6, 7); 26.2 and 27.3 (2, 3); 46.5 (9); 49.2 (8); 50.1 (1); 65.9 (4); 77.7 (5)
IR (liquid film, cm^{-1}): 1330 (NSO_2); 1460 (NSO_2); 2831 (O-CH_3); 2979 (C-H)
Mass (CI/CH_4-N_2O): 204 ($[M\text{-}OMe]^+$, 100%); 236 ($[M+H]^+$, 1.5%)
$[\alpha]_{20}^{D}$: -39.8° (c=0.176; $CHCl_3$)

Elemental analysis:
calculated (%): C: 51.04; H: 8.99; N: 5.95; S: 13.62
found (%): C: 50.48; H: 8.93; N: 5.80; S: 13.94

*4.2.5 Synthesis of 1-[(3-methylbutyl)sulfonyl]pyrrolidine **39***

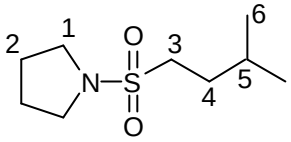
M.F.: $C_9H_{19}NO_2S$ (**M.W.** 205.31)

Following the general procedure described in 4.1 with:
0.75 ml (9 mmol, 1 eq.) of pyrrolidine
1.25 ml (9 mmol, 1 eq.) of Et_3N
1.534 ml (9 mmol, 1 eq.) of 3-methyl-1-butanesulfonyl chloride
20 ml of CH_2Cl_2

Purification by recrystallization in ether

Yield: 1.447 g (78 %)

Aspect: white crystals
TLC: R_f = 0.52 (petroleum ether : AcOEt 2 : 1)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.94 (*d*, $^3J_{6\text{-}5}$ = 6.4, 6 H, 6); 1.60-1.75 (*m*, 3 H, 4, 5); 1.90-2.00 (*m*, 4 H, 2); 2.90-3.00 (*m*, 2 H, 3); 3.30-3.40 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 22.0 (6); 25.8 (2); 27.3 (5); 31.8 (4); 47.6 (1); 48.2 (3)
IR (liquid film, cm^{-1}): 1139 (NSO_2); 1328 (NSO_2); 2875 (C-H)
Mass (EI +Q1MS): 43 ($[CH(CH_3)_2]^+$, 33%); 55 ($[CH_2CH(CH_3)_2]^+$, 15%); 70 ($[N(CH_2)_4]^+$, 100%); 71 ($[CH_2CH_2CH(CH_3)_2]^+$, 94%); 205 ($M^{\bullet+}$, 8%)
Elemental analysis:
calculated (%): C: 52.65; H: 9.32; N: 6.82
found (%): C: 52.29; H: 9.26; N: 6.66

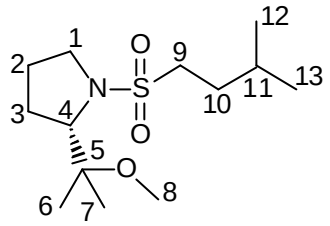
*4.2.6 Synthesis of (2S)-(1-methoxy-1-methylethyl)-1-[(3-methylbutyl) sulfonyl]pyrrolidine **44***

M.F.: $C_{13}H_{27}NO_3S$ (**M.W.** 277.42)

Following the general procedure described in 4.1 with:
1 g (6.981 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27**
970 µl (706 mg; 6.981 mmol; 1 eq.) of Et_3N
1.191 g (6.981 mmol; 1 eq.) of 3-methyl-1-butanesulfonyl chloride
10 ml of Et_2O
Flash chromatography: ether : petroleum ether 80 : 20

Yield: 1.719 g (89 %)

Aspect: colorless oil
TLC: R_f = 0.67 (ether : petroleum ether 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.93 and 0.95 (*d, $^{3}J_{12,13-11}$* = 4.2, 6 H, 12, 13); 1.14 and 1.17 (*2 s*, 6 H, 6, 7); 1.62-2.15 (*m*, 7 H, 2, 3, 10, 11); 3.00-3.20 (*m*, 3 H, 1, 9); 3.21 (*s*, 3 H, 8); 3.77-3.91 (*m*, 1 H, 1); 4.05-4.18 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 75 MHz): 20.9, 21.3, 21.9 and 22.0 (6, 7, 12, 13); 27.1 (11); 26.1 and 27.1 (2, 3); 31.7 (10); 49.0 (8); 49.8 (1); 50.4 (9); 65.9 (4); 77.7 (5)

IR (liquid film, cm^{-1}): 1140 (NSO_2); 1327 (NSO_2); 2958 (C-H)

Mass (EI +Q1MS): 70 ($[N(CH_2)_4]^+$, 30%); 73 ($[C(CH_3)_2OMe]^+$, 100%); 204 ($[M-C(CH_3)_2OMe]^+$, 66%); 246 ($[M-OMe]^+$, 4%)

$[\alpha]_{20}^{D}$: -45.1° (c=0.244; $CHCl_3$)

HRMS: calculated for $C_{13}H_{28}NO_3S^+$: 278.178991; found 278.174233; calculated for $C_{12}H_{24}NO_2S^+$ ($[M-OMe]^+$): 246.152776; found: 246.151716

4.3 Synthesis of orthoesters

*4.3.1 Synthesis of 1-(ethenylsulfonyl)pyrrolidine **40***

M.F.: $C_6H_{11}NO_2S$ (**M.W.** 161.21) **RN: 87975-58-4**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

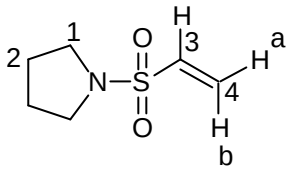
In a flame-dried three-necked flask equipped with a magnetical stirrer, 5.632 ml (4.799 g; 67.47 mmol; 1.1 eq.) of pyrrolidine and 17.1 ml (12.41 g; 122.6 mmol; 2 eq.) of Et_3N were dissolved in 60 ml of CH_2Cl_2. The solution was cooled to 0°C and 6.406 ml (10 g; 61.34 mmol; 1 eq.) of 2-chloro-1-ethanesulfonyl chloride were slowly added. After 45 minutes, the mixture was allowed to come to room temperature. 90 minutes later, 100 ml of water were added. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 25 : 75).

Yield: 6.019 g (61%)

Aspect: slightly yellow oil

TLC: R_f = 0.56 (AcOEt : petroleum ether 75 : 25)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.90 (*m*, 4 H, 2); 3.29 (*m*, 4 H, 1); 6.01 (*d*, $^{3}J_{4a-3}$ = 9.7, 1 H, 4a); 6.26 (*d*, $^{3}J_{4b-3}$ = 16.5, 1 H, 4b); 6.49 (*dd*, $^{3}J_{3-4b}$ = 16.5, $^{3}J_{3-4a}$ = 9.7, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 25.4 (2); 47.6 (1); 127.3 (4); 131.8 (3)
IR (liquid film, cm^{-1}): 1150 (NSO_2); 1344 (NSO_2); 2978 (C-H)
Mass (EI +Q1MS): 70 ([M-($SO_2CH{=}CH_2$)]$^+$, 3%); 134 ([M-($CH{=}CH_2$)]$^+$, 0.4%); 162 ([M+H]$^+$, 100%)

*4.3.2 Synthesis of (2S)-1-ethenylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **45***

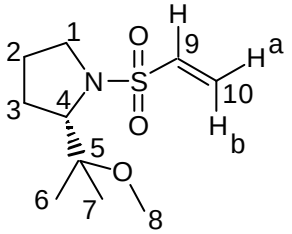
M.F.: $C_{10}H_{19}NO_3S$ (**M.W.** 233.32) **RN: 190510-68-0**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried three-necked flask equipped with a magnetical stirrer, 7.975 g (55.68 mmol; 1.1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27** and 14.11 ml (10.24 g; 101.2 mmol; 2 eq.) of Et_3N were dissolved in 50 ml of CH_2Cl_2. The mixture was cooled to 0°C and 5.286 ml (8.251 g; 50.61 mmol; 1 eq.) of 2-chloro-1-ethanesulfonyl chloride were slowly added. After stirring for 45 minutes at 0°C, the mixture was allowed to come to room temperature. The stirring was continued for 90 minutes. Then 100 ml of water were added. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered et evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 9.43 g (80 %)

Aspect: yellow oil
TLC: R_f = 0.61 (petroleum ether : AcOEt 25 : 75)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.18 and 1.22 (*2 s*, 6 H, 6, 7); 1.70-2.10 (*m*, 4 H, 2, 3); 3.19 (*s*, 3 H, 8); 3.20-3.30 (*m*, 1 H, 1); 3.49-3.59 (*m*, 1 H, 1); 3.75-3.81 (*m*, 1 H, 4); 5.94 (*d*, $^{3}J_{10a\text{-}9}$ = 9.9; 1 H, 10a); 6.24 (*d*, $^{3}J_{10b\text{-}9}$ = 16.5; 1 H, 10b); 6.46 (*dd*, $^{3}J_{9\text{-}10b}$ = 16.4; $^{3}J_{9\text{-}10a}$ = 9.6; 1 H, 9)
^{13}C NMR ($CDCl_3$, 75 MHz): 21.7 and 22.4 (2, 3); 25.4 and 26.4 (6, 7); 49.3 (1); 49.5 (8); 67.4 (4); 77.6 (5); 126.5 (10); 134.1 (9)
IR (liquid film, cm^{-1}): 1151 (NSO_2); 1345 (NSO_2); 1737; 2978 (C-H)
Mass (CI +Q1MS): 73 ($[C(CH_3)_2OMe]^+$, 2%); 202 ($[M\text{-}OMe]^+$, 100%); 234 ($[M+H]^+$, 6%)

*4.3.3 Synthesis of 3-(pyrrolidinosulfonyl)propionitrile **48***

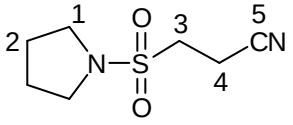
M.F.: $C_7H_{12}N_2O_2S$ (**M.W.** 188.24)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a three-necked flask equipped with a magnetical stirrer and an addition funnel, 2.179 g (13.51 mmol; 1 eq.) of 1-(ethenylsulfonyl)pyrrolidine **40** were dissolved in 53 ml of DMF. In an Erlenmeyer, 1.76 g (27.03 mmol; 2 eq.) of potassium cyanide and 1.084 g (20.27 mmol; 1.5 eq.) of ammonium chloride were dissolved in 7.8 ml of water. This solution was poured into the addition funnel and added slowly to the solution containing the sulfonamide. The reaction mixture was stirred for 65 hours at room temperature. The solvents were then evaporated under high vacuum in an evaporator with cold-trap condenser to obtain a cream-colored solid.
50 ml of water and 50 ml of CH_2Cl_2 were added to the solid. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (AcOEt : ether 50 : 50) and recrystallization from AcOEt / hexane.

Yield: 1.795 g (71 %)

Aspect: white crystals (needles)
TLC: R_f = 0.6 (AcOEt : ether 50 : 50)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.98 (*m*, 4 H, 2); 2.88 (*t*, $^{3}J_{4-3}$ = 7.2, 2 H, 4); 3.26 (*t*, $^{3}J_{3-4}$ = 7, 2 H, 3); 3.41 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 12.8 (4); 25.8 (2); 45.4 (3); 47.8 (1); 116.9 (5)
IR (solid deposit, cm^{-1}): 1140 (NSO_2); 1333 (NSO_2); 2245 (C=N); 2986 (C-H)
Mass (EI +Q1MS): 54 ($[CH_2CH_2CN]^+$, 12.3%); 70 ($[M\text{-}SO_2CH_2CH_2CN]^+$, 100%); 134 ($[M\text{-}(CH_2CH_2CN)]^+$, 21.3%); 187 ($[M\text{-}H]^+$, 21.5%); 188 ($M^{\bullet+}$, 10.5%)
m.p.: 102.5-103°C (lit.: 104°C)
GC (100/0/10/290/20): t_R = 12.22 min

*4.3.4 Synthesis of 3-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]propionitrile **49***

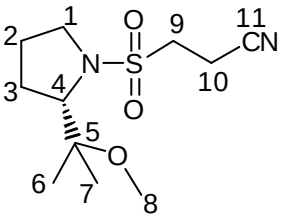
M.F.: $C_{11}H_{20}N_2O_3S$ (**M.W.** 260.35) **RN: 190510-69-1**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a three-necked flask equipped with an addition funnel, 6.77 g (29.01 mmol; 1 eq.) of (2*S*)-1-ethenylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **45** were dissolved in 115 ml of DMF. In an Erlenmeyer, 3.778 g (58.03 mmol; 2 eq.) of potassium cyanide and 2.328 g (43.52 mmol; 1.5 eq.) of ammonium chloride were dissolved in 16.75 ml of water. This solution was transferred into the addition funnel and added slowly to the flask. The mixture was stirred for 16 hours at room temperature. The solvents were evaporated under high vacuum in an evaporator with cold-trap condenser to obtain a cream-colored solid.
50 ml of CH_2Cl_2 and 50 ml of water were added to the solid obtained. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 6.27 g (83 %)

Aspect: white solid
TLC: R_f = 0.41 (petroleum ether : AcOEt 60 : 40); 0.59 (petroleum ether : AcOEt 1 : 2)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.12 and 1.15 (*2 s*, 6 H, 6, 7); 1.65-2.12 (*m*, 4 H, 2, 3); 2.87 (*t*, $^{3}J_{10\text{-}9}$ = 7.6, 2 H, 10); 3.02-3.18 (*m*, 1 H, 1); 3.23 (*s*, 3 H, 8); 3.42 (*ddd*, $^{2}J_{9\text{-}9'}$ = 13.8; $^{3}J_{9\text{-}10}$ = 7.3; $^{3}J_{9\text{-}10}$ = 7.2, 1 H, 9); 3.61 (*ddd*, $^{2}J_{9\text{-}9'}$ = 13.7; $^{3}J_{9\text{-}10}$ = 7.8; $^{3}J_{9\text{-}10}$ = 7.8; 1 H, 9); 3.89-4.01 (*m*, 1 H, 1); 4.11-4.21 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 12.8 (10); 20.0 and 21.6 (6, 7); 26.5 and 28.1 (2, 3); 48.2 (1); 49.15 (8); 50.3 (9); 66.9 (4); 78.2 (5); 117.0 (11)
Mass (EI +Q1MS): 54 ($[CH_2CH_2CN]^+$, 2%); 70 ($[N(CH_2)_4]^+$, 12%); 73 ($[C(CH_3)_2OMe]^+$, 100%); 142 ($[M\text{-}(SO_2CH_2CH_2CN)]^+$, 3%); 187 ($[M\text{-}(C(CH_3)_2OMe)]^+$, 21%); 229 ($[M\text{-}(OMe)]^+$, 7%)
$[\alpha]_{20}^{D}$: -7.7° (c=0.145; $CHCl_3$)
m.p.: 62-62.5°C (lit.: 61°C)
GC (100/0/10/290/20): t_R = 15.63 min

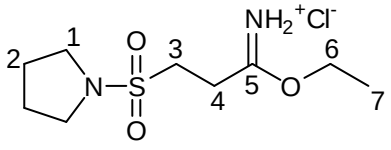
*4.3.5 Synthesis of 1-(ethyloxy)-3-(pyrrolidin-1-ylsulfonyl)propan-1-iminium chloride **50***

M.F.: $C_9H_{19}ClN_2O_3S$ (**M.W.** 270.77)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried three-necked flask equipped with a gas inlet, a gas outlet, an internal thermometer and a magnetical stirrer, 2.196 g (11.665 mmol; 1 eq.) of 3-(pyrrolidinosulfonyl)propionitrile **48** were dissolved in 9.7 ml of dry CH_2Cl_2 and 1.027 ml (806 mg; 17.497 mmol; 1.5 eq.) of dry ethanol. After complete dissolution, the mixture was cooled to -40°C. Freshly synthesized HCl, prepared by the addition of H_2SO_4 to NH_4Cl, was then bubbled through the mixture until saturation. The temperature was raised to 5°C and the mixture was stirred for 20 hours. The solvents were evaporated under reduced pressure in a rotary evaporator connected to a trap containing silica gel.
The foamy residue obtained was triturated with dry ether and the solvent evaporated under reduced pressure. This operation was repeated until a white solid was obtained.

Yield: 3.159 g (quant.)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.52 (*t*, $^{3}J_{7\text{-}6}$ = 7.0, 3 H, 7); 1.90-2.03 (*m*, 4 H, 2); 3.22 (*t*, $^{3}J_{4\text{-}3}$ = 6.4, 2 H, 4); 3.35-3.48 (*m*, 4 H, 1); 3.53 (*t*, $^{3}J_{3\text{-}4}$ = 6.7, 2 H, 3); 4.69 (*q*, $^{3}J_{6\text{-}7}$ = 7.0, 2 H, 6); 11.75 (*broad s*, 1 H, NH_2^+); 12.60 (*broad s*, 1 H, NH_2^+)
^{13}C NMR (DMSO, 200 MHz): 13.4 (7); 25.3 (2); 27.3 (4); 43.1 (3); 47.5 (1); 69.7 (6); 176.2 (5)

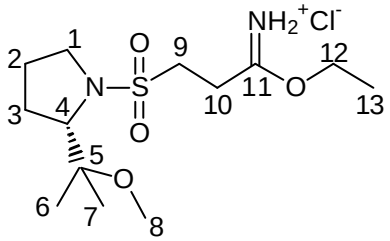
*4.3.6 Synthesis of 1-(ethyloxy)-3-({(2S)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)-propan-1-iminium chloride **51***

M.F.: $C_{13}H_{27}ClN_2O_4S$ (**M.W.** 342.88)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried three-necked flask equipped with a gas inlet, a gas outlet, an internal thermometer and a magnetical stirrer, 5.154 g (19.79 mmol; 1 eq.) of 3-[(2*S*)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]propionitrile **49** were dissolved in 16.5 ml of dry CH_2Cl_2 and 1.742 ml (1.367 g; 29.69 mmol; 1.5 eq.) of dry ethanol. After complete dissolution, the mixture was cooled to -40°C. Freshly synthesized HCl, prepared by the addition of H_2SO_4 to NH_4Cl, was then bubbled through the mixture until saturation. The temperature was raised to 5°C and the mixture was stirred for 20 hours. The solvents were evaporated under reduced pressure in a rotary evaporator connected to a trap containing silica gel.
The foamy residue obtained was triturated with dry ether and the solvent evaporated under reduced pressure. This operation was repeated until a white solid was obtained.

Yield: 6.788 g (quant.)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.14 (*s*, 6 H, 6, 7); 1.51 (*t*, $^{3}J_{13\text{-}12}$ = 7.5, 3 H, 13); 1.67-2.12 (*m*, 4 H, 2, 3); 3.09-3.89 (*m*, 6 H, 1, 9, 10); 3.20 (*s*, 3 H, 8); 4.07-4.11 (*m*, 1 H, 4); 4.65-4.73 (*m*, 2 H, 12); 11.62 (*broad s*, 1 H, NH_2^+); 12.51 (*broad s*, 1 H, NH_2^+)
^{13}C NMR ($CDCl_3$, 50 MHz): 13.2 (13); 20.2 and 21.2 (6, 7); 26.0 (10); 27.5 and 27.9 (2, 3); 47.0 (1); 48.9 (8); 50.1 (9); 66.4 (4); 71.0 (12); 77.7 (5); 176.4 (11)

*4.3.7 Synthesis of 1-[(3,3,3-triethoxypropyl)sulfonyl]pyrrolidine **52***

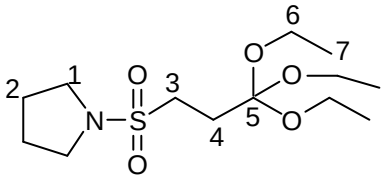
M.F.: $C_{13}H_{27}NO_5S$ (**M.W.** 309.42)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried flask, 3.158 g (11.662 mmol; 1 eq.) of freshly prepared 1-(ethyloxy)-3-[(pyrrolidin-1-yl)sulfonyl]propan-1-iminium chloride **50** were dissolved in 24 ml of dry CH_2Cl_2 and 8.2 ml of dry ethanol. The reaction mixture was stirred for 65 hours at room temperature. The precipitate (NH_4Cl) that formed during the reaction was eliminated by filtration. The filtrate was evaporated under reduced pressure. The resulting oil was dissolved in 30 ml of dry Et_2O and stirred for 10 minutes. The precipitate that formed (amide) was eliminated by filtration. The filtrate was then stirred in the presence of 30 ml of a 2N solution of KOH (hydrolysis of the ester). The stirring should be slow enough not to mix the 2 phases. It was continued until all the ester had disappeared (followed by IR). The 2 phases were separated and the aqueous phase was extracted 4 times with Et_2O. The organic phase was dried over 2 g of drierite 10-20 mesh and then filtered through a pad of dry Na_2SO_4. The drierite was washed with Et_2O and the filtrate was evaporated under reduced pressure.

Yield: 2.55 g (71 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.21 (*t*, $^3J_{7\text{-}6}$ = 7, 9 H, 7); 1.88-1.98 (*m*, 4 H, 2); 2.28 (*mult*, 2 H, 4); 3.04 (*mult*, 2 H, 3); 3.31-3.42 (*m*, 4 H, 1); 3.53 (*t*, $^3J_{6\text{-}7}$ = 7.1, 6 H, 6)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.0 (7); 25.8 (2); 26.1 (4); 44.2 (3); 47.7 (1); 57.5 (6); 113.9 (5)
IR (liquid film, cm^{-1}): 1072 (C-O); 1147 (NSO_2); 1329 (NSO_2); 2977 (C-H)

*4.3.8 Synthesis of (2S)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl)sulfonyl]pyrrolidine **10***

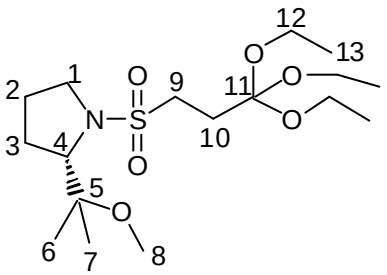
M.F.: $C_{17}H_{35}NO_6S$ (**M.W.** 381.52) **RN: 190510-70-4**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried flask, 2.265 g (6.605 mmol; 1 eq.) of freshly prepared 1-(ethyloxy)-3-({(2*S*)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)propan-1-iminium chloride **51** were dissolved in 14 ml of dry CH_2Cl_2 and 4.6 ml of dry ethanol. The reaction mixture was stirred for 65 hours at room temperature. The precipitate (NH_4Cl) that formed during the reaction was eliminated by filtration. The filtrate was evaporated under reduced pressure. The resulting oil was dissolved in 27 ml of dry Et_2O and stirred for 10 minutes. The precipitate that formed (amide) was eliminated by filtration. The filtrate was then stirred in the presence of 21 ml of a 2N solution of KOH (hydrolysis of the ester). The stirring should be slow enough not to mix the 2 phases. It was continued until all the ester had disappeared (followed by IR). The 2 phases were separated and the aqueous phase was extracted 4 times with Et_2O. The organic phase was dried over 2 g of drierite 10-20 mesh and then filtered through a pad of dry Na_2SO_4. The drierite was washed with Et_2O and the filtrate was evaporated under reduced pressure.

Yield: 1.423 g (56 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.14 and 1.18 (*2 s*, 6 H, 6, 7); 1.21 (*t*, $^3J_{13\text{-}12}$ = 7.5, 9 H, 13); 1.69-2.03 (*m*, 4 H, 2, 3); 2.28 (*mult*, 2 H, 10); 3.07-3.16 (*m*, 3 H, 1, 9); 3.20 (*s*, 3 H, 8); 3.53 (*q*, $^3J_{12\text{-}13}$ = 7.5, 6 H, 12); 3.74-3.82 (*m*, 1 H, 1); 4.05-4.11 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.1 (13); 21.4 and 21.6 (6, 7); 26.3, 26.5 and 27.2 (2, 3, 10); 47.3 (9); 49.3 (8); 50.0 (1); 57.4 (12); 66.4 (4); 77.8 (5); 113.9 (11)
IR (liquid film, cm^{-1}): 1072 (C-O); 1145 (NSO_2); 1326 (NSO_2); 2874 (OCH_3); 2978 (C-H)
$[\alpha]_{20}^{D}$: -60.8° (c=0.296; $CHCl_3$)

4.4 Synthesis of ketals

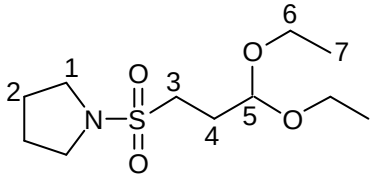
*4.4.1 Synthesis of 1-[(3,3-diethoxypropyl)sulfonyl]pyrrolidine **56***

M.F.: $C_{11}H_{23}NO_4S$ (**M.W.** 265.36)

In a flame-dried two-necked flask, 200 mg (1.34 mmol; 1 eq.) of 1-(methylsulfonyl)pyrrolidine **11** were dissolved in 10 ml of THF and 466 µl (480 mg; 2.68 mmol; 2 eq.) of HMPA. The mixture was cooled to -78°C and 670 µl (456 mg; 1.34 mmol; 1 eq.) of *n*-BuLi, 2M solution in hexane, were slowly added. After 60 minutes of reaction, 202 µl (264 mg; 1.34 mmol; 1 eq.) of bromoacetaldehyde diethyl acetal were added. The mixture was allowed to come to room temperature and the stirring was continued for 2 hours. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 200 mg (56 %)

Aspect: yellow oil
TLC: R_f = 0.77 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.19 and 1.20 (*2 t*, $^3J_{7\text{-}6}$ = 7, 6 H, 7); 1.89-1.98 (*m*, 4 H, 2); 2.09 (*mult*, 2 H, 4); 3.05 (*mult*, 2 H, 3); 3.30-3.40 (*m*, 4 H, 1); 3.51 and 3.66 (*2 mult*, 4 H, 6); 4.59 (*mult*, 1 H, 5)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.2 (7); 25.7 (2); 27.8 (4); 44.8 (3); 47.6 (1); 62.1 (6); 101.0 (5)
IR (liquid film, cm^{-1}): 1145 (NSO_2); 1330 (NSO_2); 2976 (C-H)
Mass (CI -Q1MS): 127 (45%); 264 ($[M\text{-}H]^-$, 35%)

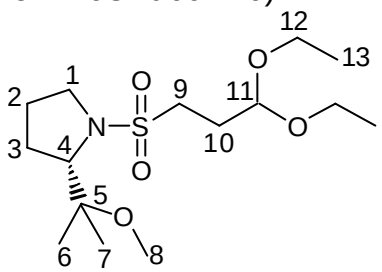
*4.4.2 Synthesis of (2S)-1-[(3,3-diethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **57***

M.F.: $C_{15}H_{31}NO_5S$ (**M.W.** 337.47)

In a flame-dried two-necked flask, 1000 mg (4.518 mmol; 1 eq.) of (2*S*)-1-methylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **14** were dissolved in 34 ml of THF and 1.572 ml (1.619 g; 9.036 mmol; 2 eq.) of HMPA. The mixture was cooled to -78°C and 2.053 ml (1.396 g; 4.518 mmol; 1 eq.) of *n*-BuLi, 2.2M solution in hexane, were slowly added. After 60 minutes of reaction, 680 µl (890 mg; 4.518 mmol; 1 eq.) of bromoacetaldehyde diethyl acetal were added. The mixture was allowed to come to room temperature and the stirring was continued for 2 hours. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 90 : 10).

Yield: 484 mg (32 %)

Aspect: colorless oil
TLC: R_f = 0.58 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.14 and 1.17 (*2 s*, 6 H, 6, 7); 1.21 (*t*, $^3J_{13\text{-}12}$ = 6.9, 6 H, 13); 1.72-2.04 (*m*, 6 H, 2, 3); 2.12 (*mult*, 2 H, 10); 3.05 (*mult*, 1 H, 1); 3.16 (*mult*, 1 H, 9); 3.21 (8); 3.51 and 3.67 (*2 mult*, 4 H, 12); 3.79 (*mult*, 1 H, 1); 4.07 (*mult*, 1 H, 4); 4.61 (*t*, $^3J_{11\text{-}10}$ = 4.6, 1 H, 11)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.2 (13); 21.2 and 21.5 (6, 7); 26.2 and 27.9 (2, 3); 27.2 (10); 47.5 (9); 49.2 (8); 49.9 (1); 62.0 (12); 66.3 (4); 77.8 (5); 101.0 (11)
IR (liquid film, cm^{-1}): 1145 (NSO_2); 1335 (NSO_2); 2975 (C-H)
Mass (CI -Q1MS): 109 (18%); 248 (100%); 336 ($[M-H]^-$, 60%)
$[\alpha]_{20}^{D}$: -18.2° (c=0.329; $CHCl_3$)

*4.4.3 Synthesis of (2S)-1-{[2-(1,3-dioxolan-2-yl)ethyl]sulfonyl}-2-(1-methoxy-1-methylethyl)-pyrrolidine **58***

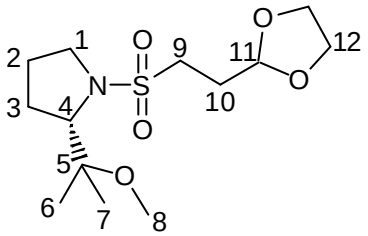
M.F.: $C_{13}H_{25}NO_5S$ (**M.W.** 307.4)

In a flame-dried two-necked flask 1000 mg, (4.518 mmol; 1 eq.) of (2*S*)-1-methylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **14** were dissolved in 34 ml of

THF and 1.572 ml (1.619 g; 9.036 mmol; 2 eq.) of HMPA. The mixture was cooled to -78°C and 2.053 ml (1.396 g; 4.518 mmol; 1 eq.) of *n*-BuLi, 2.2M solution in hexane, were added. After 60 minutes of reaction, 468 µl (754 mg; 4.518 mmol; 1 eq.) of 2-bromomethyl-1,3-dioxolane were added. The mixture was allowed to come to room temperature and after 2 hours of reaction, a few ml of a saturated solution of NH_4Cl were added. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (mounting: petroleum ether : AcOEt 95 : 5 + 10% Et_3N; elution: petroleum ether : AcOEt 95 : 5).

Yield: 686 mg (49 %)
Besides, 337 mg (34 %) of (2*S*)-1-methylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **27** were recovered.

Aspect: colorless oil
TLC: R_f = 0.32 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.12 and 1.16 (*2 s*, 6 H, 6, 7); 1.72-2.05 (*m*, 4 H, 2, 3); 2.19 (*mult*, 2 H, 10); 3.06-3.17 (*m*, 1 H, 1); 3.19-3.25 (*m*, 1 H, 9); 3.16 (*s*, 3 H, 8); 3.77-3.86 (*m*, 1 H, 1); 3.92 (*mult*, 4 H, 12); 4.05-4.11 (*m*, 1 H, 4); 5.01 (*t*, $^3J_{11\text{-}10}$ = 3.9, 1 H, 11)
^{13}C NMR ($CDCl_3$, 75 MHz): 21.0 and 21.5 (6, 7); 26.2, 27.3 and 27.9 (2, 3, 10); 49.2 (8); 46.7 and 50.0 (1, 9); 65.0 (12); 66.2 (4); 77.9 (5); 102.2 (11)
IR (liquid film, cm^{-1}): 1138 (NSO_2); 1331 (NSO_2); 2977 (C-H)
Mass (CI/CH_4-N_2O): 73 ($[C(CH_3)_2OMe]^+$, 18%); 190 (53%); 276 ($[M\text{-}OMe]^+$, 100%); 308 ($[M+H]^+$, 7%)
GC (100/0/10/290/15): t_R = 17.46 min
$[\alpha]_{20}^{D}$: -46.5° (c=0.129; $CHCl_3$)
HRMS: calculated for $C_{13}H_{25}NO_5S^+$: 308.153170; found: 308.152277

4.5 Synthesis of ethers and thioethers

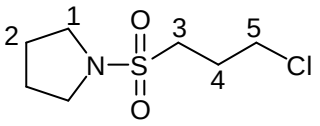
*4.5.1 Synthesis of 1-[(3-chloropropyl)sulfonyl)]pyrrolidine **41***

M.F.: $C_7H_{14}ClNO_2S$ (**M.W.** 211.7) **RN: 146475-49-2**

Following the general procedure described in 4.1 with:
2 ml (1.704 g; 23.95 mmol; 1 eq.) of pyrrolidine
3.33 ml (2.424 g; 23.95 mmol; 1 eq.) of Et_3N
2.913 ml (4.241 g; 23.95 mmol; 1 eq.) of 3-chloropropanesulfonyl chloride
21 ml of CH_2Cl_2
Flash chromatography: AcOEt : CH_2Cl_2 1 : 1

Yield: 5.23 g (quant.)

Aspect: white solid
TLC: R_f = 0.29 (CH_2Cl_2 100%)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.96 (*mult*, 4 H, 2); 2.30 (*mult*, 2 H, 4); 3.14 (*t*, $^3J_{3\text{-}4}$ = 11.2, 2 H, 3); 3.34-3.41 (*m*, 4 H, 1); 3.70 (*t*, $^3J_{5\text{-}4}$ = 9.0, 2 H, 5)
^{13}C NMR ($CDCl_3$, 75 MHz): 25.8 (2); 26.6 (4); 43.0 (5); 46.6 (3); 47.7 (1)
Mass (CI/CH_4-N_2O): 70 ($[NC_4H_8]^+$, 100%); 77 ($[C_3H_6Cl]^+$, 26%); 212 ($[M+H]^+$ (^{35}Cl), 48%); 214 ($[M+H]^+$ (^{37}Cl), 25%)

*4.5.2 Synthesis of 1-[6-chlorohexyl)sulfonyl]pyrrolidine **42***

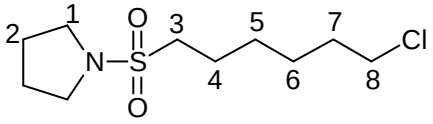
M.F.: $C_{10}H_{20}ClNO_2S$ (M.W. 253.78)

Following the general procedure described in 4.1 with:
200 µl (170 mg; 2.395 mmol; 1 eq.) of pyrrolidine
333 µl (242 mg; 2.395 mmol; 1 eq.) of Et_3N
525 mg (2.395 mmol; 1 eq.) of 6-chlorohexylsulfonyl chloride
3.4 ml of CH_2Cl_2
Flash chromatography: petroleum ether : AcOEt 70 : 30

Yield: 424 mg (70%)

Aspect: white solide

TLC: Rf = 0.25 (petroleum ether : AcOEt 80 : 20); 0.33 (petroleum ether : AcOEt 70 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.42-1.55 (*m*, 4 H, 5, 6); 1.74-1.90 (*m*, 4 H, 4, 7); 1.94 (*mult*, 4 H, 2); 2.96 (*mult*, 2 H, 3); 3.36 (*mult*, 4 H, 1); 3.54 (*t*, $^{3}J_{8\text{-}7}$ = 6.5, 2 H, 8)

^{13}C NMR ($CDCl_3$, 50 MHz): 23.1 (4); 25.8 (2); 26.3 (6); 27.7 (5); 32.1 (7); 41.6 (1); 44.7 (8); 49.4 (3)

Mass (CI/CH_4-N_2O): 218 ($[M\text{-}Cl]^+$, 16%); 254 ($[M+H]^+$ (^{35}Cl), 100%); 256 ($[M+H]^+$ (^{37}Cl), 43%)

m.p.: 55-56°C

Elemental analysis:

calculated (%): C: 47.33; H: 7.94; N: 5.52; S: 12.63

found (%): C: 47.11; H: 7.97; N: 5.11; S: 13.02

*4.5.3 Synthesis of (2S)-1-[(3-chloropropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **46***

M.F.: $C_{11}H_{22}ClNO_3S$ (**M.W.** 283.81)

Following the general procedure described in 4.1 with:

5 g (34.9 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27**

4.852 ml (3.532 g; 34.9 mmol; 1 eq.) of Et_3N

4.244 ml (6.18 g; 34.9 mmol; 1 eq.) of 3-chloropropanesulfonyl chloride

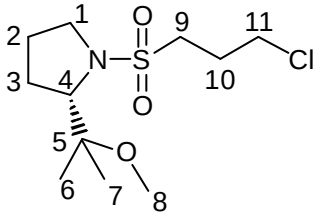
50 ml of Et_2O

Flash chromatography: petroleum ether : AcOEt 70 : 30

Yield: 8.74 g (88 %)

Aspect: slightly yellow oil

TLC: R_f = 0.67 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.13 and 1.17 (*2 s*, 6 H, 6, 7); 1.70-2.07 (*m*, 4 H, 2, 3); 2.30 (*mult*, 2 H, 10); 3.04-3.18 (*m*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.28 (*t*, $^{3}J_{9\text{-}10}$ = 7.4, 2 H, 9); 3.69 (*t*, $^{3}J_{11\text{-}10}$ = 6.2, 2 H, 11); 3.77-3.92 (*m*, 1 H, 4); 4.05-4.14 (*m*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 20.9 and 21.5 (6, 7); 26.3 (10); 26.7 and 27.4 (2, 3); 43.1 (11); 49.2 (8); 49.6 and 50.0 (1, 9); 66.3 (4); 77.9 (5)
IR (liquid film, cm^{-1}): 1141 (NSO_2); 1327 (NSO_2); 2977 (C-H)
Mass (CI/CH_4-N_2O): 252 ([M-OMe]$^+$ (^{35}Cl), 100%); 254 ([M-OMe]$^+$ (^{37}Cl), 48%); 284 ([M+H]$^+$ (^{35}Cl), 3%); 286 ([M+H]$^+$ (^{37}Cl), 1.5%)
GC (100/0/10/290/20): t_R = 16.06 min
HRMS: calculated for $C_{11}H_{21}ClNO_3S^+$: 282.093068; found: 282.092264

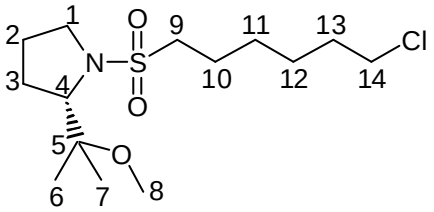
*4.5.4 Synthesis of (2S)-1-[(6-chlorohexyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **36***

M.F.: $C_{14}H_{28}ClNO_3S$ (**M.W.** 325.89)

Following the general procedure described in 4.1 with:
400 mg (2.792 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidine **27**
388 µl (282 mg; 2.792 mmol; 1 eq.) of Et_3N
612 mg (2.792 mmol; 1 eq.) of 6-chlorohexylsulfonyl chloride
4 ml of CH_2Cl_2
Flash chromatography: petroleum ether : AcOEt 70 : 30

Yield: 462 mg (51%)

Aspect: colorless oil
TLC: Rf = 0.61 (petroleum ether : AcOEt 70: 30)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.13 and 1.16 (*2 s*, 6 H, 6, 7); 1.40-1.53 (*m*, 4 H, 11, 12); 1.69-2.04 (*m*, 8 H, 2, 3, 10, 13); 3.05-3.17 (*m*, 1 H, 1); 3.07 (*t*, $^{3}J_{9\text{-}10}$ = 7.8, 2 H, 9); 3.21 (*s*, 3 H, 8); 3.54 (*t*, $^{3}J_{14\text{-}13}$ = 6.4, 2 H, 14); 3.74-3.86 (*m*, 1 H, 1); 4.04-4.14 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 21.1 and 21.5 (6, 7); 23.2 (10); 26.3 (12); 27.2-26.2 (2, 3); 27.6 (11); 32.1 (13); 44.7 (14); 49.2 (8); 51.9-49.9 (1, 9); 66.0 (4); 77.8 (5)
IR (Film liquide (FT), cm^{-1}): 1146 (NSO_2); 1330 (NSO_2); 2943 (C-H)

Mass (CI/CH4-N2O): 83 (100%); 165 (49%); 294 ($[M\text{-}OMe]^+$ (^{35}Cl), 55%); 296 ($[M\text{-}OMe]^+$ (^{37}Cl), 28%); 326 ($[M+H]^+$ (^{35}Cl), 4%); 328 ($[M+H]^+$ (^{37}Cl), 2%)

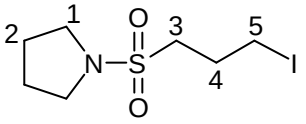
*4.5.5 Synthesis of 1-[(3-iodopropyl)sulfonyl]pyrrolidine **55***

M.F.: $C_7H_{14}INO_2S$ (**M.W.** 303.15)

A mixture of 5.23 g (24.7 mmol; 1 eq.) of 1-[(3-chloropropyl)sulfonyl]pyrrolidine **41** and of 3.814 g (25.44 mmol; 1.03 eq.) of sodium iodide in 29 ml of acetone was refluxed in a flask equipped with a reflux condenser for 16 hours. The mixture was cooled to room temperature, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (CH_2Cl_2 : AcOEt 50 : 50).

Yield: 6.12 g (82%)

Aspect: yellow solid



^{1}H NMR ($CDCl_3$, 300 MHz): 1.92-2.00 (*m*, 4 H, 2); 2.33 (*mult*, 2 H, 4); 3.09 (*mult*, 2 H, 3); 3.32 (*t*, $^3J_{5\text{-}4}$ = 6.6, 2 H, 5); 3.33-3.42 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 3.7 (5); 25.8 (2); 27.1 (4); 47.7 (1); 49.9 (3)
IR (solid deposit, cm^{-1}): 736; 1133 (NSO_2); 1327 (NSO_2); 2976 (C-H)
Mass (CI/CH_4-N_2O): 70 ($[N(CH_2)_4]^+$, 14%); 176 ($[M\text{-}I]^+$, 100%); 304 ($[M+H]^+$, 58%)
m.p.: 84-85°C

*4.5.6 Synthesis of 1-[(6-iodohexyl)sulfonyl]pyrrolidine **60***

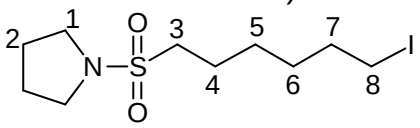
M.F.: $C_{10}H_{20}INO_2S$ (**M.W.** 345.23)

A mixture of 424 mg (1.67 mmol; 1 eq.) of 1-[6-(chlorohexyl)sulfonyl]pyrrolidine **42** and of 288 mg (1.921 mmol; 1.15 eq.) of sodium iodide in 2ml of acetone was refluxed in a flask equipped with a reflux condenser for 16 hours. The mixture was cooled to room temperature, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 70 : 30).

Yield: 404 mg (70%)

Aspect: yellow solid

TLC: Rf = 0.53 (petroleum ether : AcOEt 70 : 30)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.40-1.51 (*m*, 4 H, 4, 7); 1.74-1.89 (*m*, 4 H, 5, 6); 1.94 (*mult*, 4 H, 2); 2.96 (*mult*, 2 H, 3); 3.20 (*t*, $^{3}J_{8\text{-}7}$ = 6.9, 2 H, 8); 3.36 (*mult*, 4 H, 1)

^{13}C NMR ($CDCl_3$, 50 MHz): 6.7 (8); 23.0 (4); 25.8 (2); 27.3 (5); 29.8 (6); 32.9 (7); 47.6 (1); 49.2 (3)

Mass (CI/CH_4-N_2O): 70 ($[C_4H_8N]^+$, 100%); 218 ($[M\text{-}I]^+$, 57%); 346 ($[M+H]^+$, 38%)

m.p.: 52-53°C

Elemental analysis:

calculated (%): C: 34.79; H: 5.84; N: 4.06; S: 9.29

found (%): C: 34.77; H: 6.00; N: 3.92; S: 9.15

*4.5.7 Synthesis of (2S)-1-(3-iodopropane-1-sulfonyl)-2-(1-methoxy-1-methylethyl)pyrrolidine **61***

M.F.: $C_{11}H_{22}INO_3S$ (**M.W.** 375.26)

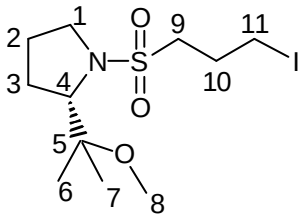
In a flask equipped with a reflux condenser, 2.94 g (10.35 mmol; 1 eq.) of (2*S*)-1-(3-chloropropane-1-sulfonyl)-2-(1-methoxy-1-methylethyl)pyrrolidine **46** and 1.599 g (10.66 mmol; 1.03 eq.) of sodium iodide in 12 ml of acetone were refluxed for 16 hours. The mixture cooled down to room temperature was filtered and evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 70 : 30).

Yield: 3.75 g (96 %)

Aspect: yellow oil

TLC: R_f = 0.41 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.13 and 1.17 (*2 s*, 6 H, 6, 7); 1.73-2.08 (*m*, 4 H, 2, 3); 2.34 (*mult*, 2 H, 10); 3.21 (*t*, $^{3}J_{11\text{-}10}$ = 6.3, 2 H, 11); 3.22 (*s*, 3 H, 8); 3.05-3.16 (*m*, 1 H, 1); 3.31 (*mult*, 2 H, 9); 3.78-3.87 (*m*, 1 H, 1); 4.07-4.13 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 75 MHz): 3.6 (11); 21.0 and 21.5 (6, 7); 26.7 (10); 26.3 and 27.4 (2, 3); 49.3 (8); 50.0 and 52.9 (1, 9); 66.3 (4); 77.9 (5)
Mass (CI/CH_4-N_2O): 85 (100%); 248 ($[M-I]^+$, 12%); 344 ($[M-OMe]^+$, 26%); 376 ($[M+H]^+$, 1%)
HRMS: calculated for $C_{11}H_{23}INO_3S^+$: 376.044343; found: 376.043432

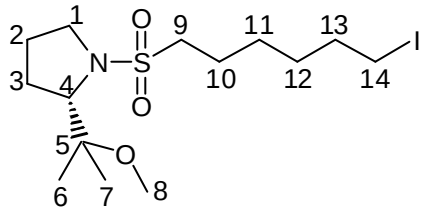
*4.5.8 Synthesis of (2S)-1-(6-iodohexane-1-sulfonyl)-2-(1-methoxy-1-methylethyl)pyrrolidine **62***

M.F.: $C_{14}H_{28}INO_3S$ (**M.W.** 417.34)

In a flask equipped with a reflux condenser, 462 mg (1.417 mmol; 1 eq.) of (2*S*)-1-[(6-chlorohexyl)sulfonyl]-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidine **36** and 244 mg (1.63 mmol; 1.15 eq.) of sodium iodide in 2 ml of acetone were refluxed for 16 hours. The mixture cooled down to room temperature was filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 466 mg (99%)

Aspect: white solid
TLC: Rf = 0.26 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.49-1.52 (*m*, 4 H, 11, 12); 1.71-2.01 (*m*, 8 H, 2, 3, 10, 13); 3.07 (*t*, $^3J_{9\text{-}10}$ = 8.0, 2 H, 9); 3.19 (*t*, $^3J_{14\text{-}13}$ = 6.8, 2 H, 14); 3.21 (*s*, 3 H, 8); 3.74-3.86 (*m*, 1 H, 1); 4.04-4.12 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 6.5 (14); 21.3 and 21.6 (6, 7); 23.2 (10); 26.3 and 27.3 (2, 3, 11); 29.9 (12); 33.0 (13); 49.2 (4); 50.0 and 52.1 (1, 9); 66.2 (8); 77.9 (5)
Mass (CI/CH_4-N_2O): 73 ($[C_4H_7N]^+$, 33%); 110 (35%); 142 ($[N^*]^+$, 27%); 260 ($[M-I-OMe]^+$, 100%); 294 (31%); 386 ($[M-OMe]^+$, 5%); 418 ($[M+H]^+$, 1%)
m.p.: 53-54°C

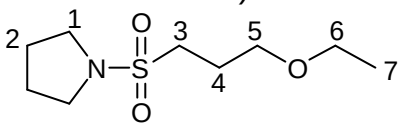
*4.5.9 Synthesis of 1-[(3-ethoxypropyl)sulfonyl]pyrrolidine **59***

M.F.: $C_9H_{19}NO_3S$ (**M.W.** 221.31)

In a flame-dried two-necked flask equipped with a reflux condenser, 152 mg (6.597 mmol; 2 eq.) of sodium were reacted with 10 ml of ethanol. When all the sodium had reacted, 1 g (3.298 mmol; 1 eq.) of 1-[(3-iodopropyl)sulfonyl]pyrrolidine **55** dissolved in 29 ml of ethanol and 7 ml of THF was added. The mixture was then refluxed for 4 hours. Once cooled down to room temperature, some water was added. The solvents were evaporated. The residue was dissolved in a mixture of water and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

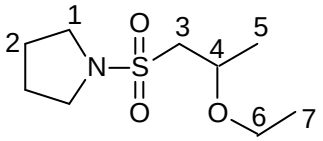
Yield: 359 mg (49 %)

Aspect: colorless oil
TLC: R_f = 0.23 (petroleum ether : AcOEt 2 : 1)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.20 (*t*, $^3J_{7\text{-}6}$ = 12.0, 3 H, 7); 1.89-1.98 (*m*, 4 H, 2); 2.00-2.16 (*m*, 2 H, 4); 3.18 (*mult*, 2 H, 3); 3.32-3.41 (*m*, 4 H, 1); 3.50 (*mult*, 4 H, 5, 6)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.3 (7); 23.8 (4); 25.7 (2); 46.5 (3); 47.6 (1); 66.1 and 68.1 (5, 6)
IR (liquid film, cm^{-1}): 1147 (NSO_2); 1329 (NSO_2); 2974 (C-H)
Mass (CI/CH_4-N_2O): 151 ($[M\text{-}NC_4H_8]^+$, 1%); 176 ($[M\text{-}OEt]^+$, 89%); 222 (M^+, 100%)
GC (100/0/10/290/15): t_R = 13.22 min

Besides, 350 mg (48 %) of 1-{[2-(ethyloxy)propyl]sulfonyl}pyrrolidine **68** were obtained:



^{1}H NMR ($CDCl_3$, 300 MHz): 1.20 (*t*, $^3J_{7\text{-}6}$ = 7.0, 3 H, 7); 1.33 (*d*, $^3J_{5\text{-}4}$ = 6.7, 3 H, 5); 1.94 (*mult*, 4 H, 2); 2.95 (*dd*, $^2J_{3\text{-}3'}$ = 14.4, $^3J_{3\text{-}4}$ = 5.5, 1 H, 3); 3.28 (*dd*, $^2J_{3\text{-}3'}$ = 14.4, $^3J_{3\text{-}4}$ = 6.7, 1 H, 3); 3.34 (*mult*, 4 H, 1); 3.49 and 3.60 (*2 mult*, 2 H, 6); 3.98 (*sext*, $^3J_{4\text{-}3}$ = $^3J_{4\text{-}5}$ = 5.9, 1 H, 4)

^{13}C NMR ($CDCl_3$, 75 MHz): 70.3 (4); 63.9 (6); 55.2 (3); 47.4 (1); 25.6 (2); 19.9 (5); 15.3 (7)
IR (liquid film, cm^{-1}): 1149 (NSO_2); 1326 (NSO_2); 2976 (C-H)

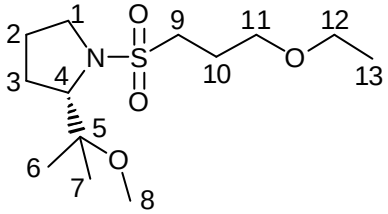
*4.5.10 Synthesis of (2S)-1-[(3-ethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **65***

M.F.: $C_{13}H_{27}NO_4S$ (**M.W.** 293.42)

In a flame-dried two-necked flask, 182 mg (7.909 mmol; 2 eq.) of sodium were reacted with 12 ml of dry EtOH. The mixture was stirred until complete reaction of the sodium. In a second flask, 1.389 g (3.954 mmol; 1 eq.) of (2*S*)-1-[(3-iodopropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **61** were dissolved in 35 ml of dry EtOH and 8.4 ml of THF. This solution was added to the first flask and the resulting mixture was refluxed for 4 hours. The mixture was cooled to room temperature and some water was added. The solvents were evaporated under reduced pressure. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 580 mg (50 %)

Aspect: colorless oil
TLC: R_f = 0.48 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.14 and 1.17 (*2 s*, 6 H, 6, 7); 1.19 (*t*, $^3J_{13\text{-}12}$ = 7.3, 3 H, 13); 1.72-2.17 (*m*, 6 H, 2, 3, 10); 3.04-3.23 (*m*, 3 H, 1, 9); 3.21 (*s*, 3 H, 8); 3.50 (*mult*, 4 H, 11, 12); 3.73-3.86 (*m*, 1 H, 1); 4.04-4.13 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.0 (13); 21.1 and 21.5 (6, 7); 23.9 (10); 26.1 and 27.1 (2, 3); 49.1 (8); 49.2 and 49.9 (1, 9); 66.2 (4); 66.0 and 68.3 (11, 12); 77.8 (5)
IR (liquid film, cm^{-1}): 1140 (NSO_2); 1327 (NSO_2); 2976 (C-H)
Mass (CI +Q1MS): 69 ($[NC_4H_7]^{\bullet+}$, 23%); 73 ($[C(CH_3)_2OMe]^+$, 100%); 85 (94%); 101 (74%); 146 (95%); 161 (31%); 294 ($[M+H]^+$, 22%)
GC (100/0/10/290/20): t_R = 17.1 min
[a]$^D_{20}$: -34.1° (c=0.176; $CHCl_3$)

HRMS: calculated for $C_{13}H_{28}NO_4S^+$: 294.173905; found: 294.173008

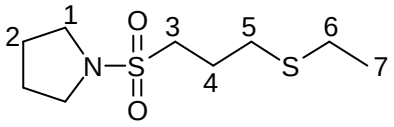
*4.5.11 Synthesis of 1-{[3-(ethylsulfanyl)propyl]sulfonyl}pyrrolidine **63***

M.F.: $C_9H_{19}NO_2S_2$ (**M.W.** 237.37)

In a flame-dried two-necked flask, 500 mg (1.649 mmol; 1 eq.) of 1-[(3-iodopropyl)sulfonyl]pyrrolidine **55** and 205 mg (2.437 mmol; 1.47 eq.) of sodium ethanethiolate were dissolved in 25 ml of THF. The mixture was stirred for 18 hours at room temperature. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted twice with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 281 mg (72 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.26 (*t*, $^3J_{7\text{-}6}$ = 7.4, 3 H, 7); 1.94 (*mult*, 4 H, 2); 2.11 (*mult*, 2 H, 4); 2.55 (*q*, $^3J_{6\text{-}7}$ = 7.4, 2 H, 6); 2.67 (*t*, $^3J_{5\text{-}4}$ = 6.9, 2 H, 5); 3.11 (*mult*, 2 H, 3); 3.37 (*mult*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.6 (7); 23.0 (4); 25.6 (6); 25.8 (2); 30.0 (5); 47.6 (1); 47.8 (3)
Mass (CI +Q1MS): 70 ($[N(CH_2)_4]^+$, 4%); 167 ($[M\text{-}N(CH_2)_4]^+$, 100%); 176 ($[M\text{-}SEt]^+$, 32%); 212 (54%); 238 ($[M+H]^+$, 12%)
GC (100/0/10/290/15): t_R = 16.87 min

*4.5.12 Synthesis of (2S)-1-{[3-(ethylsulfanyl)propyl]sulfonyl}-2-(1-methoxy-1-methylethyl)-pyrrolidine **66***

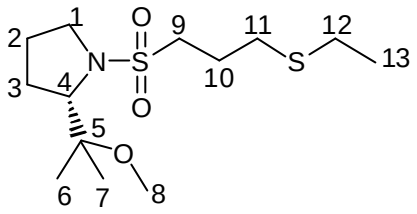
M.F.: $C_{13}H_{27}NO_3S_2$ (**M.W.** 309.48)

In a flame-dried two-necked flask, 1 g (2.664 mmol; 1 eq.) of (2*S*)-1-[(3-iodopropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)-pyrrolidine **61** and 331 mg (3.937 mmol; 1.47 eq.) of sodium ethanethiolate were dissolved in 40 ml of THF. After 18 hours of stirring the reaction was quenched by the addition of a saturated

solution of NH_4Cl. The aqueous phase was extracted twice with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 768 mg (93 %)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.13 and 1.17 (*2 s*, 6 H, 6, 7); 1.26 (*t*, $^3J_{13\text{-}12}$ = 7.4, 3 H, 13); 1.72-2.06 (*m*, 4 H, 2, 3); 2.11 (*mult*, 2 H, 10); 2.54 (*q*, $^3J_{12\text{-}13}$ = 7.4, 2 H, 12); 2.66 (*t*, $^3J_{11\text{-}10}$ = 7.1, 2 H, 11); 3.06-3.17 (*m*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.21 (*t*, $^3J_{9\text{-}10}$ = 7.7, 2 H, 9); 3.76-3.85 (*m*, 1 H, 1); 4.05-4.11 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 14.6 (13); 21.1 and 21.5 (6, 7); 23.2 (10); 25.5 and 26.2 (2, 3); 27.3 and 30.0 (11, 12); 49.2 (8); 49.9 and 50.8 (1, 9); 66.2 (4); 77.8 (5)
IR (liquid film, cm^{-1}): 1142 (NSO_2); 1326 (NSO_2); 2976 (C-H)
Mass (CI +Q1MS): 155 (87%); 252 (100%); 278 ($[M\text{-}OMe]^+$, 28%); 310 ($[M+H]^+$, 9%)
GC (100/0/10/290/20): t_R = 19.64 min
$[\alpha]_{20}^{D}$: -41.8° (c=0.263; $CHCl_3$)
HRMS: calculated for $C_{13}H_{28}NO_3S_2^+$: 310.151063; found: 310.149812

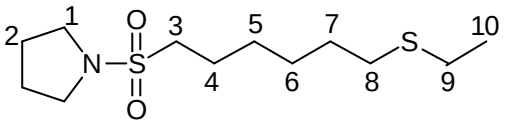
*4.5.13 Synthesis of 1-{[6-(ethylsulfanyl)hexyl]sulfonyl}pyrrolidine **64***

M.F.: $C_{12}H_{25}NO_2S_2$ (**M.W.** 279.45)

In a flame-dried two-necked flask, 160 mg (463.4 µmol; 1 eq.) of 1-[(6-iodohexyl)sulfonyl]pyrrolidin **60** and 58 mg (684.8 µmol; 1.47 eq.) of sodium ethanethiolate were dissolved in 7 ml of THF. The mixture was stirred for 18 hours at room temperature. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted twice with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 70 : 30).

Yield: 96 mg (74 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.25 (*t*, $^{3}J_{10\text{-}9}$ = 7.3, 3 H, 10); 1.37-1.54 (*m*, 4 H, 6, 7); 1.55-1.70 (*m*, 2 H, 5); 1.72-1.89 (*m*, 2 H, 4); 1.94 (*mult*, 4 H, 2); 2.53 (*q*, $^{3}J_{9\text{-}10}$ = 7.4, 2 H, 9); 2.53 (*t*, $^{3}J_{8\text{-}7}$ = 7.3, 2 H, 8); 2.96 (*mult*, 2 H, 3); 3.36 (*mult*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.7 (10); 23.1 (4); 25.8 (2, 6); 28.0 (5); 28.3 (6); 29.1 (7); 31.4 (8); 47.6 (1); 49.3 (3)
IR (liquid film, cm^{-1}): 1140 (NSO_2); 1330 (NSO_2); 2975 (C-H)
Mass (CI/CH_4-N_2O): 59 (100%); 209 ($[M\text{-}NC_4H_8]^+$, 15%); 280 ($[M+H]^+$, 7%)
HRMS: calculated for $C_{12}H_{26}NO_2S_2^+$: 280.140498; found: 280.139857

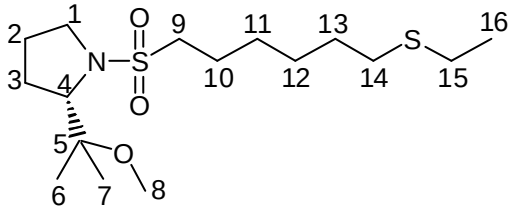
*4.5.14 Synthesis of (2S)-1-{[6-(ethylsulfanyl)hexyl]sulfonyl}-2-(1-methoxy-1-methylethyl)-pyrrolidine **67***

M.F.: $C_{16}H_{33}NO_3S_2$ (**M.W.** 351.56)

In a flame-dried two-necked flask, 450 mg (1.078 mmol; 1 eq.) of (2*S*)-1-[(6-iodohexyl)sulfonyl]-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidine **62** and 134 mg (1.593 mmol; 1.47 eq.) of sodium ethanethiolate were dissolved in 16 ml of THF. After 18 hours of stirring, the reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted twice with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 332 mg (88%)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.14 and 1.17 (*2 s*, 6 H, 6, 7); 1.26 (*t*, $^{3}J_{16\text{-}15}$ = 7.4, 3 H, 16); 1.38-1.52 (*m*, 4 H, 12, 13); 1.54-1.68 (*m*, 2 H, 11); 1.71-2.02 (*m*, 6 H, 2, 3, 10); 2.53 (*t*, $^{3}J_{14\text{-}13}$ = 7.2, 2 H, 14); 2.54 (*q*, $^{3}J_{15\text{-}16}$ = 7.4, 2 H, 15); 3.07 (*t*, $^{3}J_{9\text{-}10}$ = 7.4, 2 H, 9); 3.12-3.22 (*m*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.72-3.86 (*m*, 1 H, 1); 4.04-4.12 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 50 MHz): 14.7 (16); 21.2 and 21.5 (6, 7); 23.2 (10); 25.8 (15); 26.2 (11); 28.0 (12); 28.3 (13); 27.2 and 29.1 (2, 3); 31.4 (14); 49.2 (8); 49.9 and 52.0 (1, 9); 66.0 (4); 77.9 (5)

IR (liquid film, cm^{-1}): 1139 (NSO_2); 1330 (NSO_2); 2974 (C-H)

Mass (CI/CH_4-N_2O): 258 ([M-OMe-SCH_2CH_3]$^+$, 100); 320 [M-OMe]$^+$, 15%); 352 ([M+H]$^+$, 1%)

$[\alpha]_{20}^{D}$: -29.3° (c=0.273; $CHCl_3$)

HRMS: calculated for $C_{16}H_{34}NO_3S_2^+$: 352.198013; found: 352.197477

*4.5.15 Synthesis of of 1-[(2-ethoxyethyl)sulfonyl]pyrrolidine **69***

M.F.: $C_8H_{17}NO_3S$ (**M.W.** 207.28)

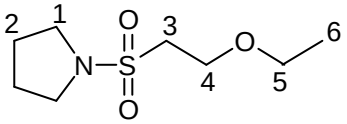
In a flame-dried two-necked flask 71 mg (3.101 mmol; 1 eq.) of sodium were reacted with 9.1 ml of EtOH. After complete reaction, 500 mg (3.101 mmol; 1 eq.) of 1-(ethenylsulfonyl)pyrrolidine **40** dissolved in 4.55 ml of EtOH were slowly added. The mixture was stirred for 2 hours at room temperature and then quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 589 mg (92%)

Aspect: yellow oil

TLC: R_f = 0.38 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.21 (*t*, $^3J_{6\text{-}5}$ = 7.0, 3 H, 6); 1.92 (*mult*, 4 H, 2); 3.26 (*t*, $^3J_{3\text{-}4}$ = 6.2, 2 H, 3); 3.37 (*mult*, 4 H, 1); 3.53 (*q*, $^3J_{5\text{-}6}$ = 7, 2 H, 5); 3.82 (*t*, $^3J_{4\text{-}3}$ = 6.0, 2 H, 4);

^{13}C NMR ($CDCl_3$, 50 MHz): 15.0 (6); 25.8 (2); 47.6 (1); 49.8 (3); 64.3 (5); 66.7 (4)

IR (liquid film, cm^{-1}): 1145 (NSO_2) ; 1330 (NSO_2) ; 2976 (C-H)

Mass (CI +Q1MS): 208 ([M+H]$^+$, 100%) ; 415 ([2M+H]$^+$, 15%)

GC (100/0/10/290/15): t_R = 12.62 min

Elemental analysis:

calculated (%): C: 46.35; H: 8.26; N: 6.75; O: 23.15; S: 15.46

found (%): C: 46.45; H: 8.26 ; N: 6.77 ; O: 23.06; S: 15.46

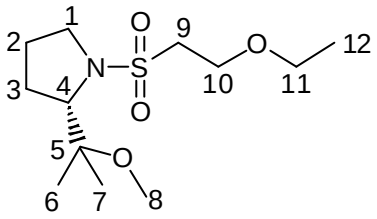
*4.5.16 Synthesis of (2S)-1-[(2-ethoxyethyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **70***

M.F.: $C_{12}H_{25}NO_4S$ (**M.W.** 279.39)

In a flame-dried two-necked flask 76 mg (3.3 mmol; 1 eq.) of sodium were reacted with 9.7 ml of EtOH. After complete reaction, 770 mg (3.3 mmol; 1 eq.) of (2*S*)-1-ethenylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **45** dissolved in 4.8 ml of EtOH were slowly added. The mixture was stirred for 2 hours at room temperature and then quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 750 mg (81%)

Aspect: colorless oil
TLC: R_f = 0.62 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.15 and 1.17 (*2 s*, 6 H, 6, 7); 1.21 (*t*, $^3J_{12\text{-}11}$ = 7.0, 3 H, 12); 1.72-2.06 (*m*, 4 H, 2, 3); 3.06-3.20 (*m*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.35 (*mult*, 2 H, 9); 3.53 (*q*, $^3J_{11\text{-}12}$ = 7.0, 2 H, 11); 3.71-3.90 (*m*, 3 H, 1, 10); 4.02-4.11 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.9 (12); 21.4 and 21.6 (6, 7); 26.0 and 27.2 (2, 3); 49.2 (8); 49.8 (1); 52.1 (9); 64.4 and 66.6 (10, 11); 66.4 (4); 77.9 (5)
IR (liquid film, cm^{-1}): 1152 (NSO_2); 1330 (NSO_2); 2977 (C-H)
Mass (CI +Q1MS) : 248 ($[M\text{-}OMe]^+$, 100%) ; 280 ($[M+H]^+$, 15%)
GC (100/0/10/290/15): t_R = 16.09 min
[a]$^D_{20}$: -110° (c=0.291; $CHCl_3$)

5 Synthesis of Michael acceptors

5.1 Synthesis of unsaturated lactams

*5.1.1 Synthesis of 1-methyl-3-phenylsulfanylpyrrolidin-2-one **76***

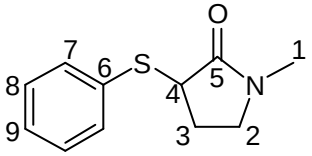
M.F.: $C_{11}H_{13}NOS$ (**M.W.** 207.29) **RN: 59953-50-3**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flame-dried three-necked flask, 2.906 ml (2.098 g; 20.73 mmol; 2 eq.) of diisopropylamine were dissolved in 12 ml of THF. The mixture was cooled to 0°C and 8.295 ml (20.73 mmol; 2 eq.) of *n*-BuLi, 2.5M solution in hexane, were added. The mixture was stirred for 10 minutes and then cooled to -78°C. 1 ml (1.028 g; 10.36 mmol; 1 eq.) of 1-methyl-2-pyrrolidinone dissolved in 6 ml of THF was slowly added. After 35 minutes at -78°C, 2.264 g (10.36 mmol; 1 eq.) of phenyl disulfide dissolved in 5 of THF and 1.804 ml (1.858 g; 10.36 mmol; 1eq.) of HMPA were added. The stirring was continued for 35 minutes, then the temperature was raised to -20°C over a period of 30 minutes and finally the mixture was allowed to come to room temperature. The mixture was poured into 100 ml of water and the aqueous phase was extracted 3 times with ether. The organic phase was washed with a 10% solution of NaOH, with water, with a 10% solution of HCl and with water. It was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 50 : 50).

Yield: 1.292 g (60 %)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.94-2.13 (*m*, 1 H, 3); 2.35-2.56 (*m*, 1 H, 3); 2.78 (*s*, 3 H, 1); 2.94-3.09 (*m*, 1 H, 2); 3.11-3.25 (*m*, 1 H, 2); 3.72-3.82 (*m*, 1 H, 4); 7.20-7.69 (*2 m*, 5 H, 7, 8, 9)
^{13}C NMR ($CDCl_3$, 50 MHz): 26.2 (3); 29.9 (1); 47.0 (2); 47.4 (4); 127.7 (9); 128.6 and 128.8 (7, 8); 132.8 (6); 171.9 (5)
IR (liquid film, cm^{-1}): 1682 (C=O); 2879 (C-H); 3056 (C-H arom)
Mass (CI +Q1MS): 98 ($[M-SC_6H_5]^+$, 8%); 111 ($[SC_6H_5]^+$, 7%); 130 ($[M-C_6H_5]^+$, 18%); 180 (100%); 208 ($[M+H]^+$, 58%)

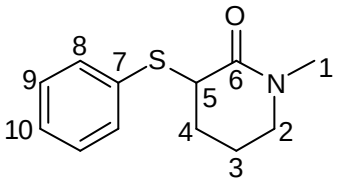
*5.1.2 Synthesis of 1-methyl-3-(phenylsulfanyl)piperidin-2-one **77***

M.F.: $C_{12}H_{15}NOS$ (**M.W.** 221.31) **RN: 59953-51-4**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flame-dried three-necked flask, 4.954 ml (3.576 g; 35.34 mmol; 2 eq.) of diisopropylamine were dissolved in 21 ml of THF. The mixture was cooled to 0°C and 14.13 ml (35.34 mmol; 2 eq.) of *n*-BuLi, 2.5M solution in hexane, were added. The mixture was stirred for 10 minutes and then cooled to -78°C. 2 ml (2 g; 17.67 mmol; 1 eq.) of 1-methylpiperidin-2-one dissolved in 11 ml of THF were slowly added. After 35 minutes at -78°C, 3.858 g (17.67 mmol; 1 eq.) of phenyl disulfide dissolved in 8.5 ml of THF and 3.075 ml (3.167 g; 17.67 mmol; 1 eq.) of HMPA were added. The stirring was continued for 35 minutes, then the temperature was raised to -20°C over a period of 30 minutes and finally the mixture was allowed to come to room temperature. The mixture was poured into 100 ml of water and the aqueous phase was extracted 3 times with ether. The organic phase was washed with a 10% solution of NaOH, with water, with a 10% solution of HCl and with water. It was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 50 : 50).

Yield: 2.99 g (76 %)
TLC: R_f = 0.38 (CH_2Cl_2 : AcOEt 1 : 1)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.71-2.19 (*m*, 4 H, 3, 4); 2.97 (*s*, 3 H, 1); 3.26-3.32 (*m*, 2 H, 2); 3.88 (*t*, $^3J_{5-4}$ = 3, 1 H, 5); 7.21-7.6 (*2 m*, 5 H, 8, 9, 10)
^{13}C NMR ($CDCl_3$, 50 MHz): 20.2 (3); 28.5 (4); 35.1 (1); 48.7 (5); 49.75 (2); 127.2 (10); 128.8 and 132.3 (8, 9); 134.7 (7); 168.1 (6)
IR (liquid film, cm^{-1}): 1645 (C=O); 2934 (C-H); 3055 (C-H arom)
Mass (CI +Q1MS): 89 (17%); 167 (100%); 195 (16%); 222 ($[M+H]^+$, 6%)

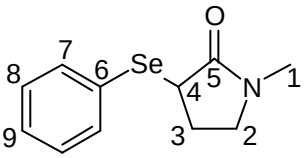
*5.1.3 Synthesis of 1-methyl-3-(phenylselanyl)pyrrolidin-2-one **80***

M.F.: $C_{11}H_{13}NOSe$ (**M.W.** 254.19) **RN: 59953-52-5**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flame-dried three-necked flask, 2.906 ml (2.098 g; 20.73 mmol; 2 eq.) of diisopropylamine were dissolved in 12 ml of THF. The mixture was cooled to 0°C and 8.295 ml (20.73 mmol; 2 eq.) of *n*-BuLi, 2.5M solution in hexane, were added. The mixture was stirred for 10 minutes and then cooled to -78°C. 1 ml (1.028 g; 10.36 mmol; 1 eq.) of 1-methyl-2-pyrrolidinone dissolved in 6 ml of THF was slowly added. After 35 minutes at -78°C, 1.986 g (10.36 mmol; 1 eq.) of phenylselenenyl chloride dissolved in 5 of THF et 1.804 ml (1.858 g; 10.36 mmol; 1 eq.) of HMPA were added. The stirring was continued for 35 minutes, then the temperature was raised to -20°C over a period of 30 minutes and finally the mixture was allowed to come to room temperature. The mixture was poured into 100 ml of water and the aqueous phase was extracted 3 times with ether. The organic phase was washed with a 10% solution of NaOH, with water, with a 10% solution of HCl and with water. It was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 50 : 50).

Yield: 1.580 g (60 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 2.15 (*mult*, 1 H, 3); 2.54 (*mult*, 1 H, 3); 2.74 (*s*, 3 H, 1); 2.82 (*mult*, 1 H, 2); 3.15 (*dt*, $^{3}J_{2\text{-}3}$ = 9.5, $^{2}J_{2\text{-}2'}$ = 3.3, 1 H, 2); 3.87 (*dd*, $^{3}J_{4\text{-}3}$ = 9.3, $^{3}J_{4\text{-}3}$ = 3.8, 1 H, 4); 7.20-7.49 (*m*, 3 H, 8, 9); 7.59-7.72 (*m*, 2 H, 7)
^{13}C NMR ($CDCl_3$, 75 MHz): 27.1 (3); 30.0 (1); 40.9 (4); 47.7 (2); 127.3 (6); 128.4 (9); 129.1 (8); 135.7 (7); 173.1 (5)
Mass (Cl/CH_4-N_2O): 83 ($[NCH_2CH_2CHC{=}O]^{\bullet+}$, 100%); 252 ($[M+H]^+$ (^{76}Se), 2%); 254 ($[M+H]^+$ (^{78}Se), 5%); 256 ($[M+H]^+$ (^{80}Se), 9%)

*5.1.4 Synthesis of 1-methyl-3-phenylselanylpiperidin-2-one **81***

M.F.: $C_{12}H_{15}NOSe$ (**M.W.** 268.21)

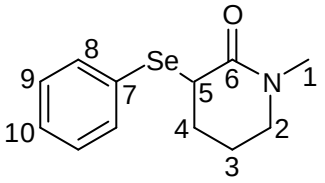
Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flame-dried two-necked flask, 1.406 ml (1.015 g; 10.03 mmol; 2 eq.) of diisopropylamine were dissolved in 6 ml of THF. The mixture was cooled to 0°C. 4.182 ml (10.03 mmol; 2 eq.) of *n*-BuLi, 2.5M solution in hexane, were added and the

mixture was stirred for 10 minutes. It was then cooled to -78°C and 569.6 µl (567 mg; 5.018 mmol; 1 eq.) of 1-methylpiperid-2-one dissolved in 3 ml of THF were slowly added. After 35 minutes of stirring at -78°C, 961 mg (5.018 mmol; 1 eq.) of phenylselenenyl chloride in 2.5 ml of THF and 873 µl (899 mg; 5.018 mmol; 1 eq.) of HMPA were added. The stirring was continued for 35 minutes, then the temperature was raised to -20°C over a period of 30 minutes and finally the mixture was allowed to come to room temperature. The mixture was poured into 100 ml of water and the aqueous phase was extracted 3 times with ether. The organic phase was washed with a 10% solution of NaOH, with water, with a 10% solution of HCl and with water. It was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 883 mg (65 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.98-2.19 (*m*, 4 H, 3, 4); 2.96 (*s*, 3 H, 1); 3.29 (*t*, $^{3}J_{2\text{-}3}$ = 4.8, 2 H, 2); 4.04 (*t*, $^{3}J_{5\text{-}4}$ = 3.6, 1 H, 5); 7.22-7.72 (*2 m*, 5 H, 8, 9, 10)
^{13}C NMR ($CDCl_3$, 75 MHz): 22.7 (3); 27.9 (1); 34.8 (4); 46.1 (2); 49.5 (5); 129.0 (10); 129.1 (8); 129.2 (7); 129.2 (9); 172.1 (6)
Mass (CI -Q1MS): 153 ($[C_6H_5Se]^-$ (^{76}Se), 23%); 155 ($[C_6H_5Se]^-$ (^{78}Se), 58%); 157 ($[C_6H_5Se]^-$ (^{80}Se), 100%); 268 ($[M\text{-}H]^-$ (^{80}Se), 4%)

*5.1.5 Synthesis of 1-methyl-3-(phenylsulfinyl)pyrrolidin-2-one **78***

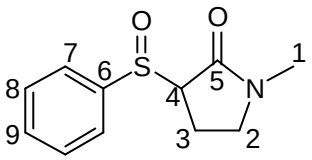
M.F.: $C_{11}H_{13}NO_2S$ (**M.W.** 223.28) **RN: 63914-40-9**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flask, 775 mg (3.738 mmol; 1 eq.) of 1-methyl-3-phenylsulfanylpyrrolidin-2-one **76** were dissolved in 12 ml of MeOH. The mixture was cooled to 0°C and 808 mg (3.738 mmol; 1 eq.) of sodium periodate dissolved in a minimum amount of water were added. The ice bath was removed and the stirring was maintained for 1 hour. The reaction mixture was filtered and the precipitate was washed several times with MeOH. The filtrate was evaporated. The residue was dissolved in Et_2O, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 912 mg (quant.) as a mixture of 2 diastereomers

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.70, 2.08, 2.22 and 2.44-2.64 (3 *mult* + *m*, 2 H, 3); 2.56 and 2.94 (*2 s*, 3 H, 1); 3.04 and 3.33 (*2 mult*, 2 H, 2); 3.55 and 4.20 (*2 mult*, 1 H, 4); 7.45-7.68 (*2 m*, 5 H, 7, 8, 9)
^{13}C NMR ($CDCl_3$, 75 MHz): 13.8 and 15.3 (3); 29.4 and 30.0 (1); 47.6 and 47.8 (2); 65.3 and 66.6 (4); 123.9 and 124.8 (7); 128.6 and 129.1 (8); 130.8 and 131.6 (9); 143.2 (6); 166.4 and 168.0 (5)
IR (liquid film, cm^{-1}): 1048 (S-O); 1684 (C=O); 2928 (C-H)
Mass (CI/CH_4-N_2O): 98 ($[M\text{-}SOC_6H_5]^+$, 100%); 208 ($[M\text{-}Me]^+$, 8%); 224 ($[M+H]^+$, 4%)

*5.1.6 Synthesis of 1-methyl-3-(phenylsulfinyl)piperidin-2-one **79***

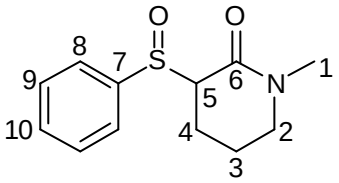
M.F.: $C_{12}H_{15}NO_2S$ (**M.W.** 237.31)

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flame-dried two-necked flask, 1.161 g (5.245 mmol; 1 eq.) of 1-methyl-3-(phenylsulfanyl)piperidin-2-one **77** were dissolved in 27 ml of CH_2Cl_2. The mixture was cooled to 0°C and 1.122 g (5.245 mmol; 1 eq.) of sodium periodate dissolved in a minimum amount of water were added. The ice bath was removed and the stirring continued for 1 hour. The mixture was then filtered and the precipitate washed several times with MeOH. The filtrate was evaporated. The residue was dissolved in Et_2O, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (CH_2Cl_2 : AcOEt 50 : 50 + 10% EtOH)

Yield: 850 mg (68 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.44-2.32 (*2 m*, 4 H, 3, 4); 2.84 and 3.04 (*2 s*, 3 H, 1); 3.25-3.40 (*2 mult*, 2 H, 2); 4.70 (*mult*, 1 H, 5); 7.45-7.69 (*m*, 5 H, 8, 9, 10)
^{13}C NMR ($CDCl_3$, 75 MHz): 17.7 (3); 21.3 (4); 35.3 (1); 49.6 (2); 66.1 (5); 124.3 (8); 128.9 (9); 131.1 (10); 142.7 (7); 164.6 (6)
IR (liquid film, cm^{-1}): 1045 (S-O); 1646 (C=O); 2935 (C-H)
Mass (CI/CH_4-N_2O): 112 ($[M-SOPh]^+$, 100%); 238 ($[M+H]^+$, 5%)

*5.1.7 Synthesis of 1-methyl-1,5-dihydro-2*H*-pyrrol-2-one **73***

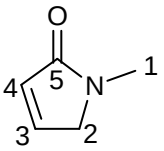
M.F.: C_5H_7NO (**M.W.** 97.11) **RN: 13950-21-5**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

In a flask equipped with a reflux condenser, 910 mg (4.075 mmol; 1 eq.) of 1-methyl-3-(phenylsulfinyl)pyrrolidin-2-one **78** were dissolved in 23 ml of toluene. 411 mg (4.89 mmol; 1.2 eq.) of sodium bicarbonate were added and the mixture was refluxed for 75 minutes. After that time, the mixture was cooled to room temperature and filtered over celite. The celite was washed with CH_2Cl_2 and the filtrate was evaporated under reduced pressure.
The product was purified by flash chromatography (Et_2O : CH_2Cl_2 50 : 50).

Yield: 213 mg (54 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 3.05 (*s*, 3 H, 1); 3.99 (*s*, 2 H, 2); 6.19 (*m*, 1 H, 4); 7.05 (*m*, 1 H, 3)
^{13}C NMR ($CDCl_3$, 75 MHz): 27.8 (1); 54.5 (2); 123.7 (4); 142.2 (3); 171.3 (5)
Mass (CI +Q1MS): 98 ($[M+H]^+$, 100%)

*5.1.8 Synthesis of 5,6-dihydro-1-methyl-2(1H)-pyridinone **74***

M.F.: C_6H_9NO (**M.W.** 111.14) **RN: 69003-17-4**

Reference: Zoretic, P.A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.

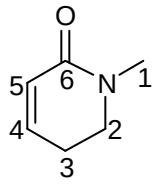
From 1-methyl-3-(phenylsulfinyl)piperidin-2-one **79**:
In a flask equipped with a reflux condenser, 850 mg (3.581 mmol; 1 eq.) of 1-methyl-3-(phenylsulfinyl)piperidin-2-one **79** were dissolved in 20 ml of toluene. 361 mg (4.298 mmol; 1.2 eq.) of sodium bicarbonate were added and the mixture was heated to reflux for 75 minutes. The mixture was cooled to room temperature and filtered over celite. The celite was washed with CH_2Cl_2 and the filtrate was evaporated.
The product was purified by flash chromatography (Et_2O + 10% EtOH).

Yield: 308 mg (77 %)

From 1-methyl-3-phenylselanylpiperidin-2-one **81**:
300 mg (1.118 mmol; 1 eq.) of 1-methyl-3-phenylselanylpiperidin-2-one **81** were dissolved in 7 ml of CH_2Cl_2. 98 µl (108 mg; 1.118 mmol; 1 eq.) of hydrogen peroxide were then slowly added. When the oxidation was complete (2 hours), the organic phase was washed 5 times with a saturated solution of $NaHCO_3$, twice with water and twice with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (Et_2O + 10% EtOH).

Yield: 105 mg (85 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 2.41 (*mult*, 2 H, 3); 2.99 (*s*, 3 H, 1); 3.41 (*t*, $^3J_{2\text{-}3}$ = 7.2, 2 H, 2); 5.92 (*td*, $^3J_{5\text{-}4}$ = 6.5, $^4J_{5\text{-}3}$ = 1.3, 1 H, 5); 6.53 (*dt*, $^3J_{4\text{-}5}$ = 6.6, $^3J_{4\text{-}3}$ = 2.7, 1 H, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 23.8 (3); 34.2 (1); 47.3 (2); 125.2 (5); 139.0 (4); 165.0 (6)
IR (liquid film, cm^{-1}): 818; 1664 (C=O); 2941 (C-H)
GC (100/0/10/290/20): t_R = 10.06 min

5.2 Synthesis of 2,2-dimethylhex-4-en-3-one 75

*5.2.1 Synthesis of 5-hydroxy-2,2-dimethylhexan-3-one **83***

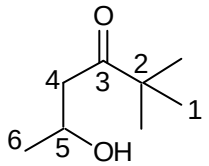
M.F.: $C_8H_{16}O_2$ (**M.W.** 144.21) **RN: 173343-33-4**

Reference (reaction conditions): Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem.* **1974**, *39*, 3459-3460.

In a flame-dried two-necked flask equipped with an addition funnel, 6.164 ml (4.45 g; 43.98 mmol; 1.1 eq.) of diisopropylamine were dissolved in 60 ml of THF. The mixture was cooled to 0°C and 17.59 ml (12.19 g; 43.98 mmol; 1.1 eq.) of *n*-BuLi, 2.5M solution in hexane, were added. After 15 minutes at 0°C, the mixture was cooled to -78°C. 5 ml (4.005 g; 39.98 mmol; 1 eq.) of pinacolone were added and the stirring was continued for 30 minutes. Then 2.235 ml (1.761 g; 39.98 mmol; 1 eq.) of acetaldehyde in 100 ml of THF were slowly added. After 15 minutes, the dry-ice bath was removed and the reaction was immediately quenched by the addition of 2.5 ml (2.641 g; 43.98 mmol; 1.1 eq.) of acetic acid dissolved in Et_2O. Water was added to dissolve the salts formed. The two phases were separated and the aqueous phase was extracted 2 times with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was obtained sufficiently pure to be used without purification.

Yield: 5.76 g (quant.)

Aspect: yellow oil
TLC: R_f = 0.7 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.15 (*s*, 9 H, 1); 1.21 (*d*, $^3J_{6\text{-}5}$ = 6.4, 3 H, 6); 2.53 (*dd*, $^2J_{4'\text{-}4}$ = 17.5, $^3J_{4'\text{-}5}$ = 8.9, 1 H, 4'); 2.70 (*dd*, $^2J_{4\text{-}4'}$ = 17.5, $^3J_{4\text{-}5}$ = 2.7, 1 H, 4); 4.19 (*mult*, 1 H, 5);
^{13}C NMR ($CDCl_3$, 75 MHz): 22.2 (6); 26.2 (1); 44.3 (2); 44.5 (4); 64.0 (5); 217.9 (3)
IR (liquid film, cm^{-1}): 1703 (C=O); 2972 (C-H); 3447 (O-H)
Mass (CI +Q1MS): 85 ($[OCC(CH_3)_3]^+$, 100%); 127 (($[M\text{-}OH]^+$, 56%); 145 ($[M+H]^+$, 78%)

*5.2.2 Synthesis of (*E*)-2,2-dimethylhex-4-en-3-one **75***

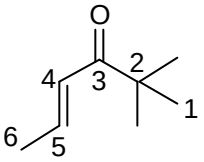
M.F.: $C_8H_{14}O$ (**M.W.** 126.19) **RN: 20971-19-1**

Reference (reaction conditions): Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem.* **1974**, *39*, 3459-3460.

In a flask equipped with a Dean-Stark apparatus, 5.17 g (35.85 mmol; 1 eq.) of 5-hydroxy-2,2-dimethylhexan-3-one **83** and 617 mg (3.585 mmol; 0.1 eq.) of *para*-toluenesulfonic acid were mixed in 127 ml of toluene. The mixture was heated to reflux until the volume of recovered water was constant. The solution was cooled to room temperature and washed with a saturated solution of $NaHCO_3$. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20) or by distillation (75°C at 18 mmHg).

Yield: 2.884 g (64 %)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.15 (*s*, 9 H, 1); 1.90 (*dd*, $^3J_{6\text{-}5}$ = 10.2, $^4J_{6\text{-}4}$ = 1.4, 3 H, 6); 6.46 (*qd*, $^3J_{4\text{-}5}$ = 20.4, $^4J_{4\text{-}6}$ = 1.4, 1 H, 4); 6.88 (*qd*, $^3J_{5\text{-}4}$ = 22.4, $^3J_{5\text{-}6}$ = 10.0, 1 H, 5)
^{13}C NMR ($CDCl_3$, 50 MHz): 18.1 (6); 26.2 (1); 42.7 (2); 125.8 (4); 142.4 (5); 203.9 (3)
IR (liquid film, cm^{-1}): 1691 (C=O); 2970 (C-H)
Mass (CI/CH_4-N_2O): 85 ($[OCC(CH_3)_3]^+$, 37); 127 ($[M+H]^+$, 100%)
b.p.: 75°C (18 mmHg)
GC (60/0/10/290/10): t_R = 5.74 min

6 Michael addition of sulfonamides

6.1 General procedure

In a flame-dried three-necked flask, HMPA, THF and a small quantity of *o*-phenantroline were introduced. *n*-BuLi was then slowly added until the color changed to red. 1 eq. of the sulfonamide was added and the mixture was cooled down to -78°C. 1.05 eq of 2.5M *n*-BuLi were then added. After 1 hour, 1.1 eq. of the Michael

acceptor were added. The reaction mixture was maintained at -78°C for 1 hour, after which 3.5 eq. of Et_3N were added followed by 3.85 eq. of chlorotrimethylsilane. The stirring was continued for 30 minutes and the mixture was allowed to come to room temperature. A few ml of diluted HCl were then added. The solution was concentrated under reduced pressure. Ether was added and the organic phase was washed 5 times with a saturated solution of NaCl to remove HMPA, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The products were separated and purified by flash chromatography.

6.2 Michael addition of achiral sulfonamides to cyclohexenone

*6.2.1 Addition of 1-methylsulfonylpyrrolidine **11***

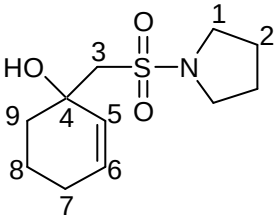
Following the general procedure described in 6.1 with:
28 mg (186 µmol; 1 eq.) of 1-methylsulfonylpyrrolidine **11**
132 µl (195.3 µmol; 1.05 eq.) of *n*-BuLi, 1.48M solution in hexane
20 µl (20 mg; 204.6 µmol; 1.1 eq.) of 2-cyclohexen-1-one
91 µl (66 mg; 655.5 µmol; 3.52 eq.) of Et_3N
91 µl (78 mg; 717.9 µmol; 3.85 eq.) of TMSCl
259 µl (267 mg; 1.488 mmol; 8 eq.) of HMPA
1.8 ml of THF
Flash chromatography: petroleum ether : AcOEt 50 : 50

Only 1,2-addition product was obtained:

*1-[(pyrrolidin-1-ylsulfonyl)methyl]cyclohex-2-en-1-ol **84***
M.F.: $C_{11}H_{19}NO_3S$ (**M.W.** 245.33)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

Yield: 43 ml (95%)
Aspect: viscous oil



^{1}H NMR ($CDCl_3$, 200 MHz): 5.89 (*dt*, $^{3}J_{6\text{-}5}$ = 10.2, $^{3}J_{6\text{-}7}$ = 3.5, 6); 5.75 (*d*, $^{3}J_{5\text{-}6}$ = 10.2, 5); 3.75 (*s*, 1 H, OH); 3.13-3.45 (*m,* 4 H, 1); 3.17 (*s*, 2 H, 3); 1.50-2.50 (*m*, 6 H, 7, 8, 9); 1.90-1.98 (*m*, 4 H, 2)
^{13}C NMR ($CDCl_3$, 50 MHz): 18.7 (8); 24.8 (9); 25.7 (2); 35.4 (7); 47.6 (1); 57.4 (3); 68.2 (4); 130.0 and 130.9 (5, 6)
IR (liquid film, cm^{-1}): 1145 (NSO_2); 1325 (NSO_2); 2935 (C-H); 3470 (O-H)
Mass (CI/CH_4-N_2O): 97 ($[C_6H_8O]^+$, 100%); 180 (44%); 193 (34%); 228 ($[M\text{-}OH]^+$, 7%); 246 ($[M+H]^+$, 2%)

*6.2.2 Addition of 1-ethylsulfonylpyrrolidine **38***

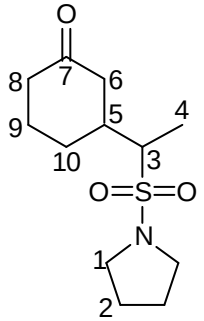
Following the general procedure described in 6.1 with:
500 mg (3.063 mmol; 1 eq.) of 1-(ethylsulfonyl)pyrrolidine **38**
1.3 ml (2.665 mmol; 0.87 eq.) of *n*-BuLi, 2.05 M solution in hexane
326 µl (324 mg; 3.369 mmol; 1.1 eq.) of 2-cyclohexen-1-one
1.5 ml (1.092 g; 10.79 mmol; 3.52 eq.) of Et_3N
1.5 ml (1.284 g; 11.81 mmol; 3.85 eq.) of TMSCl
4.263 ml (4.391 g; 24.5 mmol; 8 eq.) of HMPA
29 ml of THF
Flash chromatography: petroleum ether : AcOEt 50 : 50

1,4- and 1,2-addition products were obtained in a 65 : 35 ratio. After purification we obtained:

*3-[1-(pyrrolidin-1-ylsulfonyl)ethyl]cyclohexanone **85***
M.F.: $C_{12}H_{21}NO_3S$ (**M.W.** 259.36)

Yield: 500 mg (55%) as a mixture of 2 diastereomers (ratio: 83 : 17)

Aspect: viscous oil
TLC: R_f = 0.37 (petroleum ether : AcOEt 50 : 50)

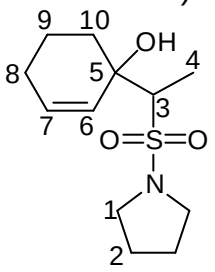


^{1}H NMR ($CDCl_3$, 200 MHz): 1.36 (*d*, $^{3}J_{4-3}$ = 7.1, 3 H, 4); 1.50-2.20 (*m*, 4 H, 9, 10); 1.79-2.01 (*m*, 4 H, 2); 2.20-2.75 (*m*, 5 H, 5, 6, 8); 2.97* (*dq*, $^{3}J_{3-4}$ = 7.2, $^{3}J_{3-5}$ = 3, 1 H, 3*); 3.12 (*dq*, $^{3}J_{3-4}$ = 6.6, $^{3}J_{3-5}$ = 2.7, 1 H, 3); 3.28-3.47 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 10.5 (4); 24.9 (9); 26.0 (2); 29.6 (10); 38.7 (5); 40.9 (8); 43.3 (6); 48.1 (1); 59.3 (3*); 60.8 (3); 210.0 (7)
IR (liquid film, cm^{-1}): 1141 (NSO_2); 1320 (NSO_2); 1705 (C=O); 2961 (C-H)
Mass (CI +Q1MS): 59 (22%); 125 (9%); 154 (25%); 190 (7%); 208 (100%); 257 (19%); 260 ($[M+H]^+$, 51%)
HRMS: calculated for $C_{12}H_{22}NO_3S^+$: 260.132041; found: 260.131466

1-[1-(pyrrolidinyl-1-sulfonyl)ethyl]cyclohex-2-en-1-ol ***86***
M.F.: $C_{12}H_{21}NO_3S$ (**M.W.** 259.36)

Yield: 211 mg (25 %)

Aspect: viscous oil
TLC: R_f = 0.48 (petroleum ether : AcOEt 50 : 50)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.36 (*d*, $^{3}J_{4-3}$ = 7.1, 3 H, 4); 1.45-2.45 (*m*, 6 H, 8, 9, 10); 1.86-2.00 (*m*, 4 H, 2); 3.01 (*mult*, 1 H, 3); 3.32-3.48 (*m*, 4 H, 1); 5.90-5.40 (*m*, 2 H, 6, 7)
^{13}C NMR ($CDCl_3$, 75 MHz): 13.8 (4); 17.9 (9); 24.7 (10); 25.9 (2); 34.2 (8); 48.3 (1); 70.8 and 71.5 (3); 71.7 (5); 129.9 (6); 132.1 (7)
IR (liquid film, cm^{-1}): 1141 (NSO_2); 1311 (NSO_2); 1648 (C=C); 2943 (C-H); 3481 (O-H)
Mass (CI +Q1MS): 59 (45%); 72 (24%); 89 (27%); 97 (11%); 107 (27%); 136 (100%); 164 (85%); 178 (20%); 204 (30%); 242 ($[M-OH]^+$, 49%); 258 ($[M-H]^+$, 16%)
HRMS: calculated for $C_{12}H_{22}NO_3S^+$: 260.132041; found: 260.131705

* minor isomer

*6.2.3 Addition of 1-[(3-methylbutyl)sulfonyl]pyrrolidine **39***

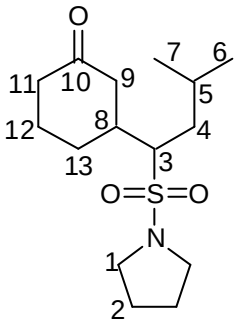
Following the general procedure described in 6.1 with:
500 mg (2.435 mmol; 1 eq.) of 1-(3-methyl-1-butanesulfonyl)pyrrolidine **39**
1.022 ml (2.557 mmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane
259 µl (257 mg; 2.678 mmol; 1.1 eq.) of 2-cyclohexen-1-one
1.192 ml (868 mg; 8.579 mmol; 3.52 eq.) of Et_3N
1.192 ml (1.02 g; 9.396 mmol; 3.85 eq.) of TMSCl
3.389 ml (3.491 g; 19.48 mmol; 8 eq.) of HMPA
23 ml of THF
Flash chromatography: ether : AcOEt 80 : 20

1,4- and 1,2-addition products were obtained in a 79 : 21. After purification we obtained:

*3-[3-methyl-1-(pyrrolidin-1-ylsulfonyl)butyl]cyclohexanone **95***
M.F.: $C_{15}H_{27}NO_3S$ (**M.W.** 301.44)

Yield: 529 mg (72 %) as a mixture of 2 diastereomers (ratio: 86 : 14)

Aspect: viscous oil
TLC: R_f = 0.35 (ether : AcOEt 80 : 20)



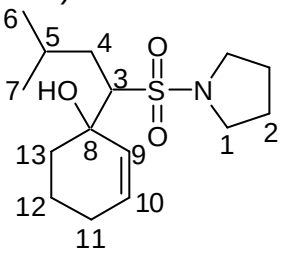
^{1}H NMR ($CDCl_3$, 300 MHz): 0.96 (*mult*, 6 H, 6, 7); 1.50-2.20 (*m*, 7 H, 4, 5, 12, 13); 1.85-2.00 (*m*, 4 H, 2); 2.20-2.69 (*m*, 5 H, 8, 9, 11); 2.96 (*dt*, $^3J_{3\text{-}4}$ = 5.8, $^3J_{3\text{-}8}$ = 2.4, 1 H, 3); 3.32-3.48 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 22.1 and 22.4 (6, 7); 25.0 (12); 25.7 (2); 26.1 (5); 28.2 (13); 35.1 (4); 39.0 (8); 40.8 (11); 44.5 (9); 47.8 (1); 63.4 (3*); 63.5 (3); 210.0 (10)
IR (liquid film, cm^{-1}): 1129 (NSO_2); 1317 (NSO_2); 1710 (C=O); 2965 (C-H)
Mass (CI +Q1MS): 97 ($[C_6H_9O]^+$, 52%); 136 (12%); 149 (9%); 167 (6%); 193 (11%); 204 ($[M\text{-}C_6H_9O]^+$, 79%); 206 (100%); 302 ($[M+H]^+$, 10%)
HRMS: calculated for $C_{15}H_{28}NO_3S^+$: 302.178991; found: 302.178435

* minor isomer

1-[3-methyl-1-(pyrrolidine-1-sulfonyl)butyl]cyclohex-2-enol ***96***
M.F.: $C_{15}H_{27}NO_3S$ (**M.W.** 301.44)

Yield: 99 mg (13 %)

Aspect: viscous oil
TLC: R_f = 0.66 (ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 0.92 (*d*, $^3J_{6,7-5}$ = 6, 6 H, 6, 7); 1.15-2.45 (*m*, 13 H, 2, 4, 5, 11, 12, 13); 3.05-3.22 (*m*, 1 H, 3); 3.30-3.55 (*m*, 4 H, 1); 5.45-6.00 (*m*, 2 H, 9, 10)
^{13}C NMR ($CDCl_3$, 50 MHz): 17.8 (12); 22.7 and 23.0 (6, 7); 24.6 (13); 25.8 (2); 27.0 (5); 31.6 (4); 36.6 (11); 47.6 (1); 68.5 (3); 72.1 (8); 130.0 (9); 132.0 (10)
IR (liquid film, cm^{-1}): 1137 (NSO_2); 1313 (NSO_2); 1634 (C=C); 2957 (C-H); 3481 (O-H)
Mass (CI +Q1MS): 79 (6%); 84 (10%); 136 (11%); 149 (8%); 179 (28%); 206 ([M-C_6H_9O]$^+$, 100%); 215 (36%); 284 ([M-OH]$^+$, 13%); 292 (23%); 302 ([M+H]$^+$, 5%)
HRMS: calculated for $C_{15}H_{28}NO_3S^+$: 302.178991; found: 302.178070

6.2.4 Addition of 1-[(3-ethoxypropyl)sulfonyl]pyrrolidine ***59***

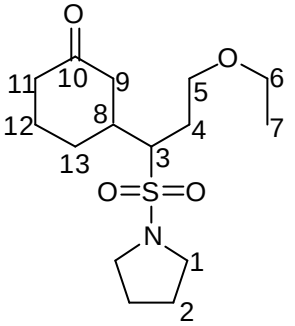
Following the general procedure described in 6.1 with:
150 mg (681.6 µmol; 1 eq.) of (3-ethoxypropane)sulfonylpyrrolidine **59**
447 µl (715.7 µmol; 1.05 eq.) of *n*-BuLi, 1.6M solution in hexane
72 µl (72 mg; 749.8 µmol; 1.1 eq.) of 2-cyclohexen-1-one
333 µl (243 mg; 2.401 mmol; 3.52 eq.) of Et_3N
333 µl (286 mg; 2.630 mmol; 3.85 eq.) of TMSCl
949 µl (977 mg; 5.453 mmol; 8 eq.) of HMPA
6.4 ml of THF
Flash chromatography: petroleum ether : AcOEt 60 : 40

1,4- and 1,2 addition products were obtained in a 83 : 17 ratio. After purification we obtained:

3-[3-ethoxy-1-(pyrrolidin-1-ylsulfonyl)propyl]cyclohexanone ***97***
M.F.: $C_{15}H_{27}NO_4S$ (**M.W.** 317.44)

Yield: 112 mg (52 %) as amixture of 2 diastereomers (ratio: 87 : 13)

Aspect: colorless oil
TLC: R_f = 0.10 (petroleum ether : AcOEt 60 : 40)



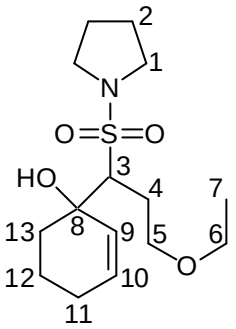
^{1}H NMR ($CDCl_3$, 300 MHz): 1.19 (*t*, $^3J_{7\text{-}6}$ = 7.2, 3 H, 7); 1.53-1.86 (*m*, 4 H, 12, 13); 1.90-1.97 (*m*, 4 H, 2); 2.08-2.46 (*m*, 7 H, 4, 8, 9, 11); 3.19 (*dt*, $^3J_{3\text{-}4}$ = 6.1, $^3J_{3\text{-}8}$ = 2.4, 1 H, 3); 3.34-3.41 (*m*, 4 H, 1); 3.44 (*q*, $^3J_{6\text{-}7}$ = 7.8, 2 H, 6); 3.43-3.60 (*m*, 2 H, 5)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.1 (7); 25.1 (12); 25.8 (2); 26.7 (4); 28.3 (13); 39.0 (8); 40.9 (11); 44.5 (9); 47.8 (1); 62.0 (3*); 62.1 (3); 66.2 and 67.7 (5, 6); 210.0 (10)
IR (liquid film, cm^{-1}): 1142 (NSO_2); 1320 (NSO_2); 1711 (C=O); 2972 (C-H)
Mass (CI/CH_4-N_2O): 193 ($[(CH_2)_4NSO_2(CH_2)_3O]^{\bullet+}$, 43%); 222 ($[M\text{-}C_6H_9O]^+$, 100%); 272 ($[M\text{-}OEt]^+$, 3%); 318 ($[M+H]^+$, 7%)
GC (100/0/10/250/20): t_R = 25.70 min (minor); t_R = 26.26 min (major)
HRMS: calculated for $C_{15}H_{28}NO_4S^+$: 318.173905; found: 318.173511

1-[3-ethoxy-1-(pyrrolidin-1-ylsulfonyl)propyl]cyclohex-2-en-1-ol ***98***
M.F.: $C_{15}H_{27}NO_4S$ (**M.W.** 317.44)

Yield: 22 mg (10 %)

Aspect: colorless oil

* minor isomer



^{1}H NMR ($CDCl_3$, 300 MHz): 1.07 (*t*, $^{3}J_{7\text{-}6}$ = 7, 3 H, 7); 1.45-2.40 (*m*, 12 H, 2, 4, 11, 12, 13); 3.05-3.51 (*m*, 9 H, 1, 3, 5, 6); 5.55-5.97 (*m*, 2 H, 9, 10)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.2 (7); 24.7 (4); 25.6 (12); 25.75 (2); 28 (13); 47.4 (11); 47.6 (1); 65.9 and 66.0 (5, 6); 68.3 (3); 69.5 (8); 130.5 (10); 131.6 (9)
IR (liquid film, cm^{-1}): 1142 (NSO_2); 1324 (NSO_2); 2956 (C-H); 3483 (O-H)
Mass (CI +Q1MS): 72 (55%); 165 (68%); 236 (99%); 255 ($[M\text{-}OH\text{-}EtO]^{\bullet+}$, 17%); 300 ($[M\text{-}OH]^{+}$, 49%); 318 ($[M+H]^{+}$, 7%); 374 (100%)
GC (100/0/10/250/20): t_R = 22.86 min (minor); t_R = 22.96 min (major)

*6.2.5 Addition of 1-{[3-(ethylsulfanyl)propyl]sulfonyl}pyrrolidine **63***

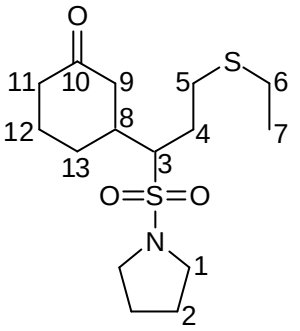
Following the general procedure described in 6.1 with:
150 mg (631.9 µmol; 1 eq.) of 1-{[(3-ethylsulfanyl)propyl]sulfonyl}pyrrolidine **63**
301 µl (663.5 µmol; 1.05 eq.) of *n*-BuLi, 2.2M solution in hexane
67 µl (67 mg; 695.1 µmol; 1.1 eq.) of 2-cyclohexen-1-one
309 µl (225 mg; 2.226 mmol; 3.52 eq.) of Et_3N
309 µl (265 mg; 2.438 mmol; 3.85 eq.) of TMSCl
880 µl (906 mg; 5.055 mmol; 8 eq.) of HMPA
5.9 ml of THF
Flash chromatography: petroleum ether : AcOEt 90 : 10

Only 1,4-addition product was obtained:

*3-[3-(ethylsulfanyl)-1-(pyrrolidin-1-ylsulfonyl)propyl]cyclohexanone **99***
M.F.: $C_{15}H_{27}NO_3S_2$ (**M.W.** 333.5)

Yield: 122 mg (58 %) as a mixture of 2 diastereomers (ratio: 90 : 10)

Aspect: colorless viscous oil
TLC: R_f = 0.5 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.21 (*t*, $^{3}J_{7\text{-}6}$ = 7.1, 3 H, 7); 1.50-2.40 (*m*, 11 H, 4, 8, 9, 11, 12, 13); 1.81-1.95 (*m*, 4 H, 2); 2.49 (*q*, $^{3}J_{6\text{-}7}$ = 7.1, 2 H, 6); 2.67 (*t*, $^{3}J_{5\text{-}4}$ = 7.1, 2 H, 5); 3.18 (*dt*, $^{3}J_{3\text{-}4}$ = 5.8 $^{3}J_{3\text{-}8}$ = 2.3, 1 H, 3); 3.26-3.4 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.6 (7); 25.0 (12); 25.8 (2); 25.9 (4); 28.6 (13); 29.8 (5); 29.9 (6); 38.8 (8); 40.8 (11); 44.2 (9); 47.8 (1); 63.5 (3*); 63.7 (3); 210.1 (10)
IR (liquid film, cm^{-1}): 1139 (NSO_2); 1317 (NSO_2); 1712 (C=O); 2963 (C-H)
Mass (CI +Q1MS): 176 (100%), 352 ($[M+H]^+$, 1%)
GC (100/0/10/290/15): t_R = 22.11 min (minor); t_R = 22.44 min (major)

*6.2.6 Addition of 1-{[3,3,3-tris(ethyloxy)propyl]sulfonyl}pyrrolidine **52***

Following the general procedure described in 6.1 with:
398 mg (1.221 mmol; 1 eq.) of 1-{[3,3,3-tris(ethyloxy)propyl]sulfonyl}pyrrolidine **52**
661 µl (1.282 mmol; 1.05 eq.) of *n*-BuLi, 1.94M solution in hexane
130 µl (129 mg; 1.343 mmol; 1.1 eq.) of 2-cyclohexen-1-one
598 µl (435 mg; 4.303 mmol; 3.52 eq.) of Et_3N
598 µl (512 mg; 4.713 mmol; 3.85 eq.) of TMSCl
1.7 ml (1.751 g; 9.773 mmol; 8 eq.) of HMPA
11.5 ml of THF

Only 1,4-addition product was obtained:

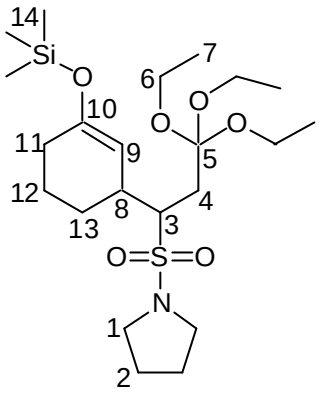
*1-[(3,3,3-tris(ethyloxy)-1-{3-[(trimethylsilyl)oxy]cyclohex-2-en-1-yl}propyl)sulfonyl] pyrrolidine **100***
M.F.: $C_{22}H_{43}NO_6SSi$ (**M.W.** 477.73)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

Yield: 580 mg (quant.)

* minor isomer

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.20 (*s*, 9 H, 14); 1.12 (*t*, $^{3}J_{7\text{-}6}$ = 6.9, 9 H, 7); 1.87 (*mult*, 4 H, 2); 1.55-2.44 (*m*, 8 H, 4, 11, 12, 13); 2.96-3.06 (*m*, 1 H, 8); 3.22-3.28 (*m*, 1 H, 2); 3.36 (*mult*, 4 H, 1); 3.52 (*mult*, 6 H, 6); 4.98 (*broad s*, 1 H, 9)
^{13}C NMR ($CDCl_3$, 75 MHz): 0.3 (14); 14.8 (7); 22.4 (13); 25.2 (12); 25.5 (2); 26.3 (11); 29.3 (4); 36.0 (8); 47.4 (1); 57.1 (6); 61.3 (3); 105.5 (9); 113.5 (5); 151.6 (10)

6.3 Michael addition of chiral sulfonamides to cyclohexenone

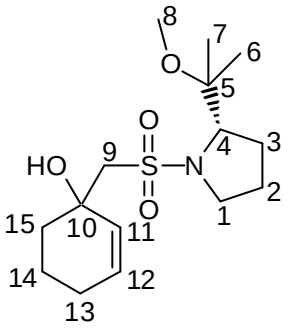
*6.3.1 Addition of (2S)-(1-methoxy-1-methylethyl)-1-methylsulfonylpyrrolidine **14***

Following the general procedure described in 6.1 with:
500 mg (2.259 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-(methylsulfonyl)pyrrolidine **14**
949 µl (2.372 mmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane
240 µl (239 mg; 2.485 mmol; 1.1 eq.) of 2-cyclohexen-1-one
1.106 ml (805 mg; 7.959 mmol; 3.52 eq.) of Et_3N
1.106 ml (947 mg; 8.716 mmol; 3.85 eq.) of TMSCl
3.144 ml (3.238 g; 18.07 mmol; 8 eq.) of HMPA
21 ml of THF

Only 1,2-addition product was obtained:

*1-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonylmethyl]cyclohex-2-enol **115***
M.F.: $C_{15}H_{27}NO_4S$ (**M.W.** 317.44)

Yield: 717 mg (quant.)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.01 and 1.03 (*2 s*, 6 H, 6 ,7); 1.30-2.12 (*m*, 10 H, 2, 3, 13, 14, 15); 3.06 (*s*, 2 H, 9); 3.06 (*s*, 3 H, 8); 3.51-3.62 (*m*, 2 H, 1, 4); 3.76-3.95 (*m*, 1 H, 1); 5.69-5.85 (*m*, 2 H, 11, 12)

^{13}C NMR ($CDCl_3$, 75 MHz): 18.6 and 18.7 (6, 7); 21.4 (15); 25.7 and 26.8 (2, 3); 26.6 and 36.2 (13, 14); 49.0 (8); 49.3 (1); 65.9 (4); 71.1 (10); 71.3 (9); 77.7 (5); 130.3 and 131.2 (11, 12)

IR (liquid film, cm^{-1}): 1140 (NSO_2); 1325 (NSO_2); 2930 (C-H); 3475 (O-H)

Mass (CI +Q1MS): 73 ($[C(CH_3)_2OMe]^+$, 7%); 111 ($[M\text{-}SO_2N^*]^+$, 4%); 190 (100%); 203 (40%); 220 ($[M\text{-}C_6H_9O]^+$, 9%); 262 (40%); 268 (27%); 277 (26%); 300 ($[M\text{-}OH]^+$, 24%)

*6.3.2 Addition of (2S)-1-ethylsulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine **43***

Following the general procedure described in 6.1 with:

500 mg (2.124 mmol; 1 eq.) of (2*S*)-1-(ethylsulfonyl)-2-(1-methoxy-1-methylethyl)pyrrolidine **43**

892 µl (2.23 mmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane

226 µl (224 mg; 2.337 mmol; 1.1 eq.) of 2-cyclohexen-1-one

1.04 ml (757 mg; 7.484 mmol; 3.52 eq.) of Et_3N

1.04 ml (890 mg; 8.197 mmol; 3.85 eq.) of TMSCl

2.957 ml (3.045 g; 16.99 mmol; 8 eq.) of HMPA

20 ml of THF

Flash chromatography: ether : petroleum ether 60 : 40

1,4- and 1,2-addition products were obtained in a 50 : 50 ratio. After purification we obtained:

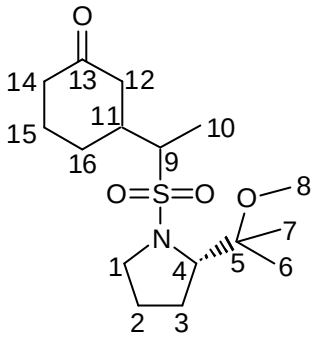
*3-{1-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]ethyl}cyclohexanone **116***

M.F.: $C_{16}H_{29}NO_4S$ (**M.W.** 331.47)

Yield: 279 mg (40 %)

Aspect: viscous oil

TLC: R_f = 0.14 (ether : petroleum ether 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.08 and 1.13 (*2 s*, 6 H, 6, 7); 1.38 (*mult*, 3 H, 10); 1.51-2.60 (*m*, 13 H, 2, 3, 11, 12, 14, 15, 16); 2.92-3.07 (*m*, 1 H, 1); 3.22 (*s*, 3 H, 8); 3.48 (*mult*, 1 H, 9); 3.86-4.01 (*m*, 1 H, 1); 4.20-4.35 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 50 MHz): 9.0 (10); 20.2 and 21.4 (6, 7); 25.0 and 26.7 (15, 16); 28.1 and 29.2 (2, 3); 38.5 (11); 42.1 and 43.6 (12, 14); 48.9 (8); 50.6 (1); 61.0 (9); 61.3 (9*); 65.5 (4); 78.1 (5); 210.0 (13)

IR (liquid film, cm^{-1}): 1141 (NSO_2); 1320 (NSO_2); 1705 (C=O); 2961 (C-H)

Mass (CI +Q1MS): 206 (12%); 248 (100%); 280 (26%); 331 ($M^{\bullet+}$, 1%)

HRMS: calculated for $C_{16}H_{30}NO_4S^+$: 332.189556; found: 332.189770

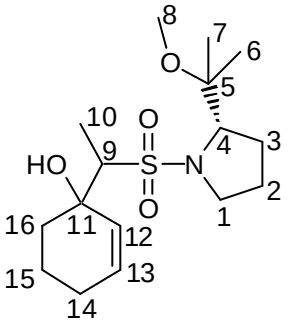
1-{1-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]ethyl}cyclohex-2-enol ***117***

M.F.: $C_{16}H_{29}NO_4S$ (**M.W.** 331.47)

Yield: 256 mg (37 %) as a mixture of 2 diastereomers (ratio: 56 : 44)

Aspect: viscous oil

TLC: R_f = 0.37 (ether : petroleum ether 60 : 40)



* minor isomer

^{1}H NMR ($CDCl_3$, 300 MHz): 1.14 and 1.17 (*2 s*, 6 H, 6, 7); 1.38 (*mult*, 3 H, 10); 1.50-2.60 (*m*, 10 H, 2, 3, 14, 15, 16); 3.00-3.15 (*m*, 1 H, 1); 3.19 (*s*, 3 H, 8); 3.48 (*mult*, 1 H, 9); 3.75-3.85 (*m*, 1 H, 1); 4.06-4.12 (*m*, 1 H, 4); 5.95-5.45 (*m*, 2 H, 12, 13)
^{13}C NMR ($CDCl_3$, 75 MHz): 7.9 (10); 21.2 and 21.5 (6, 7); 26.3 and 27.2 (2, 3); 23.0, 26.9 and 27.4 (14, 15, 16); 49.1 (8); 50.0 (1); 58.0 (9); 66.0 (4); 71.5 (11); 77.8 (5); 130.1 and 131.9 (12, 13)
IR (liquid film, cm^{-1}): 1150 (NSO_2); 1324 (NSO_2); 2977 (C-H); 3490 (O-H)
Mass (CI +Q1MS): 45 (55%); 73 ($[C(CH_3)_2OMe]^+$, 3%); 144 (25.5%); 176 (8%); 190 (12%); 204 (30%); 206 (8%); 248 (48%); 258 ($[M\text{-}C(CH_3)_2OMe]^+$, 13%); 260 (25%); 282 ($[M\text{-}OH\text{-}OMe]^+$, 100%); 300 (17%); 314 ($[M\text{-}OH]^+$, 55%); 330 ($[M\text{-}H]^+$, 8%)
HRMS: calculated for $C_{16}H_{30}NO_4S^+$: 332.189556; found: 332.189587

*6.3.3 Addition of (2S)-(1-methoxy-1-methylethyl)-1-[(3-methylbutyl) sulfonyl]pyrrolidine **44***

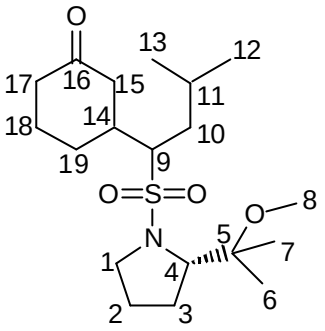
Following the general procedure described in 6.1 with:
500 mg (1.802 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-(3-methylbutyl)sulfonylpyrrolidine **44**
1.153 ml (1.892 mmol; 1.05 eq.) of *n*-BuLi, 1.64M solution in hexane
192 µl (190 mg; 1.982 mmol; 1.1 eq.) of 2-cyclohexen-1-one
882 µl (642 mg; 6.349 mmol; 3.52 eq.) of Et_3N
882 µl (755 mg; 6.953 mmol; 3.85 eq.) of TMSCl
2.508 ml (2.583 g; 14.41 mmol; 8 eq.) of HMPA
17 ml of THF
Flash chromatography: ether : petroleum ether 80 : 20

1,4- and 1,2-addition products were obtained in a 68 : 32 ratio. After purification we obtained:

*3-{1-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]-3-methylbutyl}-cyclohexanone **118***
M.F.: $C_{19}H_{35}NO_4S$ (**M.W.** 373.55)

Yield: 350 mg (52 %) as a mixture of 2 diastereomers (ratio: 90 : 10)

Aspect: brown oil
TLC: R_f = 0.63 (ether : petroleum ether 80 : 20)

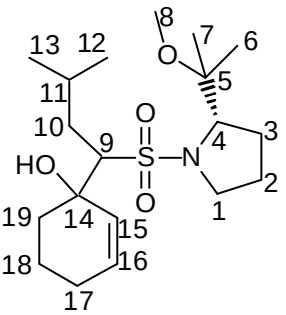


^{1}H NMR ($CDCl_3$, 200 MHz): 0.95 (*mult*, 6 H, 12, 13); 1.13 and 1.09 (*2 s*, 6 H, 6, 7); 1.2-2.6 (*m*, 15 H, 2, 3, 10, 11, 15, 17, 18, 19); 2.69-2.81 (*m*, 1 H, 14); 2.95 (*mult*, 1 H, 9); 3.21 (*s*, 3 H, 8); 3.45-3.55 (*m*, 1 H, 1); 3.90-4.04 (*m*, 1 H, 1); 4.25-4.36 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 20.2, 21.3, 21.8 and 22.7 (6, 7, 12, 13); 26.1 (11); 25.2 and 26.6 (18, 19); 28.0 and 29.5 (2, 3); 33.9 (10); 38.4 (14); 40.8 (15); 42.7 (17); 48.9 (8); 50.8 (1); 63.9 (9); 64.7 (9*); 65.5 (4); 77.9 (5); 210.0 (16)
IR (liquid film, cm^{-1}): 1140 (NSO_2); 1317 (NSO_2); 1713 (C=O); 2957 (C-H)
Mass (CI +Q1MS): 84 (100 %); 300 ($[M-C(CH_3)_2OMe]^+$, 1%); 342 ($[M-OMe]^+$, 5%); 374 ($[M+H]^+$, 2%)
HRMS: calculated for $C_{19}H_{36}NO_4S^+$: 374.236506; found: 374.235452

1-{1-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]-3-methylbutyl}-cyclohex-2-enol ***119***
M.F.: $C_{19}H_{35}NO_4S$ (**M.W.** 373.55)

Yield: 142 mg (21 %)

Aspect: brown oil



^{1}H NMR ($CDCl_3$, 200 MHz): 0.95 (*mult*, 6 H, 12, 13); 1.15 and 1.18 (*2 s*, 6 H, 6, 7); 1.23-2.50 (*m*, 13 H, 2, 3, 10, 11, 17, 18, 19); 3.02 (*mult*, 1 H, 9); 3.20 (*s*, 3 H, 8); 3.43-3.52 (*m*, 1 H, 1); 3.70-3.80 (*m*, 1 H, 1); 4.20-4.30 (*m*, 1 H, 4); 5.50-5.95 (*m*, 2 H, 15, 16)

* minor isomer

^{13}C NMR ($CDCl_3$, 75 MHz): 18.0 (18); 21.2 and 21.8 (6, 7); 22.9 (12, 13); 25.0 (19); 26.8 (11); 26.1 and 27.2 (2, 3); 31.0 (10); 36.5 (17); 49.1 (8); 50.4 (1); 65.4 (4); 68.0 (9); 72.4 (14); 77.7 (5); 130.6 and 131.4 (15, 16)
IR (liquid film, cm^{-1}): 1127 (NSO_2); 1340 (NSO_2); 2957 (C-H); 3481 (O-H)
Mass (CI +Q1MS): 73 ($[C(CH_3)_2OMe]^+$, 14%); 144 (100%); 244 (72%); 300 ($[M-C(CH_3)_2OMe]^+$, 28%); 356 ($[M-OH]^+$, 55%); 374 ($[M+H]^+$, 22%)
HRMS: calculated for $C_{19}H_{36}NO_4S^+$: 374.236506; found: 374.235807

*6.3.4 Addition of (2S)-1-[(3-ethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **65***

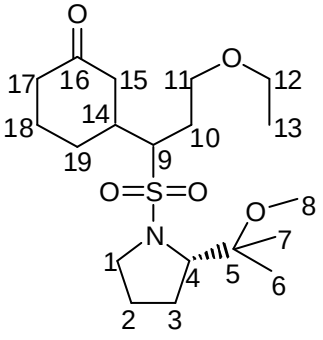
Following the general procedure described in 6.1 with:
200 mg (681.6 µmol; 1 eq.) of (2*S*)-(1-methoxy-1-methylethyl)-1-(3-ethoxypropyl)-sulfonylpyrrolidine **65**
391 µl (715.6 µmol; 1.05 eq.) of *n*-BuLi, 1.83M solution in hexane
73 µl (72 mg; 749.7 µmol; 1.1 eq.) of 2-cyclohexen-1-one
334 µl (243 mg; 2.401 mmol; 3.52 eq.) of Et_3N
334 µl (286 mg; 2.629 mmol; 3.85 eq.) of TMSCl
949 µl (977 mg; 5.452 mmol; 8 eq.) of HMPA
6.4 ml of THF
Flash chromatography: petroleum ether : AcOEt 80 : 20

Only 1,4-addition product was obtained:

*3-(3-ethoxy-1-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}propyl)-cyclohexanone **120***
M.F.: $C_{19}H_{35}NO_5S$ (**M.W.** 389.55)

Yield: 260 mg (98 %) as a mixture of 3 diastereomers (ratio: 83 : 10 : 7)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.16-1.08 (*2 s*, 6 H, 6, 7); 1.22 (*t*, $^{3}J_{13\text{-}12}$ = 6.9, 3 H, 13); 1.47-2.57 (*m*, 15 H, 2, 3, 10, 14, 15, 17, 18, 19); 2.92 (*mult*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.49 (q, $^{3}J_{12\text{-}13}$ = 6.9, 2 H, 12); 3.52-3.71 (*m*, 5 H, 9, 11); 3.92-4.01 (*m*, 1 H, 1); 4.25-4.31 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.2 (13); 20.4 and 21.5 (6, 7); 25.4, 25.5 and 26.8 (10, 18, 19); 28.2 and 29.5 (2, 3); 38.5 (14); 41.1 (15); 42.8 (17); 49.1 (8); 51.0 (1); 63.0 (9) 63.5 (9*); 65.6 (4); 66.2 and 68.5 (11, 12); 78.1 (5); 210.7 (16)
IR (liquid film, cm^{-1}): 1137 (NSO_2); 1317 (NSO_2); 1713 (C=O); 2975 (C-H)
Mass (CI/CH_4-N_2O): 73 ($[C(CH_3)_2OMe]^+$, 2%); 183 ($[M\text{-}SO_2N^*]^+$, 29%); 316 ($[M\text{-}(C(CH_3)_2OMe)]^+$, 13%); 344 ($[M\text{-}OEt]^+$, 6%); 358 ($[M\text{-}OMe]^+$, 100%); 390 ($[M+H]^+$, 66%)
GC (150/0/10/290/20): t_R = 18.33 min; 18.85 min (major); 19.14 (minor)

*6.3.5 Addition of (2S)-1-[(3-ethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **65** (0 eq. of HMPA)*

Following the general procedure with:
200 mg (681.6 µmol; 1 eq.) of (2*S*)-(1-methoxy-1-methylethyl)-1-(3-ethoxypropyl)-sulfonylpyrrolidine **65**
341 µl (715.6 µmol; 1.05 eq.) of *n*-BuLi, 2.1M solution in hexane
73 µl (72 mg; 749.7 µmol; 1.1 eq.) of 2-cyclohexen-1-one
334 µl (243 mg; 2.401 mmol; 3.52 eq.) of Et_3N
334 µl (286 mg; 2.629 mmol; 3.85 eq.) of TMSCl
0 ml of HMPA
6.4 ml THF
Flash chromatography: petroleum ether : AcOEt 80 : 20

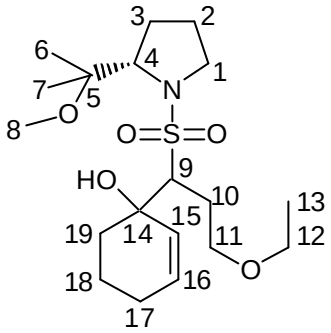
Only 1,2-addition product was obtained:

*1-(3-ethoxy-1-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}propyl)-cyclohex-2-en-1-ol **125***
M.F.: $C_{19}H_{35}NO_5S$ (**M.W.** 389.55)

Yield: 218 mg (82 %)

Aspect: yellow oil

* minor isomer



^{1}H NMR ($CDCl_3$, 200 MHz): 1.11 and 1.13 (*2 s*, 6 H, 6, 7); 1.18 (*t*, $^{3}J_{13\text{-}12}$ = 7.1, 3 H, 13); 1.60-2.50 (*m*, 12 H, 2, 3, 10, 17, 18, 19); 2.97-3.11 (*m*, 1 H, 9); 3.21 (*s*, 3 H, 8); 3.43-3.90 (*m*, 6 H, 1, 11, 12); 4.19-4.30 (*m*, 1 H, 4); 5.89-6.12 (*m*, 2 H, 15, 16)

^{13}C NMR ($CDCl_3$, 50 MHz): 15.1 (13); 21.7 and 21.8 (6, 7); 22.7 (18); 24.7 (10); 26.0 and 27.2 (2, 3); 28.0 (19); 34.4 (17); 49.0 (8); 50.1 (1); 65.4 (4); 67.5 (9); 68.6 and 69.2 (11, 12); 71.2 (14); 77.7 (5); 128.7 (16); 131.9 (15)

IR (liquid film, cm^{-1}): 1125 (NSO_2); 1319 (NSO_2); 1685 (C=C); 2974 (C-H); 3481 (O-H)

Mass (CI +Q1MS): 73 ($[C(CH_3)_2OMe]^+$, 9%); 97 ($[C_6H_9O]^+$, 95%); 216 (71%); 262 (100%); 372 ($[M\text{-}OH]^+$, 10%); 390 ($[M+H]^+$, 5%)

*6.3.6 Addition of (2S)-1-{[3-(ethylsulfanyl)propyl]sulfonyl}-2-(1-methoxy-1-methylethyl)-pyrrolidine **66***

Following the general procedure described in 6.1 with:

150 mg (484.6 µmol; 1 eq.) of (2*S*)-1-{[3-(ethylsulfanyl)propyl]sulfonyl}-2-(1-methoxy-1-methylethyl)pyrrolidine **66**

231 µl (508.9 µmol; 1.05 eq.) of *n*-BuLi, 2.2M solution in hexane

52 µl (51 mg; 533.1 µmol; 1.1 eq.) of 2-cyclohexen-1-one

237 µl (173 mg; 1.707 mmol; 3.52 eq.) of Et_3N

237 µl (203 mg; 1.87 mmol; 3.85 eq.) of TMSCl

675 µl (695 mg; 3.877 mmol; 8 eq.) of HMPA

4.6 ml of THF

Flash chromatography: petroleum ether : AcOEt 80 : 20

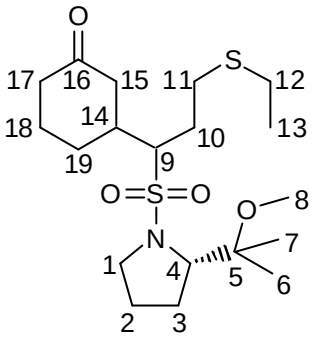
Only 1,4-additon product was obtained:

*3-(3-(ethylsulfanyl)-1-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]-sulfonyl}propyl)cyclohexanone **121***

M.F.: $C_{19}H_{35}NO_4S_2$ (**M.W.** 405.61)

Yield: 152 mg (77 %) as a mixture of 2 diastereomers (ratio: 90 : 10)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.06 and 1.13 (*2 s*, 6 H, 6, 7); 1.27 (*t*, $^{3}J_{13\text{-}12}$ = 8.3, 3 H, 13); 1.56-2.52 (*m*, 14 H, 2, 3, 10, 15, 17, 18, 19); 2.57 (*q*, $^{3}J_{12\text{-}13}$ = 8.3, 2 H, 12); 2.74-2.83 and 2.88-3.00 (*2 m*, 4 H, 1, 11, 14); 3.23 (*s*, 3 H, 8); 3.64-3.7 (*m*, 1 H, 9); 3.93-4.02 (*m*, 1 H, 1); 4.24-4.51 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 50 MHz): 14.7 (13); 20.3 and 21.5 (6, 7); 25.2 and 25.3 (18, 19); 25.8 (12); 26.8 (10); 28.2 and 29.7 (2, 3); 30.4 (11); 38.5 (14); 41.0 and 42.8 (15, 17); 49.2 (8); 51.0 (1); 64.8 (9); 65.8 (4); 66.1 (9*); 78.1 (5); 209.9 (16*); 210.4 (16)

IR (liquid film, cm^{-1}): 1134 (NSO_2); 1308 (NSO_2); 1712 (C=O); 2974 (C-H)

Mass (CI -Q1MS): 246 ($[N^*SO_2C_3H_5]^-$, 100%); 282 (58%); 344 ([M-SEt]$^-$, 3%); 404 ([M-H]$^-$, 1%)

GC (150/0/10/290/20): t_R = 21.35 min (minor); t_R = 22.22 min (major)

*6.3.7 Addition of (2S)-1-[(3,3-diethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **57***

Following the general procedure described in 6.1 with:

150 mg (416 µmol; 1 eq.) of (2*S*)-1-[(3,3-diethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **57**

199 µl (436.8 µmol; 1.05 eq.) of *n*-BuLi, 2.2M solution in hexane

44 µl (43 mg; 457.6 µmol; 1.1 eq.) of 2-cyclohexen-1-one

204 µl (148 mg; 1.465 mmol; 3.52 eq.) of Et_3N

204 µl (174 mg; 1.605 mmol; 3.85 eq.) of TMSCl

580 µl (596 mg; 3.328 mmol; 8 eq.) of HMPA

3.9 ml of THF

Flash chromatography: petroleum ether : AcOEt 80 : 20

* minor isomer

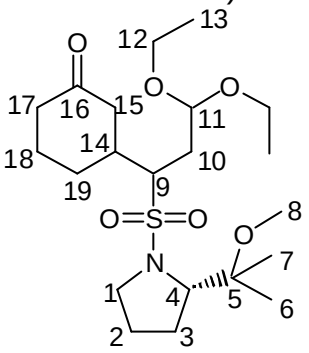
3-(3,3-diethoxy-1-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}-propyl)cyclohexanone ***122***

M.F.: $C_{21}H_{39}NO_6S$ (**M.W.** 433.6)

Yield: 137 mg (76 %) as a mixture of 2 diastereomers (ratio: 85 : 15)

Aspect: yellow oil

TLC: R_f = 0.17 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.07 and 1.13 (*2 s*, 6 H, 6, 7); 1.22 (*t*, $^3J_{13\text{-}12}$ = 6.0, 6 H, 13); 1.56-2.55 (*m*, 14 H, 2, 3, 10, 14, 15, 17, 18, 19); 2.72-2.81 (*m*, 1 H, 17); 2.95 (*mult*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.61-3.57 (*2 mult* + *m*, 5 H, 9, 12); 3.95 (*mult*, 1 H, 1); 4.24 (*mult*, 1 H, 4); 4.89 (*dd*, $^3J_{11\text{-}10}$ = 8.4, $^3J_{11\text{-}10'}$ = 3.0, 1 H, 11)

^{13}C NMR ($CDCl_3$, 75 MHz): 15.4 (13); 20.1 and 21.5 (6, 7); 25.3, 28.0, 26.8, 29.9, 29.4 (2, 3, 10, 18, 19); 38.5 (14); 41.1 (15); 42.7 (17); 49.0 (8); 50.9 (1); 62.2 (9); 62.2 (12); 66.0 (4); 78.0 (5); 101.6 (11), 210.4 (16)

IR (liquid film, cm^{-1}): 1135 (NSO_2); 1325 (NSO_2); 1713 (C=O); 2975 (C-H)

Mass (CI/CH_4-N_2O): 73 ($[C(CH_3)_2OMe]^+$, 30%); 112 (46%); 144 (61%); 181 (65%); 278 (87%); 324 (100%); 360 ($[M\text{-}C(CH_3)_2OMe]^+$, 5%); 434 ($[M+H]^+$, 1%)

GC (100/0/10/290/20): t_R = 22.97 min (minor); t_R = 23.43 min (major)

6.3.8 Addition of (2S)-1-{[2-(1,3-dioxolan-2-yl)ethyl]sulfonyl}-2-(1-methoxy-1-methylethyl)pyrrolidine ***58***

Following the general procedure described in 6.1 with:

109 mg (354.5 µmol; 1 eq.) of (2*S*)-1-{[2-(1,3-dioxolan-2-yl)ethyl]sulfonyl}-2-(1-methoxy-1-methylethyl)-pyrrolidine **58**

149 µl (372.3 µmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane

38 µl (37 mg; 390 µmol; 1.1 eq.) of 2-cyclohexen-1-one

174 µl (126 mg; 1.249 mmol; 3.52 eq.) of Et_3N

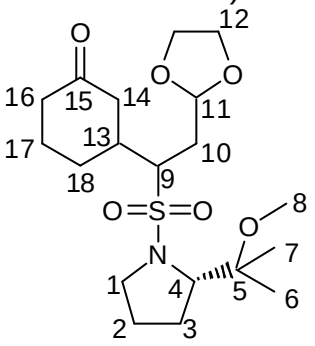
174 µl (148 mg; 1.368 mmol; 3.85 eq.) of TMSCl

493 µl (508 mg; 2.836 mmol; 8 eq.) of HMPA
3.3 ml of THF

Yield: 109 mg (76 %) as a mixture of 3 diastereomers (ratio: 69 : 29 : 2)

3-[2-(1,3-dioxolan-2-yl)-1-({(2S)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)ethyl]cyclohexanone ***123***
M.F.: $C_{19}H_{33}NO_6S$ (**M.W.** 403.53)

Aspect: colorless oil
TLC: R_f = 0.21 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.12 and 1.15 (*2 s*, 6 H, 6, 7); 1.65-2.48 (*m*, 15H, 2, 3, 10, 13, 14, 16, 17, 18); 3.02-3.11 (*m*, 1 H, 1); 3.18 (*s*, 3 H, 8); 3.75-3.98 (*2 mult + 2 m*, 6 H, 1, 9, 12); 4.99 (*t*, $^3J_{11\text{-}10}$ = 4.0, 1 H, 11)
^{13}C NMR ($CDCl_3$, 75 MHz): 20.2 and 21.4 (6, 7); 25.2, 26.7, 28.2, 29.2 and 29.8 (2, 3, 10, 17, 18); 38.5 (13); 41.0 and 42.9 (14, 16); 49.0 (8); 51.0 (1); 62.0 (9); 64.7 and 65.0 (12); 65.5 (4); 78.1 (5); 102.7 (11); 210.6 (15)
IR (liquid film, cm^{-1}): 1135 (NSO_2); 1316 (NSO_2); 1713 (C=O); 2941 (C-H)
GC (100/0/10/290/20): 23.55 min (major); 24.18 min; 24.42 min (minor)

6.3.9 Addition of (2S)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl) sulfonyl]pyrrolidine ***10***

Following the general procedure described in 6.1 with:
200 mg (524.2 µmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl) sulfonyl]pyrrolidine **10**
229 µl (550.4 µmol; 1.05 eq.) of *n*-BuLi, 2.4M solution in hexane
56 µl (55 mg; 576.6 µmol; 1.1 eq.) of 2-cyclohexen-1-one
257 µl (186 mg; 1.846 mmol; 3.52 eq.) of Et_3N
257 µl (219 mg; 2.022 mmol; 3.85 eq.) of TMSCl
730 µl (751 mg; 4.193 mmol; 8 eq.) of HMPA

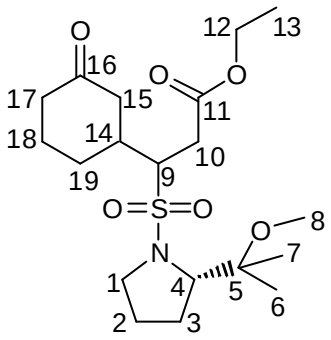
4.9 ml of THF

Only 1,4-addition product was obtained:

ethyl 3-{[(2S)-2-(1-methoxy-1-methylethyl)cyclopentyl]sulfonyl}-3-(3-oxocyclohexyl)propanoate ***124***
M.F.: $C_{19}H_{33}NO_6S$ (**M.W.** 403.53)

Yield: 228 mg (quant.)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 200 MHz): 1.06 and 1.11 (*2 s*, 6 H, 6, 7); 1.28 (*t*, $^3J_{13\text{-}12}$ = 7.0, 3 H, 13); 1.50-3.00 (*m*, 17 H, 1, 2, 3, 9, 10, 14, 15, 17, 18, 19); 3.21 (*s*, 3 H, 8); 3.80-3.91 (*m*, 1 H, 1); 4.04-4.30 (*mult* + *m*, 3 H, 4, 12)
^{13}C NMR ($CDCl_3$, 75 MHz): 14.1 (13); 20.3 and 21.4 (6, 7); 25.1 and 26.6 (2, 3); 27.8 and 29.4 (18, 19); 30.3 (10); 38.3 (14); 40.9 and 43.0 (15, 17); 49.1 (8); 50.8 (1); 61.1 (12); 62.0 (9); 65.5 (4); 77.9 (5); 171.3 (11); 209.7 (16)
IR (liquid film, cm^{-1}): 1139 (NSO_2); 1320 (NSO_2); 1715 ($C{=}O_{ketone}$); 1738 ($C{=}O_{ester}$); 2977 (C-H)
Mass (CI/CH_4-N_2O): 73 ($[C(CH_3)_2OMe]^+$, 6%); 97 ($[C_6H_9O]^+$, 100%); 180 (66%); 276 (26%); 306 ($[M\text{-}C_6H_9O]^+$, 2%); 404 ($[M+H]^+$, 1%)
HRMS: calculated for $C_{19}H_{34}NO_6S^+$: 404.210685; found: 404.209317

6.4 Michael addition to other acceptors

6.4.1 Addition of ***65*** *to crotonaldehyde*

Following the general procedure described in 6.1 with:
200 mg (681.6 µmol; 1 eq.) of (2*S*)-1-[(3-ethoxypropyl)sulfonyl]-2-(1-methoxy-1-methylethyl)pyrrolidine **65**
375 µl (715.6 µmol; 1.05 eq.) of *n*-BuLi, 1.91M solution in hexane

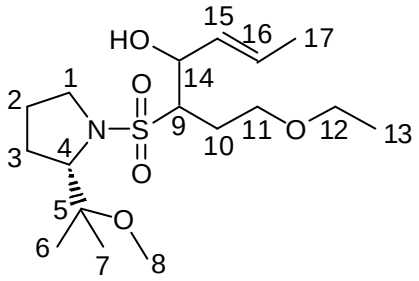
61 µl (52 mg; 749.7 µmol; 1.1 eq.) of crotonaldehyde
334 µl (242 mg; 2.401 mmol; 3.52 eq.) of Et_3N
334 µl (285 mg; 2.629 mmol; 3.85 eq.) of TMSCl
950 µl (977 mg; 5.452 mmol; 8 eq.) of HMPA
5.7 ml of THF
Flash chromatography: petroleum ether : AcOEt 60 : 40

Only 1,2-addition product was obtained:

7-(ethyloxy)-5-({(2S)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)hept-2-en-4-ol ***128***
M.F.: $C_{17}H_{33}NO_5S$ (**M.W.** 363.51)

Yield: 100 mg (40 %)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.09 and 1.12 (*2 s*, 6 H, 6, 7); 1.18 (*t*, $^3J_{13\text{-}12}$ = 7.1, 3 H, 13); 1.58-2.18 (*m*, 6 H, 2, 3, 10); 1.73 (*d*, $^3J_{17\text{-}16}$ = 6.5, 3 H, 17); 3.04 (*mult*, 1 H, 9); 3.14-3.25 (*m*, 1 H, 1); 3.22 (*s*, 3 H, 8); 3.48 and 3.61 (*2 mult + m*, 5 H, 1, 11, 12); 4.01 (*mult*, 1 H, 4); 4.29 (*dd*, ^3J = 8.8, ^3J = 6.2, 14); 4.26 (*broad s*, 1 H, OH); 5.43 (*mult*, 1 H, 16); 5.83 (*mult*, 1 H, 15)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.1 (13); 17.7 (17); 20.1 and 21.4 (6, 7); 23.4 (10); 26.9 and 28.2 (2, 3); 49.1 (8); 51.4 (1); 64.0 (4); 65.8 (9); 65.8 and 68.2 (11, 12); 69.3 (14); 78.2 (5); 127.5 (15); 129.6 (16)
IR (liquid film, cm^{-1}): 1150 (NSO_2); 1325 (NSO_2); 2980 (C-H); 3510 (O-H)
Mass (CI/CH_4-N_2O): 262 ([M-OMe-C_4H_7O]$^+$, 100%); 346 ([M-OH]$^+$, 8%); 364 ([M+H]$^+$, 10%)
GC (60/0/10/290/15): t_R = 24.68 min
HRMS: calculated for $C_{17}H_{34}NO_5S^+$: 364.215770; found: 364.215853

*6.4.2 Addition of **65** to 2,2-dimethylhex-4-en-3-one **75***

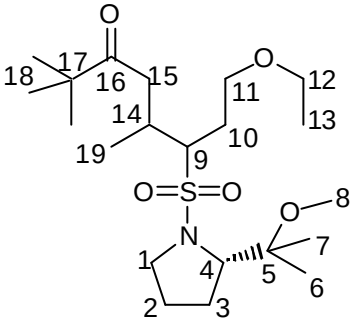
Following the general procedure with:
200 mg (681.6 µmol; 1 eq.) of (2*S*)-1-{[3-(ethyloxy)propyl]sulfonyl}-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidine **65**
330 µl (715.6 µmol; 1.05 eq.) of *n*-BuLi, 2.17M solution in hexane
95 mg (749.7 µmol; 1.1 eq.) of (*E*)-2,2-dimethylhex-4-en-3-one **75**
334 µl (242 mg; 2.401 mmol; 3.52 eq.) of Et_3N
334 µl (285 mg; 2.629 mmol; 3.85 eq.) of TMSCl
949 µl (977 mg; 5.452 mmol; 8 eq.) of HMPA
6.4 ml of THF
Flash chromatography: petroleum ether : AcOEt 60 : 40

Only 1,4-addition product was obtained:

*8-ethoxy-6-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]-2,2,5-trimethyloctan-3-one **126***
M.F.: $C_{21}H_{41}NO_5S$ (**M.W.** 419.62)

Yield: 212 mg (74 %)

TLC: R_f = 0.5 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.00 (*d*, $^3J_{19\text{-}14}$ = 6.8, 3 H, 19); 1.10 and 1.14 (*2 s*, 6 H, 6, 7); 1.12 (*s*, 9 H, 18); 1.18 (*t*, $^3J_{13\text{-}12}$ = 7.1, 3 H, 13); 1.62-2.50 (*m*, 7 H, 2, 3, 10, 14); 2.64 (*mult*, 1 H, 15); 2.82-2.98 (*m*, 1 H, 15); 3.01-3.12 (*m*, 1 H, 1); 3.18 (*s*, 3 H, 8); 3.40-3.69 (*m*, 5 H, 9, 11, 12); 3.82-3.95 (*m*, 1 H, 4); 4.25 (*mult*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 14.8 (13); 19.1 (19); 20.7 and 21.5 (6, 7); 25.4 (10); 26.2 (18); 26.6 and 27.7 (2, 3); 36.7 (14); 38.1 (15); 42.2 (17); 49.1 (8); 50.6 (1); 63.1 (9); 65.7 (4); 66.1 and 68.7 (11, 12); 78.1 (5); 207.5 (16)
IR (liquid film, cm^{-1}): 1138 (NSO_2); 1319 (NSO_2); 1705 (C=O); 2974 (C-H)
Mass (CI +Q1MS): 73 ($[C(CH_3)_2OMe]^+$, 16%); 142 ($[N^*]^+$, 19%); 213 ($[M\text{-}SO_2N^*]^+$, 100%); 346 ($[M\text{-}C(CH_3)_2OMe]^+$, 10%); 388 ($[M\text{-}OMe]^+$, 19%); 420 ($[M+H]^+$, 50%)

GC (150/0/10/290/20): t_R = 17.23 min (major); 17.42 min (minor); 17.74 min

Elemental analysis:

calculated (%): C: 60.1; H: 9.84; N: 3.33; O: 19.06; S: 7.64

found (%): C: 60.19; H: 10.28; N: 3.31; O: 18.83; S: 7.37

*6.4.3 Addition of (2S)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl) sulfonyl]pyrrolidine **10** to 2,2-dimethylhex-4-en-3-one **75***

Following the general procedure with:

200 mg (524.2 µmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl)sulfonyl]pyrrolidine **10**

246 µl (550.4 µmol; 1.05 eq.) of *n*-BuLi, 2.24M solution in hexane

73 mg (576.6 µmol; 1.1 eq.) of (*E*)-2,2-dimethylhex-4-en-3-one **75**

257 µl (186 mg; 1.846 mmol; 3.52 eq.) of Et_3N

257 µl (219 mg; 2.022 mmol; 3.85 eq.) of TMSCl

0 ml of HMPA

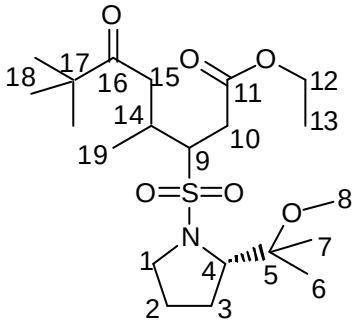
5 ml of THF

Only 1,4-addition product was obtained:

*3-[(2S)-(1-methoxy-1-methylethyl)pyrrolidine-1-sulfonyl]-4,7,7-trimethyl-6-oxo-octanoic acid ethyl ester **127***

M.F.: $C_{21}H_{39}NO_6S$ (**M.W.** 433.6)

Yield: 159 mg (70 %); the crude product was composed of 38% of the desired product and 34% of the corresponding silylated enol ether, which was hydrolyzed to **127**.



^{1}H NMR ($CDCl_3$, 200 MHz): 1.12, 1.14 and 1.15 (*3 s*, 15 H, 6, 7, 18); 1.15 (*d*, $^3J_{19\text{-}14}$ = 4.9, 3 H, 19); 1.27 (*t*, $^3J_{13\text{-}12}$ = 7.2, 3 H, 13); 1.62-2.23 (*m*, 7 H, 2, 3, 14, 15); 2.50 (*mult*, 2 H, 10); 2.83 (*mult*, 1 H 9); 2.95-3.18 (*m*, 1 H, 1); 3.21 (*s*, 3 H, 8); 3.76-3.90 (*m*, 1 H, 1); 4.02-4.15 (*m*, 1 H, 4); 4.18 (*q*, $^3J_{12\text{-}13}$ = 7.2, 2 H, 12)

^{13}C NMR ($CDCl_3$, 50 MHz): 13.9 (13); 18.9 (19); 20.0 and 21.2 (6, 7); 26.0 (18); 26.5 and 27.8 (2, 3); 30.4 (10); 36.6 (14); 39.6 (15); 44.0 (17); 48.9 (8); 60.9 (12); 62.2 (9); 62.4 (9*); 65.8 (4); 77.9 (5); 170.1 (11); 214.1 (16)
IR (liquid film, cm^{-1}): 1154 (NSO_2); 1325 (NSO_2); 1706 ($C=O_{ketone}$); 1738 ($C=O_{ester}$); 2977 (C-H)
Mass (CI/CH_4-N_2O): 276 ($[M\text{-}COC(CH_3)_3\text{-}COOEt]^+$, 100); 434 ($[M+H]^+$, 5%)
GC (150/0/10/290/15): 18.26 min (major); 18.61 (minor)
HRMS: calculated for $C_{21}H_{40}NO_6S^+$: 434.257635; found: 434.255391

*6.4.4 Addition of 1-[(3-methylbutyl)sulfonyl]pyrrolidine **39** to N,N-dimethylacrylamide*

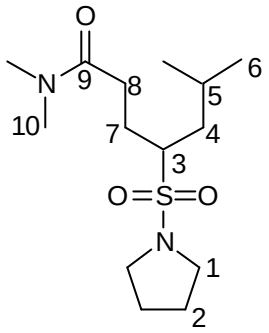
In a flame-dried two-necked flask, 150 mg (730.5 µmol; 1 eq.) of 1-(3-methyl-1-butanesulfonyl)pyrrolidine **39** were dissolved in 6.9 ml of THF. The solution was cooled to -78°C and 307 µl (767.1 µmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane, were slowly added. After 60 minutes of reaction, a mixture of 83 µl (79 mg; 803.6 µmol; 1.1 eq.) of *N,N*-dimethylacrylamide and 216 µl (246 mg; 803.6 µmol; 1.1 eq.) of triisopropylsilyl trifluoromethanesulfonate dissolved in some THF were added. The mixture was stirred for 60 minutes at -78°C then heated to room temperature. A few ml of a saturated solution of NH_4Cl were then added. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (150 ml of petroleum ether : AcOEt 80 : 20; then 150 ml of petroleum ether : AcOEt 60 : 40).

Yield: 70 mg (31.5 %)

*N,N,6-trimethyl-4-(pyrrolidin-1-ylsulfonyl)heptanamide **114***
M.F.: $C_{14}H_{28}N_2O_3S$ (**M.W.** 304.44)

Besides 42 mg (28 %) of 1-(3-methyl-1-butanesulfonyl)pyrrolidine were recovered.

* minor isomer



^{1}H NMR ($CDCl_3$, 200 MHz): 0.92 and 0.95 (*2 d*, $^{3}J_{6\text{-}5}$ = 6.0, $^{3}J_{6\text{-}5}$ = 5.9, 6 H, 6); 1.44-2.16 (*m*, 5 H, 4, 5, 7); 1.88-1.97 (*m*, 4 H, 2); 2.61 (*mult*, 2 H, 8); 2.95 and 3.02 (*2 s*, 6 H, 10); 3.18 (*mult*, 1 H, 3); 3.34-3.45 (*m*, 4 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 21.5 and 23.3 (6); 24.3 (7); 25.3 (5); 25.9 (2); 29.6 (8); 35.4 and 37.1 (10); 37.9 (4); 48.1 (1); 59.2 (3); 172.1 (9)
IR (liquid film, cm^{-1}): 1142 (NSO_2); 1320 (NSO_2); 1652 (C=O); 2957 (C-H)
Mass (CI +Q1MS): 87 (100%); 174 (10%); 265 (6%); 305 ($[M+H]^+$, 1%)
GC (100/0/10/290/15): t_R = 19.97 min

*6.4.5 Addition of pyrrolidine to 5,6-dihydro-2*H*-pyran-2-one **72***

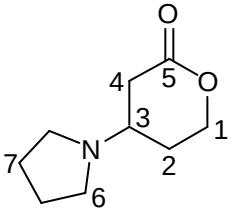
In a flame-dried two-necked flask, 145 µl (123 mg; 1.741 mmol; 1 eq.) of pyrrolidine were added to a solution of 150 µl (170 mg; 1.741 mmol; 1 eq.) of 5,6-dihydro-2*H*-pyran-2-one **72** in 4.2 ml of CH_2Cl_2. The mixture was stirred for 72 hours at room temperature. The solvent was removed under reduced pressure.
The product was purified by flash chromatography (AcOEt : CH_2Cl_2 50 : 50 + 10% EtOH).

Yield: 200 mg (68 %)

*4-pyrrolidin-1-yltetrahydro-2H-pyran-2-one **225***
M.F.: $C_9H_{15}NO_2$ (**M.W.** 169.22) **RN: 168482-09-5**

Besides, 53 mg (31 %) of 5,6-dihydro-2*H*-pyran-2-one were recovered.

Aspect: brown oil
TLC: R_f = 0.14 (CH_2Cl_2 : AcOEt 50 : 50 + 10% EtOH)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.69-2.17 (*m*, 6 H, 2, 7); 2.50-2.80 (*m*, 5 H, 3, 6); 3.82-3.45 (*2 m*, 2 H, 4); 4.37 (*mult*, 2 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 23.1 (7); 28.45 (2); 36.5 (4); 51.2 (6); 56.7 (3); 66.4 (1); 170.3 (5)
IR (liquid film, cm^{-1}): 1635; 1732 (C=O); 2968 (C-H)
Mass (CI/CH_4-N_2O): 99 ($[C_5H_7O_2]^+$, 47%); 170 ($[M+H]^+$, 100%)
GC (50/0/10/290/0): t_R = 15.31 min

*6.4.6 Addition of pyrrolidine to furan-2(5*H*)-one **71***

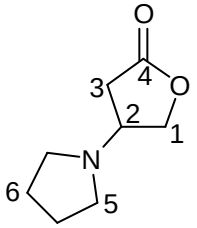
In a flame-dried two-necked flask, 235 µl (200 mg; 2.818 mmol; 1 eq.) of pyrrolidine were added to a solution of 200 µl (237 mg; 2.818 mmol; 1 eq.) of furan-2(5*H*)-one **71** in 6.8 ml of CH_2Cl_2. The mixture was stirred for 24 hours at room temperature. The solvent was removed under reduced pressure.
The product was purified by flash chromatography (AcOEt : EtOH 90 : 10).

Yield: 307 mg (70 %)

Besides, 36 mg (15 %) of furan-2(5*H*)-one were recovered

*4-pyrrolidin-1-yldihydrofuran-2(3H)-one **226***
M.F.: $C_8H_{13}NO_2$ (**M.W.** 155.19) **RN: 168482-08-4**

Aspect: yellow oil
TLC: R_f = 0.16 (AcOEt : EtOH 90 : 10)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.70-1.86 (*m*, 4 H, 6); 2.45-2.59 (*m*, 4 H, 5); 2.60 (*mult*, 2 H, 3); 3.22 (*mult*, 1 H, 2); 4.29 (*mul,* 2 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 23.0 (6); 33.8 (3); 51.5 (5); 59.6 (2); 71.6 (1); 175.4 (4)
IR (liquid film, cm^{-1}): 1179 (C-O); 1772 (C=O); 2965 (C-H)
Mass (CI/CH_4-N_2O): 156 ($[M+H]^+$, 100%); 184 ($[M+C_2H_5]^+$, 29%)
GC (50/0/10/290/0): t_R = 13.1 min

*6.4.7 Addition of pyrrolidine to 1-methyl-5,6-dihydropyridin-2(1H)-one **74***

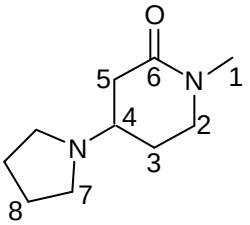
In a two-necked flask, 150 µl (127 mg; 1.799 mmol; 1 eq.) of pyrrolidine were added to a solution of 200 mg (1.799 mmol; 1 eq.) of 1-methyl-5,6-dihydropyridin-2(1*H*)-one **74** in 4.4 ml of CH_2Cl_2. The mixture was stirred for 30 hours. After this time no reaction had occurred. A small quantity of K_2CO_3 was added and the stirring continued for 70 hours. The solvent was then removed under reduced pressure. 20 ml of water and 20 ml of CH_2Cl_2 were added to the residue. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (Et_2O : EtOH 90 : 10).

Yield: 130 mg (40 %)

Besides, 70 mg (35 %) of 1-methyl-5,6-dihydropyridin-2(1*H*)-one were recovered.

*1-methyl-4-pyrrolidin-1-ylpiperidin-2-one **227***
M.F.: $C_{10}H_{18}N_2O$ (**M.W.** 182.26)

Aspect: yellow oil
TLC: R_f = 0.18 (Et_2O : EtOH 90 : 10)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.70-1.89 (*m*, 4 H, 8); 2.02-2.19 (*m*, 2 H, 3); 2.43 (*mult*, 2 H, 5); 2.50-2.72 (*m*, 5 H, 4, 7); 2.94 (*s*, 3 H, 1); 3.30 (*mult*, 2 H, 2)
^{13}C NMR ($CDCl_3$, 50 MHz): 23.15 (8); 28.6 (3); 34.1 (1); 38.3 (5); 47.25 (2); 51.5 (7); 58.5 (4); 168.6 (6)
IR (liquid film, cm^{-1}): 1341 (C-N_{amide}); 1635 (C=O); 2964 (C-H)
Mass (CI/CH_4-N_2O): 183 ($[M+H]^+$, 100%); 211 ($[M+C_2H_5]^+$, 7%)
GC (50/0/10/290/0): t_R = 18.44 min

7 Cyclization

7.1 Cyclization of cyclohexenone

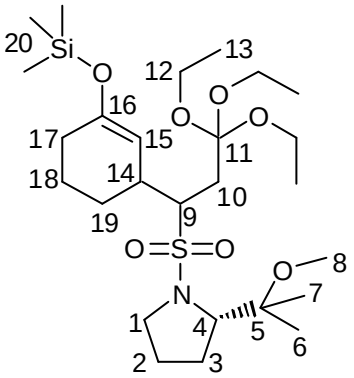
*7.1.1 Synthesis of (2S)-(1-methoxy-1-methylethyl)-1-[3,3,3-triethoxy-1-(3-trimethylsilanyloxycyclohex-2-enyl)propane-1-sulfonyl]pyrrolidine **130***

M.F.: $C_{26}H_{51}NO_7SSi$ (**M.W.** 549.83)

Following the general procedure described in 6.1 with:
200 mg (524.2 µmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl)sulfonyl]pyrrolidine **10**
323 µl (550.4 µmol; 1.05 eq.) of *n*-BuLi, 2.4M solution in hexane
56 µl (55 mg; 576.6 µmol; 1.1 eq.) of 2-cyclohexen-1-one
257 µl (186 mg; 1.846 mmol; 3.52 eq.) of Et_3N
257 µl (219 mg; 2.022 mmol; 3.85 eq.) of TMSCl
730 µl (751 mg; 4.193 mmol; 8 eq.) of HMPA
4.9 ml of THF
quenched with a saturated solution of NH_4Cl

Yield: 260 mg (90 %) crude product sufficiently pure to be used for the next step.

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.41 (20); 1.09 and 1.12 (*2 s*, 6 H, 6, 7); 1.25 (*t*, $^3J_{13\text{-}12}$ = 6.8, 13); 1.45-2.27 (*m*, 10 H, 2, 3, 17, 18, 19); 2.42 (*dd*, $^2J_{10\text{-}10'}$ = 18.1, $^3J_{10\text{-}9}$ = 4.1, 1 H, 10); 2.98 (*dd*, $^2J_{10\text{-}10'}$ = 18.1, $^3J_{10\text{-}9}$ = 6.8, 1 H, 10); 3.03-3.15 (*m*, 1 H, 1); 3.20 (*s*, 3 H, 8); 3.44-3.95 (*m*, 9 H, 1, 9, 12, 14); 4.21-4.31 (*m*, 1 H, 4); 5.14 (*s*, 1 H, 15)
^{13}C NMR ($CDCl_3$, 75 MHz): 0.3 (20); 15.1 (13); 20.8 and 21.5 (6, 7); 23.0 (18); 26.7 and 26.9 (2, 3); 27.6 (19); 28.5 (10); 29.6 (17); 35.8 (14); 49.1 (8); 50.8 (1); 57.4 (12); 62.0 (9); 66.1 (4); 77.9 (5); 105.2 (15); 113.9 (11); 152.1 (16)

*7.1.2 Synthesis of 3,3-bis(ethyloxy)-1-({(2S)-2-[1-methyl-1-(methyloxy)ethyl] pyrrolidin-1-yl}sulfonyl)octahydro-4H-inden-4-one **131***

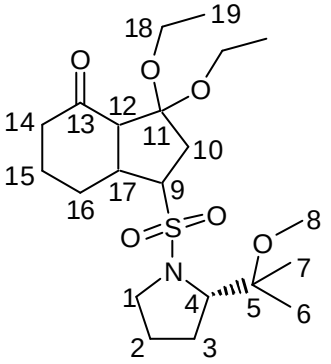
M.F.: $C_{21}H_{37}NO_6S$ (**M.W.** 431.588) **RN: 163362-43-4**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried two-necked flask equipped with a magnetical stirrer, 260 mg (472.8 µmol; 1 eq.) of (2*S*)-(1-methoxy-1-methylethyl)-1-[3,3,3-triethoxy-1-(3-trimethylsilanyloxycyclohex-2-enyl)propane-1-sulfonyl]pyrrolidine **130** were dissolved in 2.9 ml of CH_2Cl_2. The mixture was cooled to -78°C and 9 µl (10 mg; 47.28 µmol; 0.1 eq.) of trimethylsilyl trifluoromethanesulfonate were slowly added. The mixture was stirred for 45 minutes. Then a few ml of a saturated solution of $NaHCO_3$ were added and the temperature was raised to room temperature. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was washed with water and with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 97 mg (48 %)

TLC: R_f = 0.72 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.12 and 1.15 (*2 s*, 6 H, 6, 7); 1.14 and 1.20 (*2 t*, $^3J_{19\text{-}18}$ = 7.3, 6 H, 19); 1.58-2.21 (*m*, 8 H, 2, 3, 14, 15,); 2.36 and 2.56 (*2 mult*, 4 H, 10, 16); 2.77-3.10 (m, 2 H, 1, 17); 3.17 (*d*, $^3J_{12\text{-}17}$ = 9.0, 1 H, 12); 3.21 (s, 3 H, 8); 3.33-3.92 (*m*, 6 H, 1, 9, 18); 4.22 (*dd*, $^3J_{4\text{-}3}$ = 8.8, $^3J_{4\text{-}3}$ = 5.0, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50MHz): 15.2 and 15.3 (19); 20.9 and 21.5 (6, 7); 23.6 (16); 26.7 (15); 27.5 and 28.7 (2, 3); 35.4 (10); 41.8 (14); 42.4 (17); 49.2 (8); 50.8 (1); 56.7 and 58.4 (18); 59.4 (12); 64.3 (9); 66.2 (4); 78.1 (5); 110.3 (11); 208.5 (13)
IR (liquid film, cm^{-1}): 1137 (NSO_2); 1322 (NSO_2); 1704 (C=O); 2975 (C-H)

*7.1.3 Synthesis of 3,3-bis(ethyloxy)-1-({(2S)-2-[1-methyl-1-(methyloxy)ethyl] pyrrolidin-1-yl}sulfonyl)octahydro-1H-inden-4-ol **132***

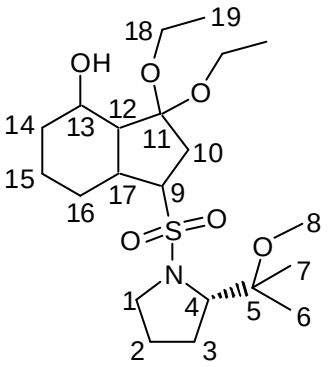
M.F.: $C_{21}H_{39}NO_6S$ (**M.W.** 433.604)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flame-dried two-necked flask equipped with a magnetical stirrer, 73 mg (169.1 µmol; 1 eq.) of 3,3-bis(ethyloxy)-1-({(2*S*)-2-[1-methyl-1-(methyloxy)ethyl] pyrrolidin-1-yl}sulfonyl)octahydro-4H-inden-4-one **131** were dissolved in 2.4 ml of CH_2Cl_2. The mixture was cooled to -78°C and 338 µl (292 mg; 338.2 µmol; 2 eq.) of diisobutylaluminum hydride were slowly added. After 20 minutes at that temperature, the reaction was quenched by the addition of a saturated solution of NH_4Cl. The mixture was allowed to come to room temperature and was acidified by the addition of HCl. The aqueous phase was extracted 4 times with CH_2Cl_2. The organic phase was washed once with a 1M solution of HCl, 3 times with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 82 mg (quant.)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.12 and 1.15 (*2 s*, 6 H, 6, 7); 1.20 and 1.22 (*2 t*, $^3J_{19\text{-}18}$ = 7.2, 6 H, 19); 1.20-2.25 (*m*, 12 H, 2, 3, 10, 14, 15, 16); 2.61-3.02 (*m*, 4 H, 1, 9, 12, 17); 3.21 (*s*, 3 H, 8); 3.34-3.78 (*2 mult + m*, 5 H, 1, 18); 4.04-4.11 (*m*, 2 H, 13, OH); 4.18-4.24 (*m*, 1 H, 4)

^{13}C NMR ($CDCl_3$, 75 MHz): 14.1 (15); 14.8 and 15.1 (19); 21.0 and 21.4 (6, 7); 24.6, 26.1 and 26.6 (2, 3, 16); 30.9 (14); 36.4 (17); 38.0 (10); 49.0 (8); 49.3 (12); 50.2 (1); 56.7 and 58.4 (18); 60.4, 64.7 and 65.4 (4, 9, 13); 78.2 (5); 109.2 (11)

IR (liquid film, cm^{-1}): 1060 (C-O); 1135 (NSO_2); 1340 (NSO_2); 2975 (C-H); 3510 (O-H)

*7.1.4 Synthesis of 7-hydroxy-3-({(2S)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)octahydro-1H-inden-1-one **133***

M.F.: $C_{17}H_{29}NO_5S$ (**M.W.** 359.482)

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

In a flask, 82 mg (189.1 µmol; 1 eq.) of 3,3-bis(ethyloxy)-1-({(2*S*)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)octahydro-1*H*-inden-4-ol **132** were dissolved in a mixture of 1 ml of acetone and 1 ml of water. The mixture was cooled to 0°C and 14 mg (56.73 µmol; 0.3 eq.) of pyridinium *para*-toluenesulfonate were added. It was stirred for 30 minutes at 0°C and for 60 minutes at room temperature. The reaction was quenched by the addition of a few ml of a saturated solution of $NaHCO_3$. The aqueous phase was extracted 5 times with CH_2Cl_2. The organic phase was washed with water and with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 45 mg of a mixture containing **133** and **134**.

*7.1.5 Synthesis of 7-hydroxy-3a,4,5,6,7,7a-hexahydro-1H-inden-1-one **134***

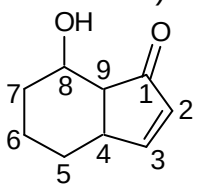
M.F.: $C_9H_{12}O_2$ (**M.W.** 152.190) **RN: 190510-64-6**

Reference: Huart, C. *PhD-Thesis UCL-ORSY*, **1995**

The crude product of 7.1.4 was passed on a flash chromatography column (petroleum ether : ether 25 : 75) to yield 7-hydroxy-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-one **134**.

Yield: 9 mg (47 %)

TLC: Rf = 0.26 (petroleum ether : ether 25 : 75)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.05-2.05 (*m*, 6 H, 5, 6, 7); 2.77 (*t*, $^3J_{9\text{-}8} = {}^3J_{9\text{-}4}$ = 5.9, 1 H, 9); 3.10 (*mult*, 1 H, 4); 4.11 (*mult*, 1 H, 8); 6.18 (*dd*, $^3J_{2\text{-}3}$ = 5.7, $^4J_{2\text{-}4}$ = 1.4, 1 H, 2); 7.76 (*dd*, $^3J_{3\text{-}2}$ = 5.7, $^3J_{3\text{-}4}$ = 3.0, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 20.1 (6); 27.3 and 30.3 (5, 7); 42.1 (4); 49.1 (9); 69.8 (8); 132.9 (2); 169.6 (3); 216.3 (1)
IR (liquid film, cm^{-1}): 1595 (C=C); 1700 (C=O); 2945 (C-H); 3455 (O-H)

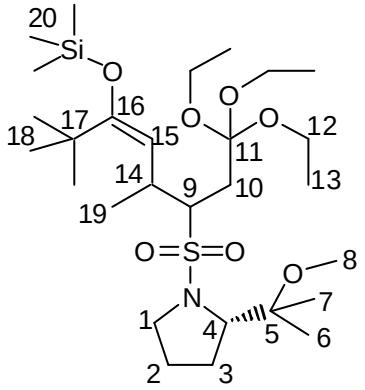
7.2 Cyclization of 2,2-dimethylhex-4-en-3-one 75 with 10

*7.2.1 Synthesis of (2S)-(1-methoxy-1-methylethyl)-1-(1,1,1-triethoxy-4,7,7-trimethyl-6-trimethylsilanyloxyoct-5-ene-3-sulfonyl)pyrrolidine **135***

M.F.: $C_{28}H_{57}NO_7SSi$ (**M.W.** 579.9)

Following the general procedure described in 6.1 with:
500 mg (1.31 mmol; 1 eq.) of (2*S*)-2-(1-methoxy-1-methylethyl)-1-[(3,3,3-triethoxypropyl)sulfonyl]-pyrrolidine **10**
550 µl (1.376 mmol; 1.05 eq.) of *n*-BuLi, 2.5M solution in hexane
182 mg (1.441 mmol; 1.1 eq.) of (*E*)-2,2-dimethylhex-4-en-3-one **75**
642 µl (467 mg; 4.617 mmol; 3.52 eq.) of Et_3N
642 µl (549 mg; 5.056 mmol; 3.85 eq.) of TMSCl
1.824 ml (1.878 g; 10.48 mmol; 8 eq.) of HMPA
12.3 ml of THF
quenched with a saturated solution of NH_4Cl

Yield: 671 mg (88 %) crude product sufficiently pure to be used in the next step.



^{1}H NMR ($CDCl_3$, 300 MHz): 0.27 (*s*, 9 H, 20); 1.04 (*s*, 9 H, 18); 1.12-1.22 (*mult*, 18 H, 6, 7, 13, 19); 1.78-1.99 (*m*, 5 H, 2, 3, 14); 2.17 (*dd*, $^2J_{10\text{-}10'}$ = 14.4, $^3J_{10\text{-}9}$ = 8.0, 1 H, 10); 2.50 (*dd*, $^2J_{10\text{-}10'}$ = 14.4, $^3J_{10\text{-}9}$ = 2.0, 1 H, 10); 2.95-3.05 (*m*, 1 H, 1); 3.18 (*s*, 3 H,

8); 3.39-3.47 (*m*, 1 H, 1); 3.50-3.69 (*m*, 7 H, 9, 12); 4.19-4.25 (*m*, 1 H, 4); 4.96 (*d*, $^{3}J_{15\text{-}14}$ = 8.9, 1 H, 15)

^{13}C NMR ($CDCl_3$, 75 MHz): 1.4 (20); 15.3 (13); 20.1 (19); 21.8 and 22.1 (6, 7); 26.5 and 27.0 (2, 3); 28.8 (18); 30.5 (14); 30.6 (10); 36.5 (17); 49.2 (8); 50.4 (1); 57.4 (12); 63.0 (9); 65.4 (4); 77.8 (5); 107.0 (15); 113.8 (11); 157.2 (16)

IR (liquid film, cm^{-1}): 844 (C-Si); 1070 (C-O); 1137 (NSO_2); 1320 (NSO_2); 1654 (C=C-O); 2974 (C-H)

*7.2.2 Synthesis of 1-[2,2-bis(ethyloxy)-5-methyl-4-({(2S)-2-[1-methyl-1-(methyloxy)ethyl]pyrrolidin-1-yl}sulfonyl)cyclopentyl]-2,2-dimethylpropan-1-one **138***

M.F.: $C_{23}H_{43}NO_6S$ (**M.W.** 461.65)

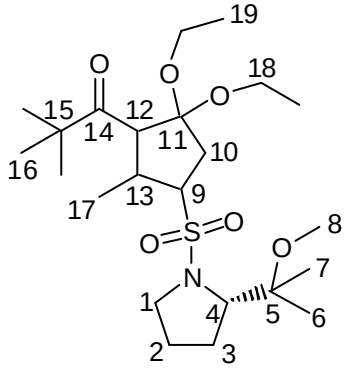
In a flame-dried two-necked flask equipped with a magnetical stirrer, 625 mg (1.157 mmol; 1 eq.) of (2*S*)-(1-methoxy-1-methylethyl)-1-(1,1,1-triethoxy-4,7,7-trimethyl-6-trimethylsilanyloxyoct-5-ene-3-sulfonyl)pyrrolidine **135** were dissolved in 7.1 ml of CH_2Cl_2. The mixture was cooled to -45°C and 22 µl (25 mg; 115.7 µmol; 0.1 eq.) of trimethylsilyl trifluoromethanesulfonate were slowly added. The mixture was stirred for 60 minutes at -45°C. The reaction was then quenched by the addition of a few ml of a saturated solution of $NaHCO_3$ and the mixture was allowed to come to room temperature. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was washed with water and with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 85 : 15).

Yield: 294 mg (55 %)

Aspect: colorless oil

TLC: R_f = 0.39 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.13 and 1.15 (*2 s*, 15 H, 6, 7, 16); 1.22 and 1.26 (*2 t*, $^3J_{19\text{-}18}$ = 7.1, 6 H, 19); 1.24 (*d*, $^3J_{17\text{-}13}$ = 7.0, 3 H, 17); 1.76-2.00 (*m*, 5 H, 2, 3, 13); 2.26 (*dd*, $^2J_{10\text{-}10'}$ = 11.5, $^3J_{10\text{-}9}$ = 6.6, 1 H, 10); 2.65 (*dd*, $^3J_{10\text{-}9}$ = 12.5, $^2J_{10\text{-}10'}$ = 11.4, 1 H, 10); 2.80 (*mult*, 1 H, 12); 3.00-3.11 (*m*, 1 H, 1); 3.18 (*s*, 3 H, 8); 3.32 (*mult*, 1 H, 9); 3.45 and 3.55 (*2 mult*, 4 H, 18), 3.67-3.76 (*m*, 1 H, 1); 4.21-4.27 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.7 and 15.2 (19); 21.2 and 21.5 (6, 7, 17); 25.8 (16); 26.4 and 26.5 (2, 3); 37.8 (10); 37.9 (13); 44.8 (15); 49.1 (8); 50.3 (1); 55.8 (12); 55.9 and 58.6 (18); 65.6 and 66.3 (4, 9); 77.7 (5); 109.1 (11); 214.2 (14)
IR (liquid film, cm^{-1}): 1135 (NSO_2); 1304 (NSO_2); 1705 (C=O); 2975 (C-H)
Mass (CI –Q1MS): 460 ($[M-H]^-$, 100%)

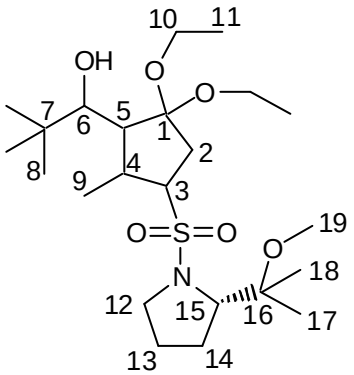
*7.2.3 Synthesis of 1-(2,2-diethoxy-4-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}-5-methylcyclopentyl)-2,2-dimethylpropan-1-ol **140***

M.F.: $C_{23}H_{45}NO_6S$ (**M.W.** 463.67)

In a flame-dried two-necked flask, a solution of 183 mg (396.3 µmol; 1 eq.) of 1-(2,2-diethoxy-4-{[(2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}-5-methyl-cyclopentyl)-2,2-dimethylpropan-1-one **138** in 5 ml of Et_2O was slowly added to a suspension of 7.5 mg (198.1 µmol; 0.5 eq.) of lithium aluminum hydride in Et_2O at 0°C. The mixture was stirred for 20 minutes at 0°C. A few ml of a saturated solution of $NaHCO_3$ were added. The aqueous phase was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 145 mg (79 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.98 (*s*, 9 H, 8); 1.15 and 1.17 (*2 s*, 15 H, 9, 17, 18); 1.24 (*mult*, 9 H, 9, 11); 1.75-2.03 (*m*, 6 H, 2, 13, 14); 2.30-2.48 (*m*, 2 H, 4, 5); 2.52-2.61

(*m*, 1 H, 3); 2.96-3.06 (*m*, 1 H, 12); 3.20 (*s*, 3 H, 19); 3.28 (*dd*, $^{3}J_{6\text{-}OH}$ = 7.7, $^{3}J_{6\text{-}5}$ = 5.0, 1 H, 6); 3.45 (*mult*, 4 H, 10); 3.71-3.79 (*m*, 1 H, 12); 4.18-4.25 (*m*, 1 H, 15); 4.33 (*d*, $^{3}J_{OH\text{-}6}$ = 7.7, 1 H, OH)

^{13}C NMR ($CDCl_3$, 75 MHz): 15.0 and 15.2 (11); 20.6 and 21.1 (17, 18); 21.7 (9); 27.0 (8); 26.6 and 28.9 (13, 14); 36.3 (7); 38.8 (2); 40.1 (4); 49.2 (19); 50.3 (12); 50.6 (5); 56.2 and 58.7 (10); 65.0 and 66.0 (3, 15); 77.8 (16); 82.3 (6); 109.7 (1)

IR (liquid film, cm^{-1}): 1055 (C-O); 1145 (NSO_2); 1323 (NSO_2); 2975 (C-H); 3441 (O-H)

Mass (CI/CH_4-N_2O): 84 (35%); 125 (100%); 211 ($[M\text{-}OEt\text{-}SO_2N^*]^+$, 64%), 464 ($[M+H]^+$, 2%)

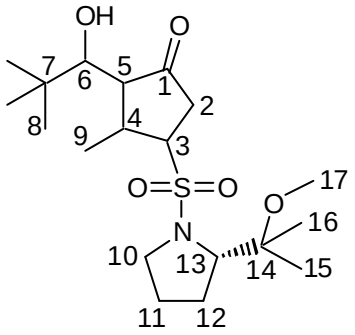
*7.2.4 Synthesis of 2-(1-hydroxy-2,2-dimethylpropyl)-4-{[(2S)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}-3-methylcyclopentanone **142***

M.F.: $C_{19}H_{35}NO_5S$ (**M.W.** 389.55)

In a two-necked flask, 134 mg (288.9 µmol; 1 eq.) of 1-(2,2-diethoxy-4-{[(2*S*)-2-(1-methoxy-1-methylethyl)pyrrolidin-1-yl]sulfonyl}-5-methylcyclopentyl)-2,2-dimethylpropan-1-ol **140** were dissolved in a mixture of 1.5 ml of acetone and 1.5 ml of H_2O. The mixture was cooled to 0°C and 22 mg (86.69 µmol; 0.3 eq) of pyridinium *para*-toluenesulfonate were added. The mixture was stirred for 30 minutes at 0°C and for 60 minutes at room temperature. A few ml of a saturated solution of $NaHCO_3$ were then added. The aqueous phase was extracted 5 times with CH_2Cl_2. The organic phase was washed with water and with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 88 mg of a mixture of **142** and **144**

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.96 (*s*, 9 H, 8); 1.10 and 1.12 (*2 s*, 6 H, 6, 7); 1.21 (*d*, $^{3}J_{9\text{-}4}$ = 7.2, 3 H, 9); 1.68-2.26 (*m*, 8 H, 2, 4, 5, 11, 12); 2.60-3.75 (*m*, 4 H, 3, 6, 10); 3.17 (*s*, 3 H, 17); 4.15-4.28 (*m*, 1 H, 13)

^{13}C NMR ($CDCl_3$, 75 MHz): 18.9 (9); 21.4 and 22.9 (15, 17); 25.8 and 26.6 (11, 12); 26.2 (8); 36.0 (7); 37.9 (2); 38.0 (4); 49.5 (17); 50.4 (1); 65.7, 66.4 and 66.7 (3, 5, 13); 77.7 (14); 79.8 (6); 214.2 (1)

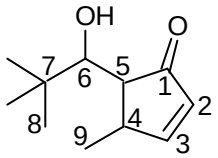
*7.2.5 Synthesis of 5-(1-hydroxy-2,2-dimethylpropyl)-4-methylcyclopent-2-en-1-one **144***

M.F.: $C_{11}H_{18}O_2$ (**M.W.** 182.26)

The crude product of 7.2.4 was passed on a flash chromatography column (petroleum ether : ether 55 : 45) to yield 5-(1-hydroxy-2,2-dimethylpropyl)-4-methylcyclopent-2-en-1-one **144**.

Yield: 32 mg (78 %)

Aspect: colorless oil
TLC: R_f = 0.50 (petroleum ether : ether 50 : 50)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.00 (*s*, 9 H, 8); 1.27 (*d*, $^{3}J_{9\text{-}4}$ = 7.2, 3 H, 9); 2.10 (*dd*, $^{3}J_{5\text{-}6}$ = 5.25, $^{3}J_{5\text{-}4}$ = 2.7, 1 H, 5); 2.92 (*mult*, 1 H, 4); 3.39 (*dd*, $^{3}J_{6\text{-}OH}$ = 6.8, $^{3}J_{6\text{-}5}$ = 5.25, 1 H, 6); 3.70 (*d*, $^{3}J_{OH\text{-}6}$ = 6.8, 1 H, OH); 6.11 (*dd*, $^{3}J_{2\text{-}3}$ = 5.7, $^{4}J_{2\text{-}4}$ = 1.9, 1 H, 2); 7.60 (*dd*, $^{3}J_{3\text{-}2}$ = 5.7, $^{3}J_{3\text{-}4}$ = 2.4, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 18.9 (9) 26.2 (8); 36.0 (7); 42.7 (4); 55.4 (5); 80.0 (6); 132.5 (2); 169.5 (3); 212.3 (1)
IR (liquid film, cm^{-1}): 1687 (C=O); 2959 (C-H); 3441 (O-H)
Mass (CI/CH_4-N_2O): 165 ($[M\text{-}OH]^+$, 100%); 183 ($[M+H]^+$, 43%)
Chiral GC (70/0/5/200/10): 21.70 min (major); 22.10 min (minor); ratio 95.6 : 4.4
$[\alpha]_{20}^{D}$: +45.2° (c=0.177; $CHCl_3$)
HRMS: calculated for $C_{11}H_{19}O_2^+$: 183.138505; found: 183.137882

7.3 Cyclization of 2,2-dimethylhex-4-en-3-one 75 with 52

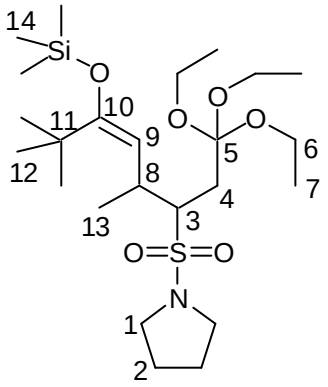
*7.3.1 Synthesis of 1-(1,1,1-triethoxy-4,7,7-trimethyl-6-trimethylsilanyloxyoct-5-ene-3-sulfonyl)pyrrolidine **136***

M.F.: $C_{22}H_{43}NO_6SSi$ (**M.W.** 477.73)

Following the general procedure described in 6.1 with:
500 mg (1.616 mmol; 1 eq.) of 1-[(3,3,3-triethoxypropyl)sulfonyl]pyrrolidine **52**
875 µl (1.697 mmol; 1.05 eq.) of *n*-BuLi, 1.94M solution in hexane
224 mg (1.777 mmol; 1.1 eq.) of (*E*)-2,2-dimethylhex-4-en-3-one **75**
790 µl (576 mg; 5.688 mmol; 3.52 eq.) of Et_3N
790 µl (677 mg; 6.222 mmol; 3.85 eq.) of TMSCl
2.250 ml (2.317 g; 12.93 mmol; 8 eq.) of HMPA
15.2 ml of THF
quenched with a saturated solution of NH_4Cl

Yield: 650 mg (84 %) crude product sufficiently pure to be used in the next step.

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.27 (*s*, 9 H, 14); 1.05 (*s*, 9 H, 12); 1.18 (*t*, $^3J_{7\text{-}6}$ = 7.2, 9 H, 7); 1.21 (*d*, $^3J_{13\text{-}8}$ = 8.1, 3 H, 13); 1.85-1.95 (*m*, 4 H, 2); 2.17 (*dd*, $^2J_{4\text{-}4'}$ = 15.3, $^3J_{4\text{-}3}$ = 6.3, 1 H, 4); 2.30 (*dd*, $^2J_{4\text{-}4'}$ = 14.4, $^3J_{4\text{-}3}$ = 1.7, 1 H, 4); 3.14-3.20 (*m*, 1 H, 3); 3.32-3.44 (*m*, 4 H, 1); 3.58 (mult, 6 H, 6); 4.96 (*d*, $^3J_{9\text{-}8}$= 9.0, 1 H, 9)
^{13}C NMR ($CDCl_3$, 75 MHz): 1.3 (14); 15.4 (7); 20.4 (13); 26.0 (2); 28.8 (12); 30.8 (4); 31.1 (8); 36.5 (11); 47.7 (1); 57.5 (6); 63.1 (3); 107.0 (9); 113.9 (5); 157.4 (10)
IR (liquid film, cm^{-1}): 845 (C-Si); 1070 (C-O); 1141 (NSO_2); 1325 (NSO_2); 1654 (C=C-O); 2974 (C-H)

*7.3.2 Synthesis of 1-[2,2-bis(ethyloxy)-5-methyl-4-(pyrrolidin-1-ylsulfonyl)-cyclopentyl]-2,2-dimethylpropan-1-one **139***

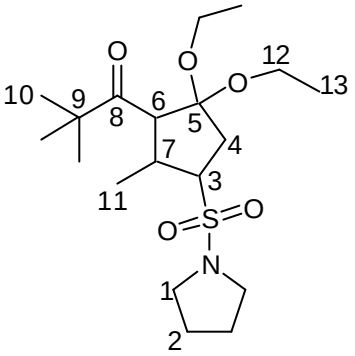
M.F.: $C_{19}H_{35}NO_5S$ (**M.W.** 389.55)

In a flame-dried two-necked flask equipped with a magnetical stirrer, 625 mg (1.308 mmol; 1 eq.) of 1-(1,1,1-triethoxy-4,7,7-trimethyl-6-trimethylsilanyloxyoct-5-

ene-3-sulfonyl)pyrrolidine **136** were dissolved in 8.1 ml of CH_2Cl_2. The mixture was cooled to -45°C and 25 µl (29 mg; 130.8 µmol; 0.1 eq.) of trimethylsilyl trifluoromethanesulfonate were slowly added. The mixture was stirred for 60 minutes at -45°C. The reaction was then quenched by the addition of a few ml of a saturated solution of $NaHCO_3$ and the mixture was allowed to come to room temperature. The aqueous phase was extracted 3 times with CH_2Cl_2. The organic phase was washed with water and with a saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 85 : 15).

Yield: 340 mg (67 %)

Aspect: colorless oil
TLC: R_f = 0.41 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.09 and 1.22 (*2 t*, $^3J_{13\text{-}12}$ = 7.2, 6 H, 13); 1.14 (*s*, 9 H, 10); 1.25 (*d*, $^3J_{11\text{-}17}$ = 7.0, 3 H, 11); 1.81-1.90 (*m*, 5 H, 2, 7); 2.26 (*dd*, $^2J_{4\text{-}4'}$ = 11.4, $^3J_{4\text{-}3}$ = 6.0, 1 H, 4); 2.60 (*t*, $^3J_{4\text{-}3}$ = $^2J_{4\text{-}4'}$ = 11.4, 1 H, 4); 2.60-2.78 (*m*, 1 H, 6); 3.26-3.60 (*m*, 9 H, 1, 3, 12)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.9 and 15.3 (13); 21.4 (11); 26.0 (2); 26.1 (10); 37.4 (4); 36.2 (7); 45.0 (9); 48.4 (1); 56.0 (6); 56.1 and 58.9 (12); 67.0 (3); 77.7 (5); 109.4 (5); 214.2 (8)
IR (liquid film, cm^{-1}): 1142 (NSO_2); 1324 (NSO_2); 1702 (C=O); 2975 (C-H)
Mass (CI –Q1MS): 153 (100%); 388 ($[M-H]^-$, 25%)

*7.3.3 Synthesis of 1-[2,2-bis(ethyloxy)-5-methyl-4-(pyrrolidin-1-ylsulfonyl)-cyclopentyl]-2,2-dimethylpropan-1-ol **141***

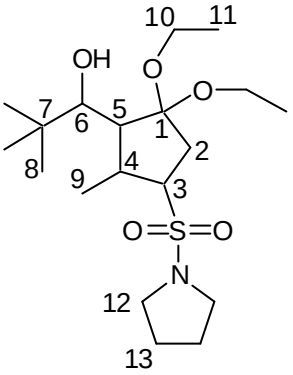
M.F.: $C_{19}H_{37}NO_5S$ (**M.W.** 391.56)

In a flame-dried two-necked flask, a solution of 300 mg (770.1 µmol; 1 eq.) of 1-[2,2-bis(ethyloxy)-5-methyl-4-(pyrrolidin-1-ylsulfonyl)cyclopentyl]-2,2-dimethylpropan-1-

one **139** in 9.7 ml of Et_2O was slowly added to a suspension of 14 mg (385 µmol; 0.5 eq.) of lithium aluminum hydride in Et_2O at 0°C. The mixture was stirred for 20 minutes at 0°C. A few ml of a saturated solution of $NaHCO_3$ were added. The aqueous phase was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 260 mg (86 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.98 (*s*, 9 H, 9); 1.22 (*mult*, 12 H, 8, 9); 1.75-1.98 (*m*, 4 H, 12); 2.38 and 2.50 (2 *mult*, 2 H, 4, 5); 3.15-3.58 (*m*, 9 H, 6, 10, 12); 4.28 (*d*, $^3J_{OH\text{-}6}$ = 7.8, 1 H, OH)
^{13}C NMR ($CDCl_3$, 75 MHz): 15.1 and 15.4 (11); 26.1 (9); 26.3 (13); 27.1 (8); 36.4 (7); 38.3 (2); 40.5 (4); 48.1 (12); 50.5 (5); 56.3 and 58.8 (10); 64.7 (3); 82.7 (6); 109.4 (1)
IR (liquid film, cm^{-1}): 1145 (NSO_2); 1324 (NSO_2); 2975 (C-H); 3490 (O-H)
Mass (CI/CH_4-N_2O): 84 (77%); 125 (100%); 167 ($[M\text{-}2OEt\text{-}SO_2NC_4H_8]^+$, 27%); 211 ($[M\text{-}OEt\text{-}SO_2NC_4H_8]^+$, 73%); 374 ($[M\text{-}OH]^+$, 1%)

*7.3.4 Synthesis of 2-(1-hydroxy-2,2-dimethylpropyl)-3-methyl-4-(pyrrolidin-1-ylsulfonyl)cyclopentanone **143***

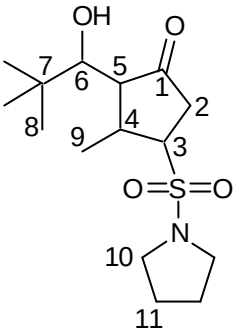
M.F.: $C_{15}H_{27}NO_4S$ (**M.W.** 317.44)

In a two-necked flask, 200 mg (511 µmol; 1 eq.) of **141** were dissolved in a mixture of 2.7 ml of acetone and 2.7 ml of H_2O. The mixture was cooled to 0°C and 38 mg (153.2 µmol; 0.3 eq) of pyridinium *para*-toluenesulfonate were added. The mixture was stirred for 30 minutes at 0°C and for 60 minutes at room temperature. A few ml of a saturated solution of $NaHCO_3$ were then added. The aqueous phase was extracted 5 times with CH_2Cl_2. The organic phase was washed with water and with a

saturated solution of NaCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 123 mg (76 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 300 MHz): 0.89 (*s*, 9 H, 8); 1.33 (*d*, 3 H, 9); 1.82-1.93 (*m*, 4 H, 11); 2.13 (*mult*, 1 H, 4); 2.52-2.68 (*m*, 3 H, 2, 5); 3.21-3.42 (*m*, 6 H, 3, 10, OH)
^{13}C NMR ($CDCl_3$, 50 MHz): 18.4 (9); 25.8 (11); 26.1 (8); 35.6 (7); 38.4 (4); 41.1 (2); 48.4 (10); 57.6 and 61.9 (3, 5); 79.1 (6); 212.3 (1)

*7.3.5 Synthesis of 5-(1-hydroxy-2,2-dimethylpropyl)-4-methylcyclopent-2-en-1-one **144***

M.F.: $C_{11}H_{18}O_2$ (**M.W.** 182.26)

The crude product of 7.3.4 was passed on a flash chromatography column (petroleum ether : ether 55 : 45) to yield 5-(1-hydroxy-2,2-dimethylpropyl)-4-methylcyclopent-2-en-1-one **144**.

Yield: 53 mg (75 %)

Analyses were identical to that of 7.2.5

8 Phase-transfer catalysis: sulfur-containing nucleophiles

8.1 Sulfones as nucleophiles

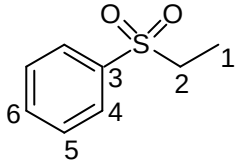
*8.1.1 Synthesis of ethylphenylsulfone **157***

M.F.: $C_8H_{10}O_2S$ (**M.W.** 170.22) **RN: 599-70-2**

To a solution of 1 ml (1.021 g; 7.386 mmol; 1 eq.) of ethylphenylsulfide in 25 ml of CH_2Cl_2 were added 4 g (16.25 mmol; 2.2 eq.) of 3-chloroperoxybenzoic acid dissolved in CH_2Cl_2. After 2 hours of reaction, the mixture was poured into a saturated solution of $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2. The organic phase was washed with a solution of 10% KOH, dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 1.263 g (quant.)

TLC: R_f = 0.63 (petroleum ether : AcOEt 60 : 40)

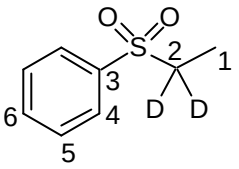


^{1}H NMR ($CDCl_3$, 200 MHz): 1.28 (*t*, $^3J_{1\text{-}2}$ = 7.4, 3 H, 1); 3.13 (*q*, $^3J_{2\text{-}1}$ = 7.4, 2 H, 2); 7.53-7.72 (*m*, 3 H, 5, 6); 7.92 (*mult*, 2 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 7.3 (1); 50.4 (2); 128.1 (4); 129.2 (5); 133.6 (6); 138.6 (3)
IR (liquid film, cm^{-1}): 1145 (S=O); 1307 (S=O); 2983 (C-H); 3065 (C-$H_{arom.}$)
Mass (CI +Q1MS): 171 ($[M+H]^+$, 100%); 341 ($[2M+H]^+$, 33%)
GC (100/0/10/290/15): t_R = 9.00 min
Elemental analysis:
calculated (%): C: 56.44; H: 5.92; O: 18.79; S: 18.83
found (%): C: 56.6; H: 5.83; O: 18.82; S: 18.75

8.1.2 Synthesis of ethylphenylsulfone d_2 ***228***

M.F.: $C_8H_8D_2O_2S$ (**M.W.** 172.234)

A mixture of 50 mg (293.7 µmol; 1 eq.) of ethylphenylsulfone **157**, 90 ml (881.1 µmol; 3 eq.) of sodium deuteroxide, 30% solution in D_2O, 99+ atom % d, 7 mg (29.37 µmol; 0.1 eq.) of benzyltriethylammonium chloride and 0.7 ml of CH_2Cl_2 was stirred for 5 hours at room temperature. After that time, 1 ml of a dilute solution of D_2SO_4 in D_2O was added. The aqueous phase was extracted wit CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
^{1}H NMR showed that the protons α to the sulfone had been replaced by deuterium.



^{1}H NMR ($CDCl_3$, 200 MHz): 1.27 (*s*, 3 H, 1); 7.61 (*mult*, 3 H, 5, 6); 7.92 (*mult*, 2 H, 4)

8.2 a-Sulfonylcarboxylic esters as nucleophiles

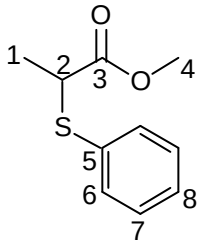
*8.2.1 Synthesis of methyl 2-(phenylsulfanyl)propanoate **160***

M.F.: $C_{10}H_{12}O_2S$ (**M.W.** 196.26) **RN: 21673-18-7**

In a flame-dried two-necked flask, 1 ml (1.497 g; 8.963 mmol; 1eq.) of methyl 2-bromopropionate, 920 µl (987 mg; 8.963 mmol; 1eq.) of thiophenol and 1.245 ml (907 mg; 8.963 mmol; 1 eq.) of Et_3N were mixed together in 23 ml of Et_2O and stirred for 16 hours. After this time, the mixture was filtered and the solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 90 : 10).

Yield: 1.629 g (93 %)

Aspect: colorless oil
TLC: R_f = 0.37 (petroleum ether : AcOEt 95 : 5); 0.8 (petroleum ether : AcOEt 90 : 10)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.49 (*d*, $^3J_{1\text{-}2}$ = 7.1, 3 H, 1); 3.67 (*s*, 3 H, 4); 3.79 (*q*, $^3J_{2\text{-}1}$ = 7.1, 1 H, 2); 7.31 (*mult*, 3 H, 6, 8); 7.45 (*mult*, 2 H, 7)

^{13}C NMR ($CDCl_3$, 75 MHz): 17.4 (1); 45.1 (2); 52.2 (4); 128.0 (8); 128.9 (7); 132.9 (5); 133.0 (6); 172.8 (3)
IR (liquid film, cm^{-1}): 1067; 1161; 1260; 1439; 1736 (C=O); 2951 (C-H)
Mass (CI +Q1MS): 137 ($[M\text{-}COOMe]^+$, 100%); 165 ($[M\text{-}OMe]^+$, 30%); 197 ($[M+H]^+$, 72%); 393 ($[2M+H]^+$, 10%)
GC (100/0/10/290/15): t_R = 9.42 min

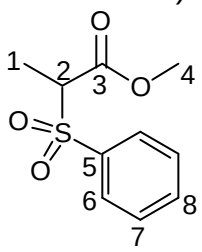
*8.2.2 Synthesis of methyl 2-(phenylsulfonyl)propanoate **158***

M.F.: $C_{10}H_{12}O_4S$ (**M.W.** 228.26) **RN: 85979-85-7**

8.345 g (33.85 mmol; 2.2 eq.) of 3-chloroperoxybenzoic acid dissolved in CH_2Cl_2 were added to a solution of 3.02 g (15.38 mmol; 1 eq.) of methyl 2-(phenylsulfanyl)propanoate **160** in 52 ml of CH_2Cl_2. After 2 hours, the reaction mixture was poured into a saturated solution of $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 2.99 g (85 %)

TLC: R_f = 0.18 (petroleum ether : AcOEt 80 : 20)



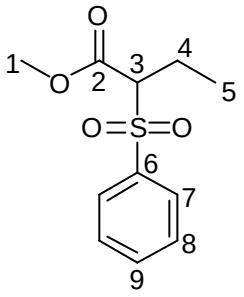
^{1}H NMR ($CDCl_3$, 300 MHz): 1.57 (*d*, $^3J_{1\text{-}2}$ = 7.2, 3 H, 1); 3.68 (*s*, 3 H, 4); 4.17 (*q*, $^3J_{2\text{-}1}$ = 7.2, 1 H, 2); 7.58 (*mult*, 2 H, 7); 7.70 (*tt*, $^3J_{8\text{-}7}$ = 7.4, $^4J_{8\text{-}6}$ = 1.26, 1 H, 8); 7.87-7.90 (*m*, 2 H, 6)
^{13}C NMR ($CDCl_3$, 50 MHz): 11.8 (1); 52.9 (4); 65.3 (2); 129.0 and 129.3 (6, 7); 134.3 (8); 137.0 (5); 166.7 (3)
IR (liquid film, cm^{-1}): 1454; 1585; 1734 (C=O); 2955 (C-H); 3003; 3066
Mass (CI +Q1MS): 89 (100%); 229 ($[M+H]^+$, 20%)
GC (100/0/10/290/15): t_R = 13.29 min

*8.2.3 Synthesis of methyl 2-(phenylsulfonyl)butanoate **161***

M.F.: $C_{11}H_{14}O_4S$ (**M.W.** 242.28) **RN: 129585-56-4**

A mixture of 780 µl (1 g; 4.667 mmol; 1 eq.) of methyl phenylsulfonylacetate, 373 µl (728 mg; 4.667 mmol; 1 eq.) of iodoethane and 645 mg (4.667 mmol; 1 eq.) of potassium carbonate in 17 ml of acetone was refluxed for 88 hours. After that time, the reaction was complete and the mixture was passed through a short pad of celite. The solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 70 : 30).

Yield: 930 mg (82 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.97 (*t*, $^3J_{5\text{-}4}$ = 7.5, 3 H, 5); 2.02 (*mult*, 2 H, 4); 3.69 (*s*, 3 H, 1); 3.89 (*dd*, $^3J_{3\text{-}4}$ = 11.4, $^3J_{3\text{-}4}$ = 4.2, 1 H, 3); 7.59 (*mult*, 2 H, 8); 7.68 (*mult*, 1 H, 9); 7.88 (*mult*, 2 H, 7)
^{13}C NMR ($CDCl_3$, 75 MHz): 11.3 (5); 20.5 (4); 52.8 (1); 72.1 (3); 128.9 and 129.2 (7, 8); 134.2 (9); 136.9 (6); 166.2 (2)
Mass (CI +Q1MS): 89 (100%); 243 ($[M+H]^+$, 87%)
GC (100/0/10/290/15): t_R = 13.93 min

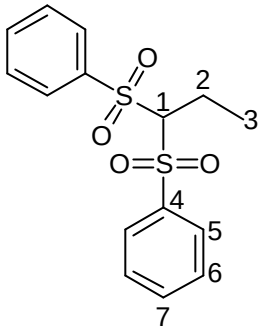
*8.2.4 Synthesis of {[1-(phenylsulfonyl)propyl]sulfonyl}benzene **162***

M.F.: $C_{15}H_{16}O_4S_2$ (**M.W.** 324.40) **RN: 110945-04-5**

In a flask equipped with a reflux condenser, a mixture of 100 mg (337.4 µmol; 1 eq.) of bis(phenylsulfonyl)methane, 27 µl (52 mg; 337.4 µmol; 1 eq.) of iodoethane, 47 mg (337.4 µmol; 1 eq.) of potassium carbonate and 8 mg (33.74 µmol, 0.1 eq.) of benzyltriethylammonium chloride in 1.2 ml of acetone was refluxed for 16 hours. After that time, the reaction was complete and the mixture was passed through a short pad of celite. The solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 105 mg (96%)

TLC: R_f = 0.59 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.17 (*t*, $^3J_{3\text{-}2}$ = 7.5, 3 H, 3); 2.21 (*mult*, 2 H, 2); 4.35 (*t*, $^3J_{1\text{-}2}$ = 5.7, 1 H, 1); 7.58 (*mult*, 4 H, 6); 7.71 (*mult,* 2 H, 7); 7.97 (*dd*, $^3J_{5\text{-}6}$ = 7.2, $^4J_{5\text{-}7}$ = 1.2, 4 H, 5)
^{13}C NMR ($CDCl_3$, 75 MHz): 12.9 (3); 19.5 (2); 85.0 (1); 129.0 and 129.4 (5, 6); 134.5 (7); 137.8 (4)
Mass (CI +Q1MS): 84 (100%); 87 (100%); 325 ($[M+H]^+$, 50%)
GC (100/0/10/290/15): t_R = 20.64 min

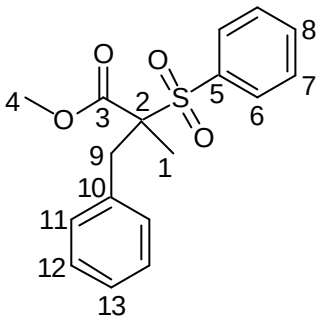
*8.2.5 Synthesis of methyl 2-methyl-3-phenyl-2-(phenylsulfonyl)propanoate **163***

M.F.: $C_{17}H_{18}O_4S$ (**M.W.** 318.38)

A mixture of 50 mg (219 µmol; 1 eq.) of methyl 2-(phenylsulfonyl)propanoate **158**, 123 mg (2.19 mmol; 10 eq.) of potassium hydroxyde and 5 mg (21.9 µmol; 0.1 eq.) of benzyltriethylammonium chloride in 0.5 ml of CH_2Cl_2 was stirred for 15 minutes. Then 130 µl (187 mg; 1.095 mmol; 5 eq.) of benzyl bromide were added and the mixture was stirred for 3 hours. It was then passed through a small pad of celite. The solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 80 : 20).

Yield: 60 mg (86 %)

Aspect: colorless oil
TLC: R_f = 0.33 (AcOEt : petroleum ether 20 : 80)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.49 (*s*, 3 H, 1); 3.07 and 3.65 (*2 d*, $^{2}J_{9\text{-}9'}$ = 12.9, 2 H, 9); 3.67 (*s*, 3 H, 4); 7.05-7.27 (*2 m*, 5 H, 11, 12, 13); 7.56-7.62 (*m*, 2 H, 7); 7.71 (*tt*, $^{3}J_{8\text{-}7}$ = 7.4, $^{4}J_{8\text{-}6}$ = 1.3, 1 H, 8); 7.88-7.91 (*m*, 2 H, 6)
^{13}C NMR ($CDCl_3$, 50 MHz): 16.1 (1); 38.5 (9); 52.8 (4); 73.8 (2); 127.4 (13); 128.5 and 128.8 (6, 7); 130.2 and 130.5 (11, 12); 134.1 (10); 134.3 (8); 135.6 (5); 168.1 (3)
IR (liquid film, cm^{-1}): 1147; 1308; 1448; 1735 (C=O); 2953 (C-H)
Mass (CI +Q1MS): 85 (60%); 91 (100%); 183 (91%); 319 ($[M+H]^+$, 2%)
GC (100/0/10/290/15): t_R = 20.8 min

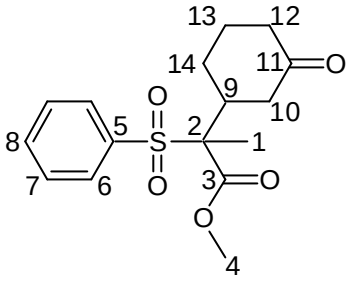
*8.2.6 Synthesis of methyl 2-(3-oxocyclohexyl)-2-(phenylsulfonyl)propanoate **164***

M.F.: $C_{16}H_{20}O_5S$ (**M.W.** 324.39)

A mixture of 100 mg (438 µmol; 1 eq.) of methyl 2-phenylsulfonylpropanoate **158**, 6 mg (43.8 µmol; 0.1 eq.) of potassium carbonate and 11 mg (43.8 µmol; 0.1 eq.) of 18-crown-6 in 2.75 ml of acetone was stirred for 15 minutes. 55 ml (55 mg, 569.5 µmol; 1.3 eq.) of 2-cyclohexen-1-one were added. As there was no reaction after 24 hours, 54 mg (394.2 µmol; 0.9 eq.) of potassium carbonate were added and the mixture was stirred for another 24 hours. It was the passed through a short pad of celite and the solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 113 mg (79 %)

Aspect: white solid
TLC: R_f = 0.51 and 0.62 (petroleum ether : AcOEt 60 : 40) (2 diastereomers)



^{1}H NMR ($CDCl_3$, 300 MHz):

1st diastereomer: 1.51-1.75 (*m*, 3 H, 13, 14); 1.64 (*s*, 3 H, 1); 1.85-1.98 (*m*, 1 H, 13, 14); 2.04 (*mult*, 1 H, 10); 2.10-2.49 (*m*, 2 H, 12); 2.50-2.62 (*m*, 1 H, 10); 2.94 (*mult*, 1 H, 9); 3.56 (*s*, 3 H, 4); 7.55 (*mult*, 2 H, 7); 7.65 (*mult*, 1 H, 8); 7.75 (*mult*, 2 H, 6)

2nd diastereomer: 1.45-1.52 (*m*, 2 H, 13 or 14); 1.64 (*s*, 3 H, 1); 2.00-2.10 (*m*, 2 H, 13 or 14); 2.25 (*mult*, 1 H, 10); 2.30-2.45 (*m*, 2 H, 12); 2.80-2.95 (m, 1 H, 9); 3.03 (*mult*, 1 H, 10); 3.59 (*s*, 3 H, 4); 7.55 (*mult*, 2 H, 7); 7.67 (*mult*, 1 H, 8); 7.82 (*mult*, 2 H, 6)

^{13}C NMR ($CDCl_3$, 50 MHz):

1st diastereomer: 12.3 (1); 24.4 and 26.3 (13, 14); 40.7 (9); 41.0 (12); 43.5 (10); 53.0 (4); 76.6 (2); 128.8 and 130.0 (6, 7); 134.3 (8); 136.7 (5); 168.1 (3); 208.6 (11)

2nd diastereomer: 12.5 (1); 24.4 and 27.4 (13, 14); 40.6 (9); 40.7 (12); 42.8 (10); 52.9 (4); 76.5 (2); 128.8 and 130.2 (6, 7); 134.2 (8); 136.5 (5); 168.4 (3); 208.6 (11)

Mass (CI +Q1MS): 69 (75%); 87 (100%); 193 (56%); 229 (24%); 325 ($[M+H]^+$, 28%)

GC (100/0/10/290/20): t_R = 21.78 min and t_R = 22.08 min (2 diastereomers)

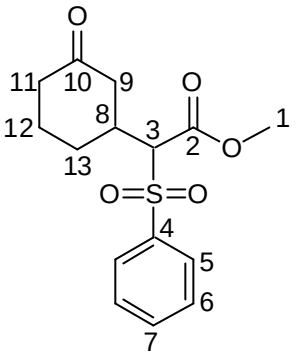
*8.2.7 Synthesis of methyl (3-oxocyclohexyl)(phenylsulfonyl)acetate **229***

M.F.: $C_{15}H_{18}O_5S$ (**M.W.** 310.36)

A mixture of 100 mg (466.7 µmol; 1 eq.) of methyl phenylsulfonylacetate, 161 mg (1.166 mmol; 2.5 eq.) of potassium carbonate and 11 mg (46.67 µmol; 0.1 eq.) of benzyltriethylammonium chloride in 2.6 ml of CH_2Cl_2 was stirred for 15 minutes at room temperature before 59 µl (58 mg; 606.8 µmol; 1.3 eq.) of 2-cyclohexen-1-one and 19 µl (14 mg; 466.7 µmol; 1 eq.) of MeOH were added. The mixture was stirred for 3 hours. It was then passed through a short pad of celite and the solvent was evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 94 mg (65 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.52-2.46 (*2 m*, 8 H, 9, 11, 12, 13); 2.58-2.89 (*2 m*, 2 H, 8); 3.51 and 3.58 (*2 s*, 3 H, 1); 3.91 and 3.97 (*2 d*, $^{3}J_{3\text{-}8}$ = 8.1, $^{3}J_{3'\text{-}8'}$ = 7.8, 1 H, 3); 7.58 (*mult*, 2 H, 6); 7.70 (*mult*, 1 H, 7); 7.91 (*mult*, 2 H, 5)
^{13}C NMR ($CDCl_3$, 50 MHz): 24.2 (12); 28.3 and 29.2 (13); 37.0 and 37.05 (8); 40.7 and 40.75 (11); 44.4 and 45.5 (9); 52.6 and 52.7 (1); 74.7 and 74.8 (3); 128.9 and 129.0 (5, 6); 134.3 (7); 138.0 (4); 165.4 (2); 207.9 (10)
Mass (CI/CH_4-N_2O): 83 (100%); 101 (35%); 311 ($[M+H]^+$, 2%)

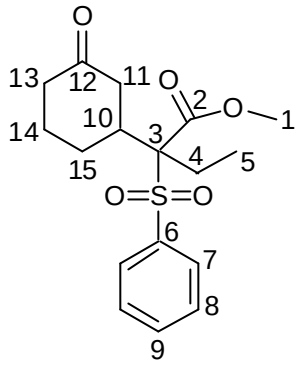
*8.2.8 Synthesis of methyl 2-(3-oxocyclohexyl)-2-(phenylsulfonyl)butanoate **230***

M.F.: $C_{17}H_{22}O_5S$ (**M.W.** 338.41)

A mixture of 75 mg (308.2 µmol; 1 eq.) of methyl 2-phenylsulfonylbutanoate **161**, 106 mg (770.6 µmol; 2.5 eq.) of potassium carbonate and 7 mg (30.82 µmol; 0.1 eq.) of benzyltriethylammonium chloride in 3 ml of *N,N*-dimethylformamide was stirred for 15 minutes before 39 µl (38 mg; 400.7 µmol; 1.3 eq.) of 2-cyclohexen-1-one and 12 µl (9.877 mg; 308.2 µmol; 1 eq.) of MeOH were added. The mixture was stirred for 90 minutes. It was then passed through a short pad of celite and the solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 31 mg (30 %)

TLC: R_f = 0.52 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.09 and 1.15 (*2 t*, $^{3}J_{5\text{-}4}$ = 7.5, 3 H, 5); 1.46-2.78 (*m*, 11 H, 4, 10', 11, 13, 14, 15); 2.92 (*mult*, 1 H, 10); 3.73 and 3.75 (*2 s*, 3 H, 1); 7.58 (*mult*, 2 H, 8); 7.69 (*mult*, 1 H, 9); 7.91 (*mult*, 2 H, 7)

^{13}C NMR ($CDCl_3$, 75 MHz): 9.5 (5); 23.3 (4); 24.9 and 26.9 (14, 15); 40.5 (10); 41.3 and 43.7 (11, 13); 52.6 (1); 75.9 (3); 128.6 and 130.7 (7, 8); 134.1 (9); 137.5 and 137.8 (6); 168.8 (2); 209.8 (12)

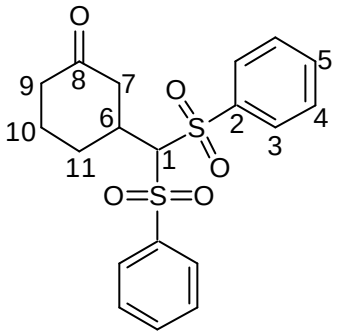
Mass (CI/CH_4-N_2O): 59 ($[COOMe]^+$, 90%); 97 ($[C_6H_7O]^+$, 73%); 193 (100%); 339 ($[M+H]^+$, 4%)

*8.2.9 Synthesis of 3-[bis(phenylesulfonyl)methyl]cyclohexanone **231***

M.F.: $C_{19}H_{20}O_5S_2$ (**M.W.** 392.48)

A mixture of 100 mg (337.4 µmol; 1 eq.) of bis-(phenylsulfonyl)methane, 116 mg (843.5 µmol; 2.5 eq.) of potassium carbonate and 8 mg (33.74 µmol; 0.1 eq.) of benzyltriethylammonium chloride in 3 ml of acetone was stirred for 15 minutes at room temperature before 42 µl (42 mg; 438.6 µmol; 1.3 eq.) of 2-cyclohexen-1-one and 14 µl (10 mg; 337.4 µmol; 1 eq.) of MeOH were added. The mixture was stirred for 16 hours. As no reaction occurred after this time, the mixture was heated to reflux for 24 hours. After being cooled to room temperature, it was passed through a short pad of celite and the solvent was removed under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 28 mg (21 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.92-1.62 (*2 m*, 4 H, 10, 11); 1.87-2.48 (*2 m*, 4 H, 7, 9); 2.78 (*mult*, 1 H, 6); 4.42 (*s*, 1 H, 1); 7.58 (*mult*, 4 H, 4); 7.72 (*mult*, 2 H, 5); 7.91 (*mult*, 4 H, 3)
^{13}C NMR ($CDCl_3$, 75 MHz): 25.05 and 27.8 (10, 11); 38.9 (6); 40.9 and 45.6 (7, 9); 86.1 (1); 129.2 and 129.4 (3, 4); 134.8 (5); 138.2 (2); 208.3 (8)
Mass (CI +Q1MS): 97 ($[C_6H_9O]^+$, 28%); 253 (100%); 393 ($[M+H]^+$, 81%)

9 Phase-transfer catalysis: nitro-containing nucleophiles

9.1 Synthesis of ketals

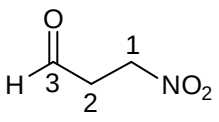
*9.1.1 Synthesis of 3-nitropropanal **166***

M.F.: $C_3H_5NO_3$ (**M.W.** 103.07) **RN: 58657-26-4**

Reference: Öhrlein, R.; Schwab, W.; Ehrler, R.; Jäger, V. *Synthesis* **1986**, 535-538.

In a flame-dried two-necked flask equipped with a reflux condenser, 20 ml (16.78 g; 299.2 mmol; 1 eq.) of acrolein and 25.83 g (374.3 mmol; 1.25 eq.) of sodium nitrite were dissolved in 120 ml of THF. The mixture was cooled to 0°C and 21.4 ml (22.44 g; 373.8 mmol; 1.24 eq.) of acetic acid were slowly added over a period of 30 minutes. The mixture was stirred for 3 hours. After that time, water was added to dissolve the salts that had formed. The aqueous phase was extracted 4 times with CH_2Cl_2. The organic phase was washed twice with a saturated solution of $NaHCO_3$, twice with a saturated solution of NaCl and once with water, then dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (60°C at $9 \cdot 10^{-3}$ mbar).

Yield: 11.02 g (36 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 3.19 (*t*, $^{3}J_{2\text{-}1}$ = 5.7, 2 H, 2); 4.69 (*t*, $^{3}J_{1\text{-}2}$ = 6.3, 2 H, 1); 9.83 (*s*, 1 H, 3)
^{13}C NMR ($CDCl_3$, 75 MHz): 39.5 (2); 67.5 (1); 196.5 (3)
IR (liquid film, cm^{-1}): 1380, 1550 (NO_2), 1720 (C=O)
Mass (CI/CH_4-N_2O): 57 ($[M\text{-}NO_2]^+$, 100%); 104 ($[M+H]^+$, 40%)
b.p.: 60°C ($9\cdot10^{-3}$ mbar)

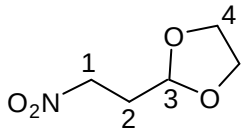
*9.1.2 Synthesis of 2-(2-nitroethyl)-1,3-dioxolane **167***

M.F.: $C_5H_9NO_4$ (**M.W.** 147.13) **RN: 82891-99-4**

In a flask equipped with a Dean-Stark apparatus, 500 mg (4.85 mmol; 1 eq.) of 3-nitropropanal **166**, 297 µl (331 mg; 5.335 mmol; 1.1 eq.) of ethylene glycol and 46 mg (242.5 µmol; 0.05 eq.) of *para*-toluenesulfonic acid monohydrate were put into 11 ml of benzene. The mixture was heated to reflux until a constant volume of water was collected. It was then cooled to room temperature and the solvent was removed under reduced pressure.
The product was purified by flash chromatography (mounting: petroleum ether : AcOEt 80 : 20 + 5% Et_3N; elution: petroleum ether : AcOEt 80 : 20).

Yield: 485 mg (68 %)

Aspect: yellow liquid



^{1}H NMR ($CDCl_3$, 200 MHz): 2.44 (*dt*, $^{3}J_{2\text{-}1}$ = 6.8 $^{3}J_{2\text{-}3}$ = 3.7, 2 H, 2); 3.97 and 3.89 (*2 mult*, 4 H, 4); 4.51 (*t*, $^{3}J_{1\text{-}2}$ = 6.8, 2 H, 1); 5.04 (*t*, $^{3}J_{3\text{-}2}$ = 3.7, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 30.7 (2); 65.1 (4); 69.9 (1); 101.0 (3)
IR (liquid film, cm^{-1}): 1045; 1141; 1377; 1556 (NO_2); 1735; 2982 (C-H)
Mass (CI/CH_4-N_2O): 73 (85%); 101 ($[M\text{-}NO_2]^+$, 100%); 148 ($[M+H]^+$, 87%)
GC (100/0/10/290/20): t_R = 5.74 min

*9.1.3 Synthesis of 1,1-diethoxy-3-nitropropane **168***

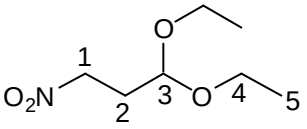
M.F.: $C_7H_{15}NO_4$ (**M.W.** 177.2) **RN: 107833-73-8**

Reference: Öhrlein, R.; Schwab, W.; Ehrler, R.; Jäger, V. *Synthesis* **1986**, 535-538.

In a flame-dried two-necked flask equipped with a tube of silicagel, 1.192 g (11.56 mmol; 1 eq.) of freshly distilled 3-nitropropanal **166** dissolved in 9 ml of EtOH were reacted with 2.308 ml (2.056 g; 13.87 mmol; 1.2 eq.) of triethyl orthoformate and 69 mg (364.7 µmol; 0.0315 eq.) of *para*-toluenesulfonic acid monohydrate for 16 hours. The volatile compounds were removed under reduced pressure. The residue was neutralized with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (65°C at $2.6 \cdot 10^{-2}$ mbar).

Yield: 2.019 g (98 %)

Aspect: yellow liquid



^{1}H NMR ($CDCl_3$, 300 MHz): 1.22 (*t*, $^3J_{5-4}$ = 6.6, 6 H, 5); 2.32 (*q*, $^3J_{2-1} = {}^3J_{2-3}$ = 5.1, 2 H, 2); 3.69-3.51 (*2 mult*, 4 H, 4); 4.49 (*t*, $^3J_{1-2}$ = 6.9, 2 H, 1); 4.61 (*t*, $^3J_{3-2}$ = 5.4, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.1 (5); 31.6 (2); 62.5 (4); 71.3 (1); 100.0 (3)
IR (liquid film, cm^{-1}): 1055; 1375; 1558 (NO_2); 1739; 3981 (C-H)
Mass (CI/CH_4-N_2O): 85 (100%); 132 ($[M\text{-}OEt]^+$, 29%)
b.p.: 65°C ($2.6 \cdot 10^{-2}$ mbar)
GC (100/0/10/290/20): t_R = 5.72 min

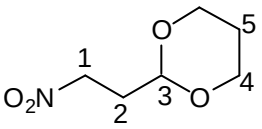
*9.1.4 Synthesis of 2-(2-nitroethyl)-1,3-dioxane **169***

M.F.: $C_6H_{11}NO_4$ (**M.W.** 161.15) **RN: 146073-16-7**

In a flame-dried two-necked flask, 297 mg (4.312 mmol; 1.17 eq.) of sodium nitrite were dissolved in 3.7 ml of DMSO. 0.5 ml (715 mg; 3.668 mmol; 1 eq.) of 2-(2-bromoethyl)-1,3-dioxane were added. The mixture was stirred for 27 hours and then poured into an Erlenmeyer containing a mixture of ice and Et_2O. The aqueous phase was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (mounting: petroleum ether : AcOEt 80 : 20 + 5% Et_3N; elution: petroleum ether : AcOEt 80 : 20).

Yield: 438 mg (74 %)

Aspect: colorless liquid



^{1}H NMR ($CDCl_3$, 300 MHz): 1.35 (*mult*, 1 H, 5_{ax}); 2.05 (*mult*, 1 H, 5_{eq}); 2.30 (*dt*, $^3J_{2\text{-}1}$ = 6.6, $^3J_{2\text{-}3}$ = 4.8, 2 H, 2); 3.76 (*dt*, $^3J_{4\text{-}5}$ = 12; $^2J_{4\text{-}4'}$ = 2.1, 2 H, 4_{ax}); 4.10 (*mult*, 2 H, 4_{eq}); 4.52 (*t*, $^3J_{1\text{-}2}$ = 6.9, 2 H, 1); 4.72 (*t*, $^3J_{3\text{-}2}$ = 4.8, 1 H, 3)
IR (liquid film, cm^{-1}): 1141; 1241; 1377; 1555 (NO_2); 1738; 2978 (C-H)
Mass (CI/CH_4-N_2O): 87 (19%); 115 ($[M\text{-}NO_2]^+$, 100%); 162 ($[M+H]^+$, 11%)
GC (100/0/10/290/20): t_R = 8.01 min

9.2 Synthesis of orthoester

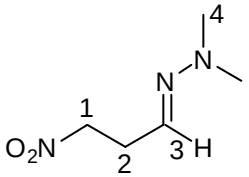
*9.2.1 Synthesis of 3-nitropropanal dimethylhydrazone **173***

M.F.: $C_5H_{11}N_3O_2$ (**M.W.** 145.16)

Reference (reaction conditions): Solladié-Cavallo, A.; Bonne, F. *Tetrahedron Asymmetry* **1996**, *7*, 171-180.

A mixture of 2 g (19.4 mmol; 1 eq.) of 3-nitropropanal **166**, 1.547 ml (1.224 g; 20.37 mmol; 1.05 eq.) of 1,1-dimethylhydrazine and 2.101 g (17.46 mmol; 0.9 eq.) of magnesium sulfate in 31.5 ml of CH_2Cl_2 was stirred for 6 hours at 0°C. It was then filtered and the solvent was removed under reduced pressure.
The product, highly unstable, is obtained sufficiently pure to be used without purification.

Yield: 2.755 g (98 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 2.75 (*s*, 6 H, 4); 2.91 (*dt*, $^3J_{2\text{-}1}$ = 6.6, $^3J_{2\text{-}3}$ = 3.9, 2 H, 2); 4.61 (*t*, $^3J_{1\text{-}2}$ = 6.6, 2 H, 1); 6.55 (*t*, $^3J_{3\text{-}2}$ = 3.9, 1 H, 3)

*9.2.2 Synthesis of 3-nitropropanenitrile **171***

M.F.: $C_3H_4N_2O_2$ (**M.W.** 100.07) **RN: 35461-45-1**

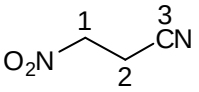
References:

reaction conditions: Fernandez, R.; Gasch, C.; Lassaletta, J. M.; Llera, J. M.; Vazquez, J. *Tetrahedron Lett.* **1993**, *34*, 141-144.

3-nitropropanenitrile **171**: Movsumzade, E. M.; Kulieva, D. A.; Mamedov, M. G.; Nasirov, Y. F. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **1985**, *28*, 12-16.

To an ice-cooled solution of 22.53 g (36.44 mmol; 2.5 eq.) of monoperoxyphthalic acid, magnesium salt hexahydrate, 80% in 114 ml of MeOH were added 2.116 g (14.57 mmol; 1 eq.) of 3-nitropropanal dimethylhydrazone **173** dissolved in 14.2 ml of MeOH. The solution was stirred for 5-10 minutes and then poured into a mixture of 355 ml of water and 355 ml of CH_2Cl_2. The organic phase was washed once with a saturated solution of NaCl, twice with water, then dried over $MgSO_4$, filtered and evaporated under reduced pressure. As only a small quantity of product was found in the organic phase, the aqueous phases were extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 921 mg (63 %)



^{1}H NMR ($CDCl_3$, 200 MHz): 3.09 (*t*, $^3J_{2\text{-}1}$ = 6.8, 2 H, 2); 4.66 (*t*, $^3J_{1\text{-}2}$ = 6.7, 2 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.6 (2); 69.1 (1); 115.4 (3)
IR (liquid film, cm^{-1}): 1380; 1560 (NSO_2); 2260 (C=N); 2980 (C-H)
Mass (CI/CH_4-N_2O): 82 (48%); 101 ($[M+H]^+$, 100%); 154 (17%); 201 ($[2M+H]^+$, 21%)
GC (100/0/10/290/15): t_R = 4.19 min

*9.2.3 Synthesis of 3-ethyloxetan-3-yl 3-bromopropanoate **176***

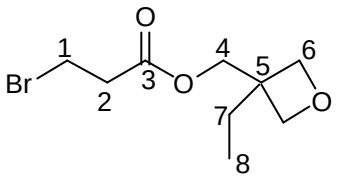
M.F.: $C_9H_{15}BrO_3$ (**M.W.** 251.12)

Reference: Keinan, E.; Sinha, S. C.; Singh, S. P. *Tetrahedron* **1991**, *47*, 4631-4638.

1 ml (1.019 g; 8.772 mmol; 1eq.) of 3-ethyl-3-oxetanemethanol was solubilized in 17.5 ml of THF and 852 µl (833 mg; 10.53 mmo; 1.2 eq.) of pyridine. The mixture was cooled to 0°C and 975 µl (1.66 g; 9.684 mmoles; 1.1 eq.) of 3-bromopropionyle

chloride were added. The mixture was stirred for 2 hours and the reaction was quenched by the addition of water. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was obtained sufficiently pure to be used without purification.

Yield: 2.194 (quant.)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.93 (*t*, $^3J_{8\text{-}7}$ = 7.5, 3 H, 8); 1.78 (*q*, $^3J_{7\text{-}8}$ = 7.2, 2 H, 7); 2.99 (*t*, $^3J_{2\text{-}1}$ = 6.6, 2 H, 2); 3.61 (*t*, $^3J_{1\text{-}2}$ = 6.9, 2 H, 1); 4.30 (*s*, 2 H, 4); 4.43 and 4.50 (*2 d*, $^2J_{6\text{-}6'}$ = 6.0, 4 H, 6)
IR (liquid film , cm^{-1}): 1740 (C=O); 2965 (C-H)
Mass (CI/CH_4-N_2O): 99 ($[M\text{-}BrCH_2CH_2CO_2]^+$, 78%), 251 ($[M+H]^+$ (^{79}Br), 96%); 253 ($[M+H]^+$ (^{81}Br), 100%)

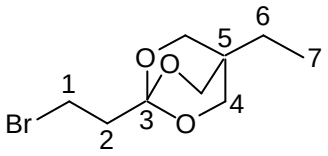
*9.2.4 Synthesis of 1-(2-bromoethyl)-4-ethyl-2,6,7-trioxabicyclo[2,2,2]octane **174***

M.F.: $C_9H_{15}BrO_3$ (**M.W.** 251.12)

Reference: Keinan, E.; Sinha, S. C.; Singh, S. P. *Tetrahedron* **1991**, *47*, 4631-4638.

In a flame-dried two-necked flask, 9 g (35.83 mmol; 1 eq.) of (3-ethyloxetan-3-yl)methyl 3-bromopropanoate were dissolved in 38.6 ml of CH_2Cl_2. The mixture was cooled to 0°C and 1.262 ml (1.424 g; 10.03 mmol; 0.28 eq.) of trifluoroborane diethyl etherate were added. After 3 hours of stirring at 0°C the reaction was quenched by the addition of 5.579 ml (4.061 g; 40.14 mmol; 1.12 eq.) of Et_3N. Et_2O was added and the precipitate that formed was eliminated by filtration. The filtrate was evaporated under reduced pressure.
The product was purified by flash chromatography (mounting: petroleum ether : AcOEt 80 : 20 + 10% Et_3N; elution: petroleum ether : AcOEt 80 : 20).

Yield: 5.949 g (66 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.83 (*t*, $^{3}J_{7\text{-}6}$ = 7.8, 3 H, 7); 1.24 (*q*, $^{3}J_{6\text{-}7}$ = 7.8, 2 H, 6); 2.26 (*mult*, 2 H, 2); 3.42 (*mult*, 2 H, 1); 3.91 (*s*, 6 H, 4)

^{13}C NMR ($CDCl_3$, 75 MHz): 7.6 (7); 22.5 (6); 26.1 (2); 33.2 (5); 40.5 (1); 71.0 (4); 108.0 (3)

Mass (CI/CH_4-N_2O): 99 (28%); 171 ($[M\text{-}Br]^+$, 44%); 251 ($[M+H]^+$ (^{79}Br), 95%); 253 ($[M+H]^+$ (^{81}Br), 100%)

Elemental analysis:

calculated (%): C: 43.05; H: 6.02; Br: 31.82

found (%): C: 43.69; H: 6.23; Br: 32.59

*9.2.5 Attempted synthesis of 4-ethyl-1-(2-nitroethyl)-2,6,7-trioxabicyclo[2.2.2]octane **232***

Reference (reaction conditions): Kornblum, N. In *Organic Reactions*; John Wiley & Sons, Inc.: New York, 1962; Vol. 12, p 101-156.

In a flame-dried flask, 97 mg (1.404 mmoles; 1.17 eq.) of sodium nitrite were put into 1.2 ml of DMSO. 300 mg (1.194 mmol; 1 eq.) of 1-(2-bromoethyl)-4-ethyl-2,6,7-trioxabicyclo[2,2,2]octane were added and the mixture was stirred for 27 hours. It was then poured into an Erlenmeyer containing a mixture of ice and Et_2O. The aqueous phase was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

The product obtained resulted from the substituion of the bromide by the nitrite and simultaneous hydrolysis of the orthoester function.

9.3 Michael addition of nitro-compounds: racemic

9.3.1 General procedure

A mixture of 1 eq. of the corresponding nitro-compound, 2.5 eq. of potassium carbonate and 0.1 eq. of the catalyst in the desired solvent were stirred for 15 minutes at room temperature before 1.3 eq. of the Michael acceptor were added. The mixture was stirred for x hours and then passed through a short pad of celite. The solvent was removed under reduced pressure.

The product was purified by flash chromatography.

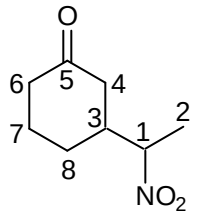
9.3.2 Addition of nitroethane to cyclohexenone

Following the general procedure described in 9.3.1 with:
50 µl (52 mg; 696 µmol; 1 eq.) of nitroethane
240 mg (1.74 mmol; 2.5 eq.) of potassium carbonate
16 mg (69.6 µmol; 0.1 eq.) of benzyltriethylammonium chloride
88 µl (86 mg; 904.8 µmol; 1.3 eq.) of 2-cyclohexen-1-one
3.8 ml of CH_2Cl_2
Reaction time: 4 hours
Flash chromatography: petroleum ether : AcOEt 60 : 40

Yield: 80 mg (67 %) as a mixture of 2 diastereomers

3-(1-nitroethyl)cyclohexanone ***177***
M.F.: $C_8H_{13}NO_3$ (**M.W.** 171.19) **RN: 59969-93-6**

Aspect: yellow oil
TLC: R_f = 0.5 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.53 (*t*, $^3J_{2\text{-}1}$ = 6.6, 3 H, 2); 1.58-2.49 (*m*, 9 H, 3, 4, 6, 7, 8); 4.49 (*mult*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 16.1 (2'); 16.3 (2); 24.2 and 26.9 (7, 8); 24.3 and 27.4 (7', 8'); 40.8 (6); 42.3 (3'); 42.4 (3); 43.2 (4'); 43.6 (4); 86.9 (1); 208.3 (5)
IR (liquid film, cm^{-1}): 1547 (NO_2); 1715 (C=O); 2950 (C-H)
Mass (CI +Q1MS): 125 ($[M\text{-}NO_2]^+$, 28%); 172 ($[M+H]^+$, 24%); 296 ($[2M\text{-}NO_2]^+$, 35%); 343 ($[2M+H]^+$, 100%)
Mass (CI -Q1MS): 57 (100%); 170 ($[M-H]^-$, 85%)
GC (100/0/10/290/15): t_R = 8.38 min; t_R = 8.77 min

9.3.3 Addition of nitropropane to cyclohexenone

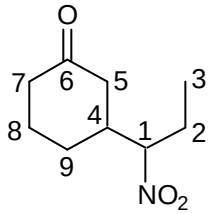
Following the general procedure described in 9.3.1 with:
62 µl (62 mg; 696 µmol; 1 eq.) of 1-nitropropane

240 mg (1.74 mmol; 2.5 eq.) of potassium carbonate
16 mg (69.6 µmol; 0.1 eq.) of benzyltriethylammonium chloride
88 µl (86 mg; 904.8 µmol; 1.3 eq.) of 2-cyclohexen-1-one
3.8 ml of CH_2Cl_2
Reaction time: 4 hours
Flash chromatography: petroleum ether : AcOEt 50 : 50

Yield: 136 mg (quant.) as a mixture of 2 diastereomers

3-(1-nitropropyl)cyclohexanone ***178***
M.F.: $C_9H_{15}NO_3$ (**M.W.** 185.22) **RN: 71759-65-4**

Aspect: yellow oil
TLC: R_f = 0.54 (petroleum ether : AcOEt 60 : 40)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.94 (*t*, $^3J_{3-2}$ = 7.5, 3 H, 3); 1.34-2.5 (*m*, 11 H, 2, 4, 5, 7, 8, 9); 4.31 (*mult*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 10.1 (3); 10.3 (3'); 23.9 and 24.1 (2, 8); 24.0 and 24.3 (2', 8'); 27.4 (9'); 27.5 (9); 40.8 (7); 41.2 (4); 41.4 (4'); 43.3 (5'); 43.7 (5); 94.6 (1); 208.6 (6)
IR (liquid film, cm^{-1}): 1547 (NO_2); 1716 (C=O); 2943 (C-H)
Mass (CI +Q1MS): 139 ($[M-NO_2]^+$, 3%); 186 ($[M+H]^+$, 4%); 324 ($[2M-NO_2]^+$, 45%); 357 (31%); 371 ($[2M+H]^+$, 100%)
GC (100/0/10/290/15): t_R = 9.21 min; t_R = 9.89 min

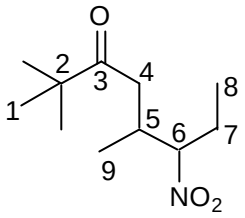
9.3.4 Addition of nitropropane to 2,2-dimethylhex-4-en-3-one ***75***

Following the general procedure described in 9.3.1 with:
60 µl (59 mg; 672 µmol; 1 eq.) of 1-nitropropane
232 mg (1.68 mmol; 2.5 eq.) of potassium carbonate
15 mg (67.2 µmol; 0.1 eq.) of benzyltriethylammonium chloride
110 mg (873.7 µmol; 1.3 eq.) of (*E*)-2,2-dimethylhex-4-en-3-one
3.7 ml of CH_2Cl_2
Reaction time: 4 hours

Flash chromatography: petroleum ether : AcOEt 70 : 30

Yield: 79 mg (55 %)

2,2,5-trimethyl-6-nitrooctan-3-one ***179***
M.F.: $C_{11}H_{21}NO_3$ (**M.W.** 215.29)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.95 (*d*, $^3J_{9\text{-}5}$ = 7.8, 3 H, 9); 0.96 (*t*, $^3J_{8\text{-}7}$ = 6.9, 3 H, 8); 1.13 and 1.15 (*2 s*, 9 H, 1); 1.65-2.15 (*2 mult*, 3 H, 5, 7); 2.56 (*mult*, 2 H, 4); 4.44 (*mult*, 1 H, 6)
^{13}C NMR ($CDCl_3$, 75 MHz): 10.4 (8); 10.5 (8'); 14.6 (9); 16.7 (9'); 24.2 (7); 24.3 (7'); 26.1 (1'); 26.3 (1); 31.7 (5); 32.2 (5'); 38.7 (4'); 40.1 (4); 44.1 (2); 93.0 (6); 94.5 (6'); 214.3 (3)
IR (liquid film, cm^{-1}): 808; 1368; 1548 (NO_2); 1706 (C=O); 2972 (C-H)
Mass (CI +Q1MS): 85 ($[(CH_3)_3CC{=}O]^+$, 35%); 169 ($[M\text{-}NO_2]^+$, 100%); 216 ($[M+H]^+$, 14%)
GC (60/0/10/290/10): t_R = 5.13 min
HRMS: calculated for $C_{11}H_{22}NO_3^+$: 216.159969; found: 216.160446

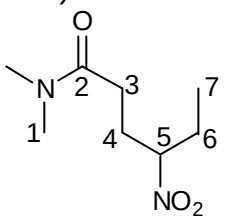
9.3.5 Addition of nitropropane to N,N*-dimethylacrylamide*

Following the general procedure described in 9.3.1 with:
62 µl (62 mg; 696 µmol; 1 eq.) of 1-nitropropane
240 mg (1.74 mmol; 2.5 eq.) of potassium carbonate
16 mg (69.6 µmol; 0.1 eq.) of benzyltriethylammonium chloride
93 µl (89 mg; 904.8 µmol; 1.3 eq.) of *N,N*-dimethylacrylamide
3.8 ml of CH_2Cl_2
Reaction time: 20 hours
Flash chromatography: AcOEt : CH_2Cl_2 50 : 50

Yield: 109 mg (83 %)

N,N*-dimethyl-4-nitrohexanamide* ***180***
M.F.: $C_8H_{16}N_2O_3$ (**M.W.** 188.22)

TLC: R_f = 0.36 (CH_2Cl_2 : AcOEt 50 : 50)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.98 (*t*, $^3J_{7\text{-}6}$ = 7.5, 3 H, 7); 1.85 and 2.01 (*2 mult*, 2 H, 6); 2.16-2.28 (*m*, 2 H, 4); 2.33 (*mult*, 2 H, 3); 2.96 and 2.97 (*2 s*, 6 H, 1); 4.56 (*mult*, 1 H, 5)

^{13}C NMR ($CDCl_3$, 75 MHz): 10.1 (7); 27.3 (6); 28.5 (4); 28.7 (3); 35.3 and 36.8 (1); 89.6 (5); 170.6 (2)

IR (liquid film, cm^{-1}): 1265 (NO_2); 1547 (NO_2); 1647 (C=O); 2974 (C-H)

Mass (CI/CH_4-N_2O): 142 ($[M\text{-}NO_2]^+$, 91%); 189 ($[M+H]^+$, 100%); 377 ($[2M+H]^+$; 20%)

HRMS: calculated for $C_8H_{17}N_2O_3^+$: 189.123918; found: 189.123025

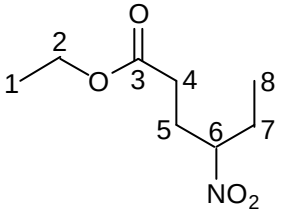
9.3.6 Addition of nitropropane to ethyl acrylate

Following the general procedure described in 9.3.1 with:
62 µl (62 mg; 696 µmol; 1 eq.) of 1-nitropropane
240 mg (1.74 mmol; 2.5 eq.) of potassium carbonate
16 mg (69.6 µmol; 0.1 eq.) of benzyltriethylammonium chloride
98 µl (90 mg; 904.8 µmol; 1.3 eq.) of ethyl acrylate
3.8 ml of CH_2Cl_2
Reaction time: 4 hours
Flash chromatography: petroleum ether : AcOEt 60 : 40

Yield: 157 mg (quant.)

ethyl 4-nitrohexanoate ***181***

M.F.: $C_8H_{15}NO_4$ (**M.W.** 189.21) **RN: 59925-14-3**



^{1}H NMR ($CDCl_3$, 200 MHz): 0.98 (*t*, $^3J_{8\text{-}7}$ = 7.4, 3 H, 8); 1.26 (*t*, $^3J_{1\text{-}2}$ = 7.2, 3 H, 1); 1.72-2.41 (*m*, 6 H, 4, 5, 7); 4.15 (*q*, $^3J_{2\text{-}1}$ = 6.3, 2 H, 2); 4.49 (*mult*, 1 H, 6)

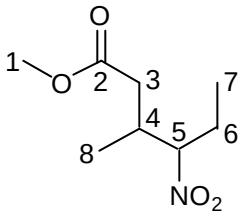
^{13}C NMR ($CDCl_3$, 50 MHz): 10.0 (8); 14.1 (1); 27.1 and 28.4 (5, 7); 29.9 (4); 60.7 (2); 89.1 (6); 171.8 (3)
IR (liquid film, cm^{-1}): 1186; 1265; 1550 (NO_2); 1735 (C=O); 2981 (C-H)
Mass (CI +Q1MS): 143 ($[M-NO_2]^+$, 100%); 190 ($[M+H]^+$, 11%)

9.3.7 Addition of nitropropane to methyl crotonate

Following the general procedure described in 9.3.1 with:
62 µl (62 mg; 696 µmol; 1 eq.) of 1-nitropropane
240 mg (1.74 mmol; 2.5 eq.) of potassium carbonate
16 mg (69.6 µmol; 0.1 eq.) of benzyltriethylammonium chloride
96 µl (90 mg; 904.8 µmol; 1.3 eq.) of methyl crotonate
3.8 ml of CH_2Cl_2
Reaction time: 24 hours
Flash chromatography: petroleum ether : AcOEt 50 : 50

Yield: 53 mg (40 %)

methyl 3-methyl-4-nitrohexanoate ***182***
M.F.: $C_8H_{15}NO_4$ (**M.W.** 189.21) **RN: 16507-08-7**



^{1}H NMR ($CDCl_3$, 200 MHz): 0.97 (*t*, $^3J_{7\text{-}6}$ = 7.3, 3 H, 7); 1.06 (*d*, $^3J_{8\text{-}4}$ = 7.4, 3 H, 8); 1.69-2.38 (*m*, 3 H, 4, 6); 2.50 (*mult*, 2 H, 3); 3.69 and 3.71 (*2 s*, 3 H, 1); 4.41 (*mult*, 1 H, 5)
^{13}C NMR ($CDCl_3$, 50 MHz): 10.3 (7'); 10.4 (7); 15.4 (8); 16.2 (8'); 23.9 (6 and 6'); 33.3 (4'); 33.4 (4); 36.9 (3'); 37.4 (3); 51.7 (1); 93.4 (5); 94.0 (5'); 164.8 (2'); 172.0 (2)
IR (liquid film, cm^{-1}): 1548 (NO_2); 1739 (C=O); 2977 (C-H)
Mass (CI +Q1MS): 143 ($[M-NO_2]^+$, 100%); 158 ($[M-OMe]^+$, 16%); 190 ($[M+H]^+$, 22%)

9.3.8 Addition of nitropropane to methyl methacrylate

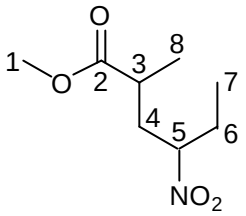
Following the general procedure described in 9.3.1 with:
60 µl (59 mg; 672 µmol; 1 eq.) of 1-nitropropane

232 mg (1.68 mmol; 2.5 eq.) of potassium carbonate
15 mg (67.2 µmol; 0.1 eq.) of benzyltriethylammonium chloride
93 µl (87 mg; 873.7 µmol; 1.3 eq.) of methyl methacrylate
3.7 ml of CH_2Cl_2
Reaction time: 4 hours
Flash chromatography: petroleum ether : AcOEt 80 : 20

Yield: 69 mg (54 %) as a mixture of 2 diastereomers

methyl 2-methyl-4-nitrohexanoate ***183***
M.F.: $C_8H_{15}NO_4$ (**M.W.** 189.21) **RN: 16507-05-4**

TLC: R_f = 0.64; 0.71 (petroleum ether : AcOEt 80 : 20)



^{1}H NMR ($CDCl_3$, 200 MHz): 0.96 and 0.97 (*2 t*, $^3J_{7\text{-}6}$ = 7.2, 3 H, 7); 1.20 and 1.23 (*2 d*, $^3J_{8\text{-}3}$ = 6.6, 3 H, 8); 1.70-2.09 (*m*, 4 H, 4, 6); 2.45 (*mult*, 1 H, 3); 3.69 and 3.71 (*2 s*, 3 H, 1); 4.49 (*mult*, 1 H, 5)
^{13}C NMR ($CDCl_3$, 50 MHz): 10.0 and 10.1 (7); 16.4 and 18.0 (8); 27.3 and 27.7 (6); 36.2 and 36.3 (3); 36.5 and 36.9 (4); 51.8 and 51.9 (1); 87.6 and 88.5 (5); 175.3 and 175.6 (2)
IR (liquid film, cm^{-1}): 1550 (NO_2); 1737 (C=O); 2978 (C-H)
Mass (CI +Q1MS): 143 ($[M\text{-}NO_2]^+$, 100%); 158 ($[M\text{-}OMe]^+$, 24%); 190 ($[M+H]^+$, 6%)

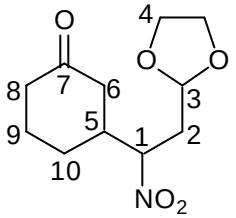
9.3.9 Addition of 2-(2-nitroethyl)-1,3-dioxolane ***167*** *to cyclohexenone*

Following the general procedure described in 9.3.1 with:
100 mg (679.6 µmol; 1 eq.) of 2-(2-nitroethyl)-1,3-dioxolane **167**
235 mg (1.699 mmol; 2.5 eq.) of potassium carbonate
15 mg (67.96 µmol; 0.1 eq.) of benzyltriethylammonium chloride
85 µl (84 mg; 883.5 µmol; 1.3 eq.) of 2-cyclohexen-1-one
3.7 ml of CH_2Cl_2
Reaction time: 3 hours
Flash chromatography: mounting: petroleum ether : AcOEt 80 : 20 + 5% Et_3N; elution: petroleum ether : AcOEt 80 : 20

Yield: 133 mg (80 %) as a mixture of 2 diastereomers

*3-[2-(1,3-dioxolan-2-yl)-1-nitroethyl]cyclohexanone **184***

M.F.: $C_{11}H_{17}NO_5$ (**M.W.** 243.25) **RN: 215236-84-3 (*R,R*)**



^{1}H NMR ($CDCl_3$, 300 MHz): 1.39-1.76 (*m*, 4 H, 9, 10); 1.82-2.27 (*m*, 4 H, 6, 8); 2.35-2.58 (*m*, 2 H, 2); 2.82 (*mult*, 1 H, 5); 3.95 (*mult*, 4 H, 4); 4.65 (*mult*, 1 H, 1); 4.95 (*mult*, 1 H, 3)

^{13}C NMR ($CDCl_3$, 75 MHz): 24.1 and 24.2 (10); 26.8 and 27.6 (9); 33.9 (2); 40.7 (8); 41.6 and 41.7 (5); 42.9 and 43.9 (6); 65.1 (4); 86.4 and 86.6 (1); 100.8 and 100.9 (3); 208.1 (7)

Mass (CI/CH_4-N_2O): 59 (100%); 73 (29%); 79 (52%); 197 ($[M-NO_2]^+$, 53%); 244 ($[M+H]^+$, 12%)

GC (100/0/10/290/20): t_R = 15.49 min; t_R = 15.77 min

*9.3.10 Addition of 2-(2-nitroethyl)-1,3-dioxane **169** to cyclohexenone*

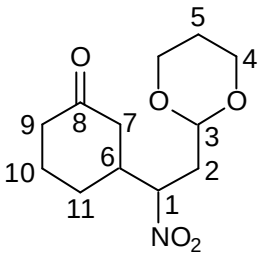
Following the general procedure described in 9.3.1 with:
100 mg (620.5 µmol; 1 eq.) of 2-(2-nitroethyl)-1,3-dioxane **169**
214 mg (1.551 mmol; 2.5 eq.) of potassium carbonate
14 mg (62.05 µmol; 0.1 eq.) of benzyltriethylammonium chloride
78 µl (77 mg, 806.6 µmol; 1.3 eq.) of 2-cyclohexen-1-one
3.4 ml of CH_2Cl_2
Reaction time: 3 hours
Flash chromatography: mounting: petroleum ether : AcOEt 70 : 30 + 5% Et_3N; elution: petroleum ether : AcOEt 70 : 30

Yield: 153 mg (96 %) as a mixture of 2 diastereomers

*3-[2-(1,3-dioxan-2-yl)-1-nitroethyl]cyclohexanone **185***

M.F.: $C_{12}H_{19}NO_5$ (**M.W.** 257.28)

Aspect: yellow oil



^{1}H NMR ($CDCl_3$, 300 MHz): 1.30-1.72 (*m*, 4 H, 10, 11); 1.83-2.56 (*m*, 8 H, 2, 5, 7, 9); 3.72 and 4.07 (*2 mult*, 4 H, 4); 4.58 (*mult*, 1 H, 3); 4.70 (*mult*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 75 MHz): 24.3 and 24.35 (10); 25.4 (5); 27.0 and 27.7 (11); 35.4 and 35.5 (2); 40.9 (9); 41.7 and 41.8 (6); 43.1 and 44.0 (7); 66.8 (4); 86.8 and 87.0 (1); 98.3 (3); 208.4 (8)
IR (liquid film, cm^{-1}): 1047; 1244; 1375 (NO_2); 1551 (NO_2); 1731 (C=O); 2979 (C-H)
Mass (CI/CH_4-N_2O): 83 (100%); 85 (73%); 87 (84%); 101 (31%); 103 (22%); 211 ([M-NO_2]$^+$, 30%); 258 ([M+H]$^+$, 15%)
GC (100/0/10/290/20): t_R = 17.58 min; t_R = 17.93 min
Chiral GC (150/0/0.4/200/10): t_R = 65.65 min and 66.00 min (1st diastereomer); 69.08 min and 69.80 min (2nd diastereomer)
HRMS: calculated for $C_{12}H_{20}NO_5^+$: 258.134148; found: 258.134773

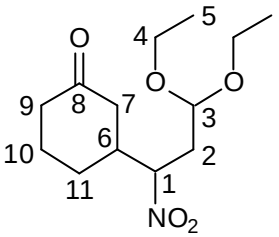
*9.3.11 Addition of 1,1-diethoxy-3-nitropropane **168** to cyclohexenone*

Following the general procedure described in 9.3.1 with:
100 mg (564.3 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **168**
195 mg (1.41 mmol; 2.5 eq.) of potassium carbonate
13 mg (56.43 µmol; 0.1 eq.) of benzyltriethylammonium chloride
71 µl (70 mg; 733.6 µmol; 1.3 eq.) of 2-cyclohexen-1-one
3.1 ml of CH_2Cl_2
Reaction time: 3 hours
Flash chromatography: mounting: petroleum ether : AcOEt 70 : 30 + 5% Et_3N; elution: petroleum ether : AcOEt 70 : 30

Yield: 126 mg (82 %) as a mixture of 2 diastereomers

*3-(3,3-diethoxy-1-nitropropyl)cyclohexanone **186***
M.F.: $C_{13}H_{23}NO_5$ (**M.W.** 273.32)

Aspect: yellow oil
TLC: R_f = 0.54 (petroleum ether : AcOEt 70 : 30)



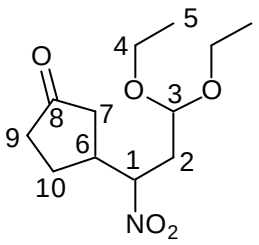
^{1}H NMR ($CDCl_3$, 300 MHz): 1.19 (*t*, $^{3}J_{5\text{-}4}$ = 6.9, 6 H, 5); 1.40-1.75 (*m*, 2 H, 10, 11); 1.82-2.01 (*m*, 2 H, 10, 11); 2.08-2.35 (*m*, 4 H, 7, 9); 2.36-2.55 (*m*, 3 H, 2, 6); 3.48 and 3.66 (*2 mult*, 4 H, 4); 4.44 (*dd*, $^{3}J_{3\text{-}2}$ = 6.0, $^{3}J_{3\text{-}2}$ = 1.9, 1 H, 3); 4.61 (*mult*, 1 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): 14.9 and 15.0 (5); 24.1 and 24.2 (10); 27.0 and 27.6 (11); 34.9 (2); 40.7 (9); 41.6 and 41.8 (6); 43.1 and 43.9 (7); 62.4 and 62.5 (4); 62.8 and 62.9 (4); 88.0 and 88.2 (1); 100.0 (3); 207.9 and 208.0 (8)
IR (liquid film, cm^{-1}): 1551 (NO_2); 1717 (C=O); 2676 (C-H)
Mass (CI/CH_4-N_2O): 97 ($[C_6H_9O]^+$, 100%); 181 (13%); 183 ($[M\text{-}2OEt]^{\bullet+}$, 2%); 228 ($[M\text{-}OEt]^+$, 2%)
GC (100/0/10/290/20): t_R = 14.64 min; t_R = 14.87 min
Chiral GC (100/0/10/150/1/220/5): t_R= 49.08 min (1st diastereomer); 50.41 min and 51.43 min (2nd diastereomer)

*9.3.12 Addition of 1,1-diethoxy-3-nitropropane **168** to cyclopentenone*

Following the general procedure described in 9.3.1 with:
100 mg (564.3 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **168**
195 mg (1.41 mmol; 2.5 eq.) of potassium carbonate
13 mg (56.43 µmol; 0.1 eq.) of benzyltriethylammonium chloride
61 µl (60 mg; 733.6 µmol; 1.3 eq.) of 2-cyclopentenone
3.1 ml of CH_2Cl_2
Reaction time: 3 hours
Flash chromatography: mounting: petroleum ether : AcOEt 60 : 40 + 5% Et_3N; elution: petroleum ether : AcOEt 60 : 40

Yield: 148 mg (quant.) as a mixture of 2 diastereomers

*2-(3,3-diethoxy-1-nitropropyl)cyclopentenone **198***
M.F.: $C_{12}H_{21}NO_5$ (**M.W.** 259.3)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.19 and 1.20 (*2 t*, $^{3}J_{5\text{-}4}$ = 7.1, 6 H, 5); 1.62-2.55 (m, 7 H, 2, 7, 9, 10); 2.57-2.78 (m, 2 H, 2); 3.49 and 3.68 (2 mult, 4 H, 4); 4.46 (mult, 1 H, 3); 4.62 (mult, 1 H, 1)

^{13}C NMR ($CDCl_3$, 50 MHz): 15.0 and 15.1 (5); 25.9 and 26.2 (10); 35.8 and 36.6 (2); 38.0 and 38.2 (9); 40.4 and 40.5 (6); 41.3 and 41.5 (7); 62.7 and 63.2 (4); 88.1 and 88.2 (1); 99.9 and 99.95 (3); 215.1 (8)

IR (liquid film, cm^{-1}): 1548 (NO_2); 1740 (C=O); 2975 (C-H)

Mass (CI/CH_4-N_2O): 59 (39%); 83 ($[C_5H_7O]^+$, 100%); 103 (34%); 141 (26%); 167 (80%); 183 (34%); 187 (35%); 214 ($[M+OEt]^+$, 17%)

GC (100/0/10/290/10): t_R = 13.79 min; t_R = 14.04 min

Chiral GC (100/010/150/0.5/225/5): t_R = 43.97 min and 44.62 min (1st diastereomer); 47.06 min (2nd diastereomer)

9.4 Synthesis of catalysts

9.4.1 General procedure

Reference: Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415.

A mixture of 1 eq. of amine and 1 eq. of aryl chloride was refluxed for 3 hours in toluene or methanol. Once cooled to room temperature, the mixture was poured into an important volume (~10 times the volume of the solvent) of Et_2O to precipitate the product. Filtration and drying under vacuum allowed to isolate the product.

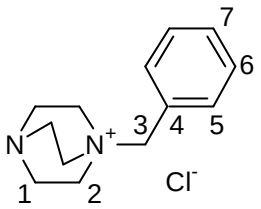
9.4.2 Monobenzylation of 1,4-diazabicyclo[2.2.2]octane

Following the general procedure described in 9.4.1 with:
200 mg (1.782 mmol; 1 eq.) of 1,4-diazabicyclo[2.2.2]octane
427 µl (469 mg; 3.708 mmol; 2.08 eq.) of benzyl chloride
5.3 ml of toluene

Yield: 425 mg (quant.)

*1-(phenylmethyl)-4-aza-1-azoniabicyclo**[**2.2.2**]**octane chloride **187***
M.F.: $C_{13}H_{19}ClN_2$ (**M.W.** 238.756) **RN: 42790-42-1**

Aspect: white solid



^{1}H NMR ($CDCl_3$, 300 MHz): 3.17 (*t*, $^{3}J_{1-2}$ = 7.5, 6 H, 1); 3.77 (*t*, $^{3}J_{2-1}$ = 7.2, 6 H, 2); 5.13 (*s*, 2 H, 3); 7.43 (*mult*, 3 H, 6, 7); 7.64 (*d*, $^{3}J_{5-6}$ = 7.5, 2 H, 5)
^{13}C NMR (CD_3OD, 50 MHz): 46.2 (1); 53.6 (2); 69.4 (3); 127.8 (4); 130.0 (6); 131.8 (7); 134.3 (5)
Mass (CI/CH_4-N_2O): 59 (79%); 91 (100%); 203 ($[M]^+$, 7%)

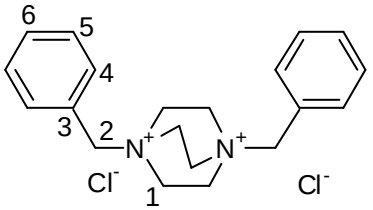
9.4.3 Dibenzylation of 1,4-diazabicyclo[2.2.2]octane

Following the general procedure described in 9.4.1 with:
200 mg (1.782 mmol; 1 eq.) of 1,4-diazabicyclo[2.2.2]octane
410 µl (451 mg; 3.565 mmol; 2 eq.) of benzyl chloride
2.7 ml of MeOH

Yield: 651 mg (quant.)

*1,4-bis(phenylmethyl)-1,4-diazoniabicyclo[2.2.2]octane dichloride **188***
M.F.: $C_{20}H_{26}Cl_2N_2$ (**M.W.** 365.345) **RN: 42790-43-2**

Aspect: white solid



^{1}H NMR (CD_3OD, 300 MHz): 3.98 (*s*, 12 H, 1); 4.83 (*s*, 4 H, 2); 7.55-7.61 (*m*, 10 H, 4, 5, 6)
^{13}C NMR (CD_3OD, 50 MHz): 52.2 (1); 69.6 (2); 127.0 (3); 130.9 (5); 132.6 (6); 134.4 (4)
Mass (CI/CH_4-N_2O): 59 (100%); 91 (63%); 131 (58%); 203 ($[M\text{-}CH_2C_6H_5]^+$, 28%)

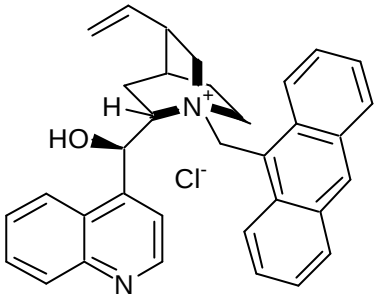
9.4.4 Reaction of cinchonidine with 9-(chloromethyl)anthracene

Following the general procedure described in 9.4.1 with:
410 mg (1.391 mmol; 1 eq.) of cinchonidine
328 mg (1.446 mmol; 1.04 eq.) of 9-(chloromethyl)anthracene
4 ml of toluene

Yield: 633 mg (87 %)

N-(9-anthrylmethyl)cinchonidinium chloride ***189***

M.F.: $C_{34}H_{33}ClN_2O$ (**M.W.** 521.10) **RN: 199588-80-2**



Spectral data identical to a commercial sample.
Mass (APCI): 191 ($[CH_3C_{14}H_8]^+$, 21%); 295 ($[M\text{-}CH_2C_{14}H_8]^+$, 100%); 485 ($M^+$, 7%)

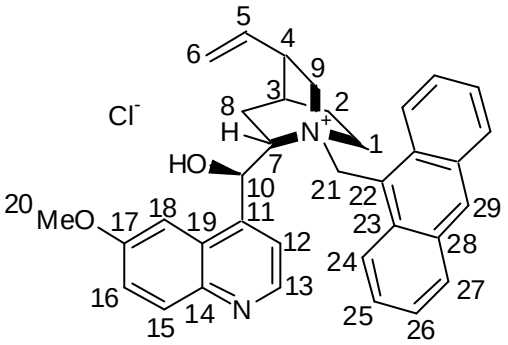
9.4.5 Reaction of quinine with 9-(chloromethyl)anthracene

Following the general procedure described in 9.4.1 with:
451 mg (1.391 mmol; 1 eq.) of quinine
328 mg (1.446 mmol; 1.04 eq.) of 9-(chloromethyl)anthracene
4 ml of toluene

Yield: 499 mg (65 %)

N-(9-anthrylmethyl)quininium chloride ***156***

M.F.: $C_{35}H_{35}ClN_2O_2$ (**M.W.** 551.12) **RN: 199588-84-6**



^{13}C NMR: 17.9 and 24.2 (2, 8); 26.9 (3); 37.1 (4); 54.6, 57.1 and 61.0 (1, 9, 21); 55.4, 60.1 and 65.8 (7, 10, 20); 99.7 (18); 117.1 and 118.1 (6, 19); 118.7, 121.2, 122.1, 124.9, 125.4, 127.8, 128.8 and 131.8 (12, 15, 16, 24, 25, 26, 27, 29); 126.4, 130.8 and 132.8 (22, 23, 28); 136.5 (5); 143.8 and 144.1 (11, 14); 147.4 (13); 158.1 (17)
Mass (APCI): 279 (100%); 325 ([M-$CH_2C_{14}H_8$]$^+$, 64%); 391 (11%); 515 (M^+, 2%)

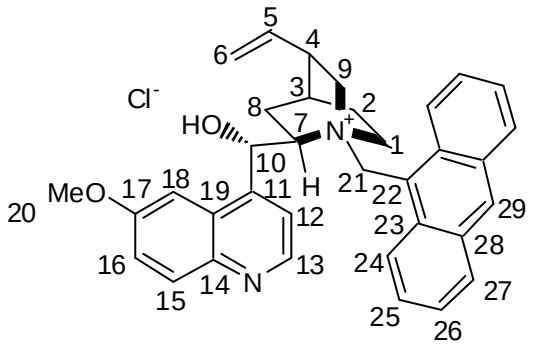
9.4.6 Reaction of quinidine with 9-(chloromethyl)anthracene

Following the general procedure described in 9.4.1 with:
451 mg (1.391 mmol; 1 eq.) of quinidine
328 mg (1.446 mmol; 1.04 eq.) of 9-(chloromethyl)anthracene
4.2 ml of toluene

Yield: 363 mg (47 %)

N-(9-anthrylmethyl)quinidinium chloride ***155***

M.F.: $C_{35}H_{35}ClN_2O_2$ (**M.W.** 551.12) **RN: 199588-78-8**



^{13}C NMR ($CDCl_3$, 50 MHz): 17.6 and 23.4 (2, 8); 27.6 (3), 37.5 (4); 48.4, 49.2 and 54.5 (1, 9, 21); 56.8, 60.0 and 66.3 (7, 10, 20); 99.6 (18); 117.7 and 118.3 (6, 19); 118.5, 122.2, 124.9, 125.0 and 131.2 (24, 25, 26, 27, 29); 120.6 and 121.2 (12, 16); 125.1 (22); 130.5 and 133.1 (23, 28); 136.3 (5); 143.6 and 144.1 (11, 14); 147.0 (13); 158.0 (17)

Mass (APCI): 282 (35%); 325 ([M-$CH_2C_{14}H_8$]+, 100%); 515 (M^+, 2%)

9.4.7 Reaction of cinchonine with 1-(chloromethyl)naphthalene

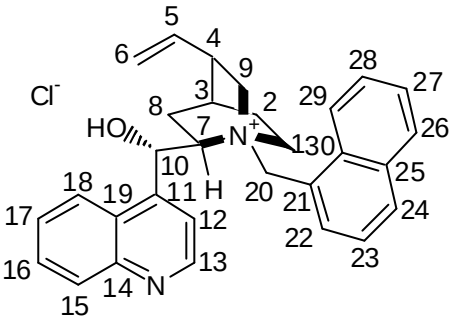
Following the general procedure described in 9.4.1 with:
409 mg (1.391 mmol; 1 eq.) of cinchonine
232 µl (255 mg; 1.446 mmol; 1.04 eq.) of 1-(chloromethyl)naphthalene
4.2 ml of toluene

Yield: 537 mg (82%)

*N-(1-naphthylmethyl)cinchoninium chloride **190***

M.F.: $C_{30}H_{31}ClN_2O$ (**M.W.** 471.03)

Aspect: white solid



^{1}H NMR ($CDCl_3$, 300 MHz): 0.65-0.80 (*m*, 2 H); 2.06 (*mult*, 2 H); 2.62 (*mult*, 1 H); 3.26 (*t*, *J* = 12.0, 1 H); 4.07 (*mult*, 2 H); 4.12-4.23 (*m*, 1 H); 4.54 (*t*, *J* = 10.4, 1 H); 5.13 (*d*, *J* = 16.8, 1 H); 5.18 (*d*, *J* = 9.6, 1 H); 5.58 (*d*, *J* = 11.2, 1 H); 5.81 (*mult*, 1 H); 6.42 (*d*, *J* = 11.2, 1 H); 6.52-6.61 (*m*, 1 H); 7.01 (*mult*, 2 H); 7.18 (*mult*, 1 H); 7.23-7.38 (*m*, 3 H); 7.50-7.62 (*m*, 4 H); 7.85-7.94 (*m*, 2 H); 8.28 (*d*, *J* = 8.0, 1 H); 8.80 (*d*, *J* = 4.0, 1 H)

^{13}C NMR ($CDCl_3$, 50 MHz): 22.0 and 23.9 (2, 8); 26.7 (3); 37.9 (4); 49.9, 54.8 and 56.4 (1, 9, 20); 66.3 and 66.5 (7, 10); 117.7 (6); 119.6 (12); 122.5 and 123.6 (19, 21); 123.4, 124.3, 124.7 and 125.6 (18, 26, 27, 28); 126.9, 127.3, 128.1, 128.5, 129.1 and 130.2 (16, 17, 22, 23, 24, 28); 132.7 and 133.0 (25, 30); 134.3 (15); 135.3 (5); 145.2 (11); 146.8 (14); 149.3 (13)

Mass (APCI): 141 ([$CH_2C_{10}H_7$]$^+$, 25 %); 295 ([M-($CH_2C_{10}H_7$]$^+$, 100%); 435 (M^+, 43%)

[α**]**$^D_{20}$: 196° (c=0.240; MeOH)

m.p.: 228°C (decomposition)

9.4.8 Reaction of cinchonine with 4-(chloromethylbiphenyl)

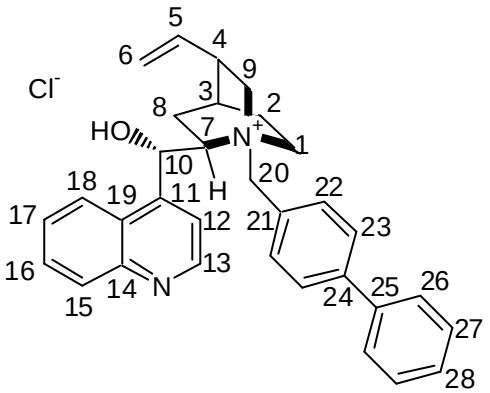
Following the general procedure described in 9.4.1 with:
400 mg (1.358 mmol; 1 eq.) of cinchonine
286 mg (1.413 mmol; 1.04 eq.) of 4-(chloromethyl)biphenyl
4.1 ml of toluene

Yield: 484 mg (72 %)

N-([1,1'-biphenyl]-4-ylmethyl)cinchoninium chloride ***191***

M.F.: $C_{32}H_{33}ClN_2O$ (**M.W.** 497.07)

Aspect: purple solid



^{1} H NMR ($CDCl_3$, 300 MHz): 0.65-0.76 (*m*, 2 H); 2.02-2.21 (*m*, 2 H); 2.65-2.78 (*m*, 1 H); 3.34 (*t*, *J* = 10.5, 1 H); 3.92-4.18 (*m*, 2 H); 4.52 (*mult*, 1 H); 5.20 (*mult*, 4 H); 5.82 (*mult*, 1 H); 6.39 (*d*, *J* = 11.7, 1 H); 6.51 (*broad s*, 1 H); 7.00 (*mult*, 2 H); 7.19-7.29 (*m*, 3 H); 7.30-7.36 (*m*, 3 H); 7.54 (*mult*, 3 H); 7.60-7.69 (*m*, 2 H); 7.89 (*d*, *J* = 4.2, 1 H); 8.30 (*d*, *J* = 8.1, 1 H); 8.82 (*d*, *J* = 4.8, 1 H)
^{13}C NMR ($CDCl_3$, 50 MHz): 21.7 and 23.7 (2, 8); 27.1 (3); 38.0 (4); 49.7, 53.5 and 56.3 (1, 9, 20); 65.7 and 67.0 (7, 10); 118.0 (6); 119.6 (12); 123.1 (18); 123.5 (19); 126.1 (21); 126.8, 127.8, 128.3 and 128.9 (22, 23, 26, 27); 129.2 and 130.1 (16, 17); 134.3 and 135.3 (5, 15); 139.4 and 142.2 (24, 25); 144.7 and 146.8 (11, 14); 149.3 (13)
Mass (APCI): 167 ($[CH_2C_6H_4C_6H_5]^+$, 67%); 295 ($[M\text{-}CH_2C_6H_4C_6H_5]^+$, 80%); 461 ($M^+$, 100%)
[α**]**$^D_{20}$: 107° (c=0.225; MeOH)
m.p.: 192° (decomposition)

9.4.9 Reaction of cinchonine with 2-(chloromethyl)naphthalene

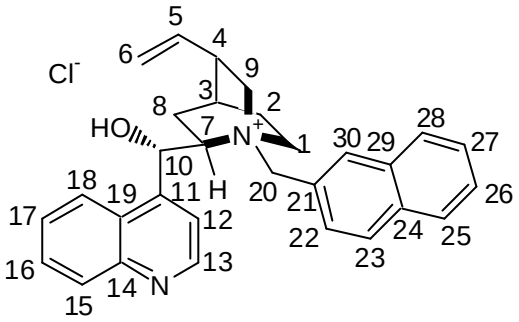
Following the general procedure described in 9.4.1 with:
400 mg (1.358 mmol; 1 eq.) of cinchonine
250 mg (1.413 mmol; 1.04 eq.) of 2-chloromethylnaphtalene
4.1 ml of toluene

Yield: 440 mg (69 %)

*N-(2-naphthylmethy)cinchoninium chloride **192***

M.F.: $C_{30}H_{31}ClN_2O$ (**M.W.** 471.04)

Aspect: white solid



^{1}H NMR ($CDCl_3$, 300 MHz): 0.63-0.75 (*m*, 2 H); 2.02 (*mult*, 2 H); 2.64 (*mult*, 2 H); 3.13 (*mult*, 1 H); 3.99-4.11 (*m*, 1 H); 4.12-4.22 (*m*, 2 H); 4.52 (*mult*, 1 H); 5.03 (*mult*, 2 H); 5.57 (*d*, *J* = 11.7, 1 H); 6.54-6.60 (*m*, 1 H); 7.03 (*mult*, 2 H); 7.14-7.21 (*m*, 1 H); 7.26-7.37 (*m*, 3 H); 7.43-7.71 (*m*, 4 H); 7.89 (*m*, 2 H); 8.37 (*d*, *J* = 9.3, 1 H); 8.80 (*d*, *J* = 4.2, 1 H)
^{13}C NMR ($CDCl_3$, 50 MHz): 21.5 and 23.5 (2, 8); 26.9 (3); 37.9 (4); 49.4, 53.6 and 56.2 (1, 9, 20); 65.5 and 66.7 (7, 10); 117.8 (6); 119.6 (12); 123.0 (18); 123.7 and 124.0 (19, 21); 126.3, 126.6, 127.1, 127.2, 127.3, 127.9, 128.0, 128.6 and 128, 7 (16, 17, 22, 24, 25, 26, 27, 29, 30); 132.2 and 133.0 (23, 28); 133.9 and 135.2 (5, 15); 145.1 and 147.4 (11, 14); 149.0 (13)
Mass (APCI): 141 ($[CH_2C_{10}H_7]^+$, 29%); 295 ($[M\text{-}CH_2C_{10}H_7]^+$, 100%); 435 ($M^+$, 27%)
$[\alpha]_{20}^{D}$: 139° (c=0.237; MeOH)
m.p.: 213°C (decomposition)

9.4.10 Reaction of cinchonidine with 1,3-bis(bromomethyl)benzene

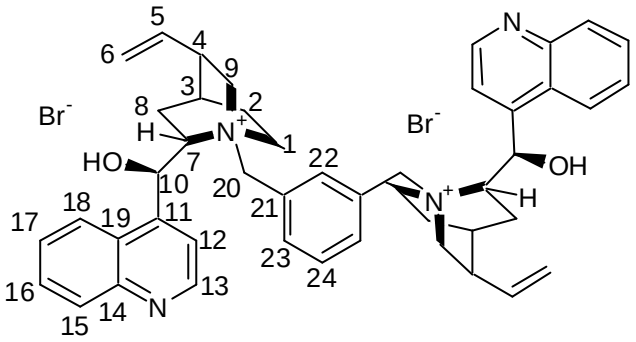
Reference: Jew, S.-S.; Jeong, B.-S.; Yoo, M.-S.; Huh, H.; Park, H.-G. *Chem. Comm.* **2001**, 1244-1245.

A mixture of 500 mg (1.698 mmol; 2.03 eq.) of cinchonidine and 220 mg (833.4 µmol; 1 eq.) of 1,3-bis(bromomethyl)benzene in 1.5 ml of DMF and 0.5 ml of $CHCl_3$ was heated to 100°C for 6 hours. Once cooled down to room temperature it was diluted with 10 ml of MeOH. Then 50 ml of ether were slowly added to precipitate the product. The precipitate was filtered and dried under high vacuum.

Yield: 701 mg (99 %)

*Catalyst **194***

M.F.: $C_{46}H_{52}Br_2N_4O_2$ (**M.W.** 852.75) **RN: 473410-07-0**



^{13}C NMR ($CDCl_3$, 75 MHz): 21.6 and 24.6 (2, 8); 26.3 (3); 37.2 (4); 51.0, 60.6 and 62.3 (1, 9, 20); 64.5 and 68.2 (7, 10); 117.1 (6); 119.6 (12); 122.4 (18); 124.1 (19); 127.9 (21); 127.9 (22); 129.2 and 129.5 (16, 17, 23); 135.4 and 136.4 (5, 15); 139.0 (22); 145.2 and 147.0 (11, 15); 149.2 (13)

Mass (APCI): 397 ([M-cinchonidinium]$^+$, 67%); 506 (100%); 530 (54%); 673 ([M-H_3O]$^+$, 93%); 692 ([M-H]$^+$, 1%)

[α**]**$^D_{20}$: -169° (c=0.189; MeOH) [lit.: -171° (c=0.276; MeOH)]

*9.4.11 Reaction of N-benzylcinchonidinium chloride **196** with allyl bromide*

Reference: Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415.

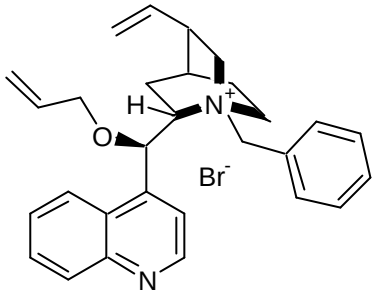
742 mg (1.727 mmol; 1 eq.) of *N*-benzylcinchonidinium chloride were put into suspension in 6.5 ml of CH_2Cl_2. 249 µl (509 mg; 9.074 mmol; 5.25 eq.) of allyl bromide and an aqueous solution of 50% of KOH (509 mg (9.074 mmol; 5.25 eq.) of potassium hydroxide in 433.5 µl of water) were then added. The mixture was stirred vigorously for 4 hours. A homogenization of the organic phase occurred. The mixture

was then diluted with water and extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 1.101 g (quant.)

O-allyl-N-benzylcinchonidinium bromide ***197***

M.F.: $C_{29}H_{33}BrN_2O$ (**M.W.** 505.49) **RN: 158195-40-5**



Spectral data identical to a commercial sample
Mass (APCI): 282 (26%); 335 ($[M-CH_2C_8H_{14}]^+$, 100%); 425 (M^+, 2%)

9.4.12 Reaction of N-(9-anthrylmethyl)cinchonidinium chloride ***189*** *with allyl bromide*

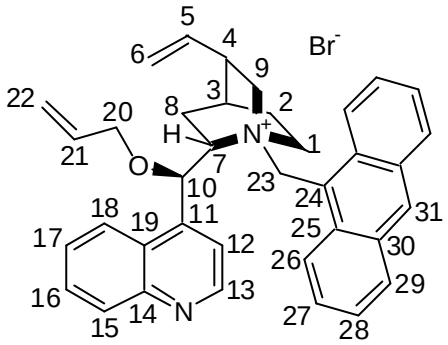
Reference: Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415.

1000 mg (1.727 mmol; 1 eq.) of N-(9-anthrylmethyl)cinchonidinium chloride were put into suspension in 6.6 ml of CH_2Cl_2. 249 µl (509 mg; 9.074 mmol; 5.25 eq.) of allyl bromide and an aqueous solution of 50% of KOH (509 mg (9.074 mmol; 5.25 eq.) of potassium hydroxide in 433.5 µl of water) were then added. The mixture was stirred vigorously for 4 hours. A homogenization of the organic phase occurred. The mixture was then diluted with water and extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 917 mg (88 %)

O-allyl-N-(9-anthrylmethyl)cinchonidinium bromide ***195***

M.F.: $C_{37}H_{37}BrN_2O$ (**M.W.** 605.61) **RN: 200132-54-3**



^{13}C NMR ($CDCl_3$, 50 MHz): 23.2 and 25.5 (2, 8); 26.0 (3); 38.3 (4); 50.8 and 54.8 (1, 23); 61.3 (9); 66.8 (7); 70.1 (20); 70.2 (10) 117.9, 118.0 and 118.3 (6, 19, 22); 123.2, 124.9, 125.6, 126.6, 127.6, 128.4, 128.9, 129.9 (12, 16, 18, 26, 27, 28, 29, 31); 131.2, 133.1, 133.6 (24, 25, 30); 132.1, 132.6 (15, 17); 136.2 and 136.5 (5, 21); 139.6 and 140.1 (11, 14); 148.5 (13)

Mass (APCI): 282 (28%); 335 ($[M\text{-}CH_2C_{14}H_8]^+$, 100%); 525 ($M^+$, 2%)

9.5 Michael addition of nitro-compounds: asymmetric

9.5.1 Addition to cyclopentenone

Following the general procedure described in 9.3.1 with the following quantities:
75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **168**
146 mg (1.058 mmol; 2.5 eq.) of potassium carbonate
0.1 eq of catalyst
46 µl (45 mg; 550.2 µmol; 1.3 eq.) of 2-cyclopentenone
3.9 ml of toluene

Catalyst	Reaction time[a]	ee	Configuration
196	16 h	21%	*S*
194	3 days	2.5%	*(S)*
189	16 h	11%	*S*
195	16 h	21%	*S*
197	16 h	12%	*S*
199	16 h	23%	*R*
150	16 h	21%	*R*
191	16 h	19%	*R*
190	16 h	20%	*R*
192	16 h	48%	*R*
200	3 days	3%	*(R)*
201	3 days	6%	*R*
202	3 days	8%	*R*
204	16 h	10%	*R*
156	16 h	15%	*R*
155	16 h	11%	*S*
205	16 h	1%	*(S)*

9.5.2 Addition to cyclohexenone

Following the general procedure described in 9.3.1 with the following quantities:
75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **168**
146 mg (1.058 mmol; 2.5 eq.) of potassium carbonate
0.1 eq of catalyst
53 µl (52 mg; 550.2 µmol; 1.3 eq.) of 2-cyclohexenone
3.9 ml of toluene

Catalyst	Reaction time[a]	ee	Configuration
196	16 h	21%	*S*
189	16 h	3%	*S*
195	16 h	13%	*S*
199	16 h	16%	*R*
150	16 h	14.5%	*R*
191	16 h	17%	*R*
190	16 h	16%	*R*

[a] reaction time until complete conversion

192	16 h	28%	*R*
200	3 days	4%	*(S)*
201	3 days	12%	*S*
202	3 days	2%	*(S)*
156	16 h	13%	*S*
155	16 h	8%	*R*

10 Michael addition of nitro-compounds: other catalytic methods

10.1 Silylated nitronates

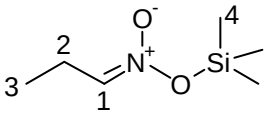
10.1.1 Synthesis of propylidene[(trimethylsilyl)oxy]azane oxide (1-aci-nitropropane trimethylsilylester) ***207***

M.F.: $C_6H_{15}NO_2Si$ (**M.W.** 161.27) **RN: 51146-38-4**

Reference: Knudsen, K. R.; Risgaard, T.; Nishiwaki, N.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2001**, *123*, 5843-5844.

In a flame-dried two-necked flask, to a solution of 2 ml (1.996 g; 22.4 mmol; 1 eq.) of 1-nitropropane in 45 ml of benzene were added 3.114 ml (2.267 g; 22.4 mmol; 1 eq.) of Et_3N, then 2.843 ml (2.433 g; 22.4 mmol; 1 eq.) of TMSCl. The mixture was stirred for 64 hours, then filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (75°C at 16 mmHg).

Yield: 2.158 g (60 %)



^{1}H NMR ($CDCl_3$, 300 MHz): 0.32 (*s*, 9 H, 4); 1.09 (*t*, $^3J_{3-2}$ = 7.8, 3 H, 3); 2.32 (*quint*, $^3J_{2-1} = {}^3J_{2-3}$ = 7.8, 2 H, 2); 6.10 (*t*, $^3J_{1-2}$ = 6.3, 1 H, 1)
^{13}C NMR ($CDCl_3$): -0.15 (4); 10.1 (3); 19.9 (2); 118.1 (1)
b.p.: 75°C (16 mmHg)

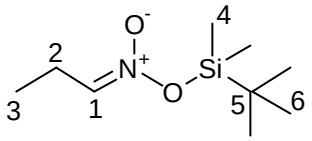
*10.1.2 Synthesis of {[*tert*-butyl(dimethyl)silyl]oxy}(propylidene)azane oxide (1-aci-nitropropane tert-butyldimethylsilylester)* ***208***

M.F.: $C_9H_{21}NO_2Si$ (**M.W.** 203.35) **RN: 77242-14-9**

Reference: Knudsen, K. R.; Risgaard, T.; Nishiwaki, N.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2001**, *123*, 5843-5844.

In a flame-dried two-necked flask, to a solution of 2 ml (1.996 g; 22.4 mmol; 1 eq.) of 1-nitropropane in 25 ml of toluene were added 3.114 ml (2.267 g; 22.4 mmol; 1 eq.) of Et_3N, then 3.376 g (22.4 mmol; 1 eq.) of *tert*-butyldimethylsilyl chloride. The mixture was stirred for 64 hours, then filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (75°C at $9 \cdot 10^{-3}$ mbar).

Yield: 1.483 g (33 %)



^{1}H NMR ($CDCl_3$, 200 MHz): 0.32 (*s*, 6 H, 4); 0.94 (*s*, 9 H, 6); 1.09 (*t*, $^3J_{3-2}$ = 7.6, 3 H, 3); 2.31 (*dq*, $^3J_{2-3}$ = 7.6, $^3J_{2-1}$ = 6.3, 2 H, 2); 6.10 (*t*, $^3J_{1-2}$ = 6.2, 1 H, 1)
^{13}C NMR ($CDCl_3$, 50 MHz): -3.7 (4); 9.7 (3); 18.5 (5); 22.0 (2); 25.4 (6); 107.8 (1)
b.p.: 75°C ($9 \cdot 10^{-3}$ mbar)

10.1.3 Synthesis of 7-ethoxy-2,2-dimethyl-3,8-dioxa-4-aza-2-siladec-4-ene 4-oxide (1-aci-nitro-3,3-diethoxypropane trimethylsilylester) ***209***

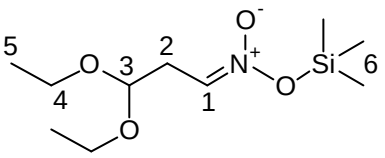
M.F.: $C_{10}H_{23}NO_4Si$ (**M.W.** 249.38)

Reference (reaction conditions): Knudsen, K. R.; Risgaard, T.; Nishiwaki, N.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2001**, *123*, 5843-5844.

In a flame-dried two-necked flask, to a solution of 500 mg (2.821 mmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **168** in 5.6 ml of benzene were added 392 µl (285 mg; 2.821 mmol; 1 eq.) of Et_3N, then 358 µl (306 mg; 2.821 mmol; 1 eq.) of TMSCl. The mixture was stirred for 64 hours, then filtered and evaporated under reduced pressure.
The product was purified by bulb-to-bulb distillation (75°C at $2.1 \cdot 10^{-2}$ mbar).

Yield: 549 mg (78 %)

Aspect: colorless oil



^{1}H NMR ($CDCl_3$, 200 MHz): 0.31 (*s*, 9 H, 6); 1.21 (*t*, $^3J_{5\text{-}4}$ = 6.9, 6 H, 5); 2.64 (*t*, $^3J_{2\text{-}1}$ = $^3J_{2\text{-}3}$ = 6.1, 2 H, 2); 3.65 and 3.51 (*2 mult*, 4 H, 4); 4.68 (*t*, $^3J_{3\text{-}2}$ = 5.6, 1 H, 3); 6.18 (*t*, $^3J_{1\text{-}2}$ = 6.3, 1 H, 1)
b.p.: 75°C ($2.1 \cdot 10^{-2}$ mbar)

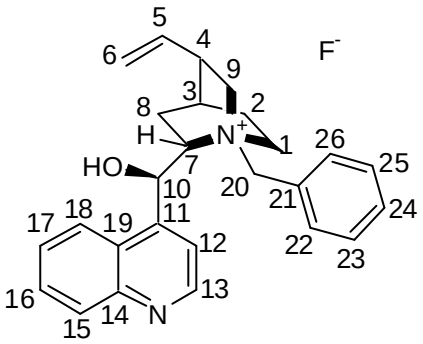
10.1.4 Synthesis of N-benzylcinchonidinium fluoride ***210***

M.F.: $C_{26}H_{29}FN_2O$ (**M.W.** 404.52) **RN: 174626-65-4**

Reference (reaction conditions): Hayami, J.; Ono, N.; Kaji, A. *Tetrahedron Lett*. **1968**, *11*, 1385-1386

A mixture of 100 mg (201.9 µmol; 1 eq.) of benzylcinchonidinium chloride and 26 mg (201.9 µmol; 1 eq.) of silver fluoride in 5 ml of water was stirred overnight. The solution was evaporated under reduced pressure. Acetonitrile was added to the residue and the solvent was evaporated under reduced pressure. To separate the product from AgCl, acetone was added to the residue and the suspension was filtered. The filtrate was evaporated under reduced pressure and the resulting residue was dried under high vacuum.

Yield: 105 mg (quant.)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.03-1.16 (*m*, 1 H); 1.51-1.65 (*m*, 1 H); 1.90-2.19 (*m* + *s*, 4 H); 2.42-2.52 (*m*, 1 H); 3.02 (*dt*, *J* = 11.8, *J* = 3.1, 1 H); 3.18 (*t*, *J* = 11.8, 1 H); 3.57 (*d*, *J* = 12.6, 1 H); 3.83 (*t*, *J* = 8.6, 1 H); 4.80-4.91 (*m*, 1 H); 4.93 (*d*, *J* = 11.0, 1 H); 5.09 (*d*, *J* = 16.5, 1 H); 5.31 (*d*, *J* = 11.8, 1 H); 5.84 (*d*, *J* = 11.8, 1 H); 6.34 (*s*, 1 H); 6.95 (*mult*, 3 H); 7.45 (*d*, *J* = 7.1, 1 H); 7.59 (*mult*, 2 H); 7.84 (*d*, *J* = 3.9, 1 H); 7.98 (*mult*, 1 H); 8.05 (*mult*, 1 H); 8.83 (*d*, *J* = 3.9, 1 H)

^{13}C NMR ($CDCl_3$, 75 MHz): 21.9 and 25.2 (2, 8); 26.7 (3); 38.1 (4); 50.2, 60.2 and 62.6 (1, 9, 20); 65.1 and 68.3 (7, 10); 117.4 (6); 119.9 (12); 123.1 (18); 124.2 and 126.8 (19, 21), 127.3, 128.2, 128.8 and 129.6 (16, 17, 22, 23, 24); 133.4 and 136.6 (5, 15); 145.5 and 147.4 (11, 14) 149.5 (13)
^{19}F NMR ($CDCl_3$, 288.5 MHz): 129.3 (*s*, F^-)

*10.1.5 Michael addition of **207**: TBAF*

Reference (reaction conditions): Colvin, E. W.; Seebach, D. *J. Chem. Soc. Chem. Commun.* **1978**, 689-691.

In a flame-dried flask, 16 mg (62 µmol; 0.1 eq.) of tetrabutylammonium fluoride and 63 µl (62 mg; 651 µmol; 1.05 eq.) of 2-cyclohexen-1-one were put into solution in 5 ml of THF. 100 mg (620 µmol; 1 eq.) of 1-*aci*-nitropropan-trimethylsilylester **207** dissolved in a small quantity of THF were then slowly added and the mixture was stirred for 4 hours. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 87 mg (76 %) of 3-(1-nitropropyl)cyclohexanone **178**

Physical data as described in 9.3.3.

*10.1.6 Michael additon of **207**: KF and benzyltriethylammonium chloride or N-(1-naphthylmethyl)cinchoninium chloride **190***

In a flame-dried flask, 3 mg (62 µmol; 0.1 eq.) of potassium fluoride and catalyst (7 mg (31 µmol; 0.05 eq.) of benzyltriethylammonium chloride or 29 mg (62 µmol; 0.1 eq.) of *N*-(1-naphthylmethyl)cinchoninium chloride) were put into suspension in 6.6 ml of toluene. 63 µl (62 mg; 651 µmol; 1.05 eq.) of 2-cyclohexen-1-one were added, followed by 100 mg (620 µmol; 1 eq.) of 1-*aci*-nitropropan-trimethylsilylester **207** in solution in a small quantity of toluene. The mixture was stirred for 4 hours before the reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

No product was obtained by this method.

*10.1.7 General procedure for the Michael addition of silylated nitronates catalyzed by N-benzylcinchonidinium fluoride **210***

In a flame-dried flask, 0.1 eq. of *N*-benzylcinchonidinium fluoride **210** and 1.05 eq. of enone were dissolved in the solvent. 1 eq. of silylated nitronate dissolved in a small quantity of solvent was added. The mixture was stirred for x hours before the reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

*10.1.8 Michael additon of **207** to cyclohexenone: N-benzylcinchonidinium fluoride **210***

Following the general procedure described in 10.1.7 with:
100 mg (620 µmol; 1 eq.) of 1-*aci*-nitropropan-trimethylsilylester **207**
63 µl (62 mg; 651 µmol; 1.05 eq.) of 2-cyclohexen-1-one
25 mg (62 µmol; 0.1 eq.) of *N*-benzylcinchonidinium fluoride **210**
5.1 ml of THF
reaction time: 1 hour

Yield: 120 mg (quant.) of 3-(1-nitropropyl)cyclohexanone **178**

Physical data as described in 9.3.3.

*10.1.9 Michael addition of **209** to cyclopentenone: N-benzylcinchonidinium fluoride **210***

Following the general procedure described in 10.1.7 with:
100 mg (400.9 µmol; 1 eq.) of 1-*aci*-nitro-3,3-diethoxypropane trimethylsilylester **209**
35 µl (34 mg; 421 µmol; 1.05 eq.) of 2-cyclopentenone
16 mg (40.09 µmol; 0.1 eq.) of *N*-benzylcinchonidinium fluoride **210**
3.3 ml of THF
reaction time: 1 hour

Complete conversion to 2-(3,3-diethoxy-1-nitropropyl)cyclopentenone **198**
Adduct **198** was obtained with 7% de and 7% ee.

*10.1.10 Michael addition of **209** to cyclohexenone: N-benzylcinchonidinium fluoride **210***

Following the general procedure described in 10.1.7 with:
100 mg (400.9 µmol; 1 eq.) of 1-*aci*-nitro-3,3-diethoxypropane trimethylsilylester **209**
41 µl (40 mg; 421 µmol; 1.05 eq.) of 2-cyclohexen-1-one
16 mg (40.09 µmol; 0.1 eq.) of *N*-benzylcinchonidinium fluoride **210**
3.3 ml of THF
reaction time: 2 days

Only 30% conversion were observed after 2 days. Reagent **209** had been transformed to 1,1-diethoxy-3-nitropropane **168**.
Adduct **186** was obtained with 4% de and 30% ee.

*10.1.11 Michael addition of **209** to cyclopentenone: N-benzylcinchonidinium fluoride **210***

Following the general procedure described in 10.1.7 with:
100 mg (400.9 µmol; 1 eq.) of 1-*aci*-nitro-3,3-diethoxypropane trimethylsilylester **209**
35 µl (34 mg; 421 µmol; 1.05 eq.) of 2-cyclopentenone
16 mg (40.09 µmol; 0.1 eq.) of *N*-benzylcinchonidinium fluoride **210**
4.3 ml of toluene
reaction time: 1 hour

Complete conversion to 2-(3,3-diethoxy-1-nitropropyl)cyclopentenone **198**
Adduct **198** was obtained with 7% de and 2% ee.

*10.1.12 Michael addition of **209** to cyclohexenone: N-benzylcinchonidinium fluoride **210***

Following the general procedure described in 10.1.7 with:
100 mg (400.9 µmol; 1 eq.) of 1-*aci*-nitro-3,3-diethoxypropane trimethylsilylester **209**
41 µl (40 mg; 421 µmol; 1.05 eq.) of 2-cyclohexen-1-one
16 mg (40.09 µmol; 0.1 eq.) of *N*-benzylcinchonidinium fluoride **210**
4.3 ml of toluene
reaction time: 2 days

Only 30% conversion were observed after 2 days. Reagent **209** had been transformed to 1,1-diethoxy-3-nitropropane **168**.
Adduct **186** was obtained with 8% de and 50% ee.

10.2 AlLi[(*R*)-binaphthoxide]$_2$ complex as catalyst

10.2.1 Preparation of a 0.1M solution of AlLi[(R)-binaphthoxide]$_2$ ((R)-ALB)

Reference: Shimizu, S.; Ohori, K.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Org. Chem.*, **1998**, *63*, 7547-7551.

To a suspension of 24 mg (625 µmol; 1 eq.) of lithium aluminum hydride in 2.5 ml of THF at 0°C were added 358 mg (1.25 mmol; 2 eq.) of (*R*)-(+)-1,1'-bi-2-naphthol dissolved in 2.5 ml of THF followed by 2x 625 µl of THF. After 30 minutes of stirring at 0°C, the mixture was stirred for 1 hour at room temperature, then left standing without stirring overnight. The supernatant was used as 0.1M solution of (*R*)-ALB in THF.

*10.2.2 Michael addition of **168** to cyclopentenone*

Reference (reaction conditions): Yamada, K.-i.; Moll, G.; Shibasaki, M. *Synlett*, **2001**, 980-982.

To 35 µl (34 mg; 423.2 µmol; 1 eq.) of 2-cyclopentenone contained in a flame-dried two-necked flask were added 423 µl (42.32 µmol; 0.1 eq.) of the previously prepared 0.1M solution of AlLi[(*R*)-binaphtoxide]$_2$. The mixture was stirred for 10 minutes, cooled to -40°C and stirred for another 10 minutes before 43 mg (380.9 µmol; 0.9 eq.) of potassium *tert*-butoxide dissolved in 78 µl of THF were added followed by 75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane. The mixture was stirred for 48 hours at -40°C. The reaction was quenched by the addtion of a saturated solution of NH_4Cl. The aqueous phase was extracted by CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Quantitative yield of racemic 2-(3,3-diethoxy-1-nitropropyl)cyclopentenone **198** was obtained.

10.3 Rubidium prolinate as catalyst

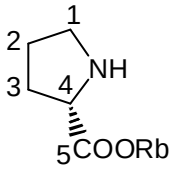
*10.3.1 Synthesis of rubidium prolinate **211***

M.F.: $C_5H_8NO_2Rb$ (**M.W.** 199.59) **RN: 151600-44-1**

Reference: Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.*, **1996**, *61*, 3520-3530.

A mixture of 2 g (17.37 mmol; 1 eq.) of L-proline and 2.093 g (17.37 mmol; 1 eq.) of rubidium hydroxyde hydrate in 36 ml of MeOH was stirred at room temperature for 2 hours. The solvent was removed under reduced pressure and the product was dried at high vacuum.

Quantitative yield of rubidium prolinate **211** was obtained.



^{1}H NMR (D_2O, 200 MHz): 1.72-1.92 (*m*, 3 H, 2, 3), 2.06-2.29 (*m*, 1 H, 3); 2.85-3.01 (*m*, 1 H, 1); 3.09-3.22 (*m*, 1 H, 1); 3.67 (*dd*, $^3J_{4\text{-}3}$ = 8.4, $^3J_{4\text{-}3}$ = 6.3, 1 H, 4)
^{13}C NMR (D_2O, 75 MHz, acetone as internal reference (29.9 ppm)): 23.9 (2); 29.4 (3); 45.2 (1); 60.6 (4); 179.0 (5)

*10.3.2 Michael addition of **209** to cyclopentenone*

Reference: Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.*, **1996**, *61*, 3520-3530.

A mixture of 75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **209**, 35 µl (34 mg; 423.2 µmol; 1 eq.) of 2-cyclopentenone and 8 mg (42.32 µmol; 0.1 eq.) of rubidium prolinate **211** in 500 µl of $CHCl_3$, previously passed through a column of basic alumina, was stirred for 72 hours at room temperature. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted by CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Quantitative yield of adduct **198** was obtained.
Diastereoselectivity: 4% de; enantioselectivity: 59% ee.

*10.3.3 Michael addition of **209** to cyclohexenone*

Reference: Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.*, **1996**, *61*, 3520-3530.

A mixture of 75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **209**, 41 µl (40 mg; 423.2 µmol; 1 eq.) of 2-cyclohexen-1-one and 8 mg (42.32 µmol; 0.1 eq.) of rubidium prolinate **211** in 500 µl of $CHCl_3$, previously passed through a column of basic alumina, was stirred for 72 hours at room temperature. The reaction was quenched by the addition of a saturated solution of NH_4Cl. The aqueous phase was extracted by CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Quantitative yield of adduct **186** was obtained.
Diastereoselectivity: 4% de; enantioselectivity: 57% ee.

10.4 L-proline as catalyst

*10.4.1 Michael addition of **209** to cyclopentenone*

Reference (reaction conditions): Hanessian, S.; Pham, V. *Org. Lett.*, **2000**, *2*, 2975-2978.

A mixture of 75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **209**, 35 µl (34 mg; 423.2 µmol; 1eq.) of 2-cyclopentenone, 49 mg (430.5 µmol; 1.01 eq.) of *trans*-2,5-dimethylpiperazine and 1 mg (15.65 µmol; 0.0369 eq.) of L-proline in 3.3 ml of $CHCl_3$, previously passed through a column of basic alumina, was stirred for 46 hours. It was then diluted with CH_2Cl_2, washed with a 3% solution of HCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Quantitative yield of adduct **198** was obtained.
Diastereoselectivity: 1% de; enantioselectivity: 77% ee.

*10.4.2 Michael addition of **209** to cyclohexenone*

Reference (reaction conditions): Hanessian, S.; Pham, V. *Org. Lett.*, **2000**, *2*, 2975-2978.

A mixture of 75 mg (423.2 µmol; 1 eq.) of 1,1-diethoxy-3-nitropropane **209**, 41 µl (40 mg; 423.2 µmol; 1 eq.) of 2-cyclohexen-1-one, 49 mg (430.5 µmol; 1.01 eq.) of *trans*-2,5-dimethylpiperazine and 1 mg (15.65 µmol; 0.0369 eq.) of L-proline in 3.3 ml of $CHCl_3$, previously passed through a column of basic alumina, was stirred for 46 hours. It was then diluted with CH_2Cl_2, washed with a 3% solution of HCl, dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Quantitative yield of adduct **186** was obtained.
Diastereoselectivity: 25% de; enantioselectivity: 69% ee.

11 Chemical modification of adducts

11.1 Cyclization

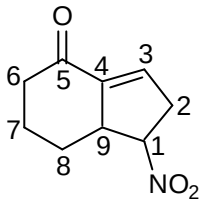
*11.1.1 Cyclization of adduct **186***

Reference: Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5045-5050.

A mixture of 200 mg (731.7 µmol; 1 eq.) of 3-(3,3-diethoxy-1-nitropropyl)cyclohexanone **186**, 3.3 ml of THF and 100 µl (90 mg; 1.25 mmol; 1.7 eq.) of a 12.5N solution of hydrochloric acid was stirred for 2 hours at room temperature. It was then neutralized with a 5% solution of $NaHCO_3$ and diluted with Et_2O. The organic phase was washed 3 times with water and once with a saturated solution of NaCl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.
The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 87 mg (66 %) as a mixture of 2 diastereomers

*1-nitro-1,2,5,6,7,7a-hexahydro-4H-inden-4-one **218***
M.F.: $C_9H_{11}NO_3$ (**M.W.** 181.19) **RN: 182298-16-4**



^{1}H NMR ($CDCl_3$, 200 MHz): 1.12-2.75 (*m*, 6 H, 6, 7, 8); 3.05 and 3.18 (*2 mult*, 2 H, 2); 3.34-3.56 (*m*, 1 H, 9); 4.92 (*q*, $^{3}J_{1\text{-}2}$ = $^{3}J_{1\text{-}9}$ = 8.7, 1 H, 1); 5.32 (*dt*, $^{3}J_{1\text{-}2}$ = 7.4, $^{3}J_{1\text{-}9}$ = 1.2, 1 H, 1); 6.50 (*mult*, 1 H, 3); 6.69 (*mult*, 1 H, 3)

^{13}C NMR ($CDCl_3$, 50 MHz): major isomer: 22.9 (8); 29.8 (7); 36.8 (2); 39.7 (6); 50.3 (9); 90.7 (1); 132.7 (3); 140.8 (4); 196.7 (5); minor isomer: 25.5 (8); 29.8 (7); 36.2 (2); 39.6 (6); 49.7 (9); 88.3 (1); 135.0 (3); 140.7 (4); 197.1 (5)

Mass (CI/CH_4-N_2O): 59 (58%); 63 (37%); 89 (100%); 135 ($[M\text{-}NO_2]^+$, 69%); 151 (28%); 166 (12%); 182 ($[M+H]^+$, 5%)

*11.1.2 Cyclization of **198***

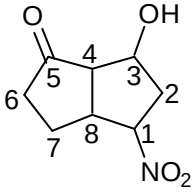
A mixture of 100 mg (385.6 µmol; 1 eq.) of 2-(3,3-diethoxy-1-nitropropyl)cyclopentenone **198**, 1.7 ml of THF and 0.263 ml (658.8 µmol; 1.7 eq.) of a 2.5N solution of hydrochloric acid was stirred for 2 hours at room temperature. It was then neutralized with a 5% solution of $NaHCO_3$ and diluted with Et_2O. The organic phase was washed 3 times with water and once with a saturated solution of NaCl. The aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 55 mg (77%)

*6-hydroxy-4-nitrohexahydropentalen-1(2H)-one **219***

M.F.: $C_8H_{11}NO_4$ (**M.W.** 185.18)



^{1}H NMR ($CDCl_3$, 200 MHz): 1.94-2.66 (*mult* + *m*, 8 H, 2, 4, 6, 7, 8); 3.30-3.46 (*m*, 1H, 3); 4.69-4.80 (*m*, 1 H, 1)

^{13}C NMR ($CDCl_3$, 50 MHz): 26.2 (7); 39.8 (2); 41.6 (6); 47.0 (8); 56.3 (4); 72.4 (3); 90.2 (1); 213.2 (5)

Mass (CI/CH_4-N_2O): 121 ($[M\text{-}NO_2\text{-}OH]^+$, 100%]; 139 ($[M\text{-}NO_2]^+$, 77%); 168 ($[M\text{-}OH]^+$, 60%); 186 ($[M+H]^+$, 16%)

11.2 The Nef reaction

*11.2.1 Nef reaction of adduct **178***

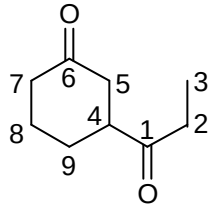
Reference (reaction conditions): Akita, Y.; Inaba, M.; Uchida, H.; Ohta, A. *Synthesis* **1977**, 792-794.

In a flask equipped with a reflux condenser 400 mg (2.159 mmol; 1 eq.) of 3-(1-nitropropyl)cyclohexanone **178** were dissolved in 2.2 ml (1.708 g) of MeOH. 1.99 g (16.19 mmol; 7.5 eq.) of chromium(II) chloride dissolved in 54 ml of a 3% solution of HCl were added and the mixture was refluxed for 2 hours. After being cooled to room temperature the reaction mixture was extracted with Et_2O. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure.

Yield: 298 mg (89 %)

*3-propionylcyclohexanone **221***
M.F.: $C_9H_{14}O_2$ (**M.W.** 154.2) **RN: 88017-43-0**

TLC: R_f = 0.37 (petroleum ether : AcOEt 70 : 30)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.07 (*t*, $^3J_{3\text{-}2}$ = 7.2, 3 H, 3); 1.62-1.82 (*m*, 2 H, 8); 2.00-2.16 (*m*, 2 H, 9); 2.25-2.62 (*m*, 6 H, 2, 5, 7); 2.82-2.98 (*m*, 1 H, 4)
^{13}C NMR ($CDCl_3$, 50 MHz): 7.5 (3); 24.8 and 27.3 (8, 9); 34.1 (2); 40.7 and 42.5 (5, 7); 49.8 (4); 209.6 (6); 210.8 (1)
Mass (CI/CH_4-N_2O): 155 ($[M+H]^+$, 100%)
GC (100/0/10/290/15): t_R = 7.4 min

*11.2.2 Nef reaction of **186***

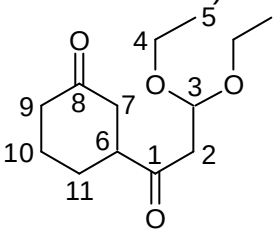
Reference (reaction conditions): Barton, D. H. R.; Motherwell, W. B.; Simon, E. S.; Zard, S. Z. *J. Chem. Soc. Perkin Trans. 1* **1986**, 2243-2252.

In a flame-dried two-necked flask 147 mg (539.8 µmol; 1 eq.) of 3-(3,3-diethoxy-1-nitropropyl)cyclohexanone **186** and 290 mg (1.328 mmol; 2.46 eq.) of phenyl disulfide were dissolved in 2.175 ml of THF. 507 µl (412 mg; 2.036 mmol; 3.77 eq.) of tri-*n*-butylphosphine were added to this mixture, which was stirred for 3 hours at room temperature. After this time 435 µl of water were added and the mixture was stirred overnight at room temperature. The solvents were removed under reduced pressure. The product was purified by flash chromatography (petroleum ether : AcOEt 60 : 40).

Yield: 88 mg (67 %)

3-(3,3-diethoxypropanoyl)cyclohexanone ***222***
M.F.: $C_{13}H_{22}O_4$ (**M.W.** 242.31)

TLC: R_f = 0.38 (petroleum ether : AcOEt 70 : 30)



^{1}H NMR ($CDCl_3$, 300 MHz): 1.18 and 1.19 (*2 t*, $^3J_{5-4}$ = 6.6, 6 H, 5); 1.61-1.81 (*m*, 2 H, 11); 2.01-2.13 (*m*, 2 H, 10); 2.25-2.56 (*m*, 4 H, 7, 9); 2.79 (*d*, $^3J_{2-3}$ = 6.0, 2 H, 2); 2.88-2.99 (*m*, 1 H, 6); 3.53 and 3.66 (*2 mult*, 4 H, 4); 4.89 (*t*, $^3J_{3-2}$ = 5.7, 1 H, 3)
^{13}C NMR ($CDCl_3$, 50 MHz): 15.2 (5); 24.7 and 26.7 (10, 11); 40.9 and 42.1 (7, 9); 46.0 (2); 51.0 (6); 62.6 and 62.7 (4); 100.2 (3); 207.7 (8); 209.9 (1)
Mass (CI/CH_4-N_2O): 103 (37%); 111 (29%); 151 ([M-2OEt]$^+$, 52%); 197 ([M-OEt]$^+$, 100%); 242 ($M^{\bullet+}$, 3%)
GC (100/0/10/290/15): t_R = 13.24 min

Bibliography

1. Von Euler, U. S.; Eliasson, R., *Prostaglandins*; Academic Press: New York, 1967.
2. Achab, S.; Das, B. C. *J. Chem. Soc. Perkin Trans. 1* , **1990**, 2863.
3. Kusaka, T.; Yamamoto, H.; Shibata, M.; Muroi, M.; Kishi, T.; Mizuno, K. *J. Antibiot.*, **1968**, *21*, 255-263.
4. Fieser, L. F.; Fieser, M., *Steroids*; Reinhold Publishing: New York, 1959.
5. Tori, M.; Sono, M.; Nishigaki, Y.; Nakashima, K.; Asakawa, Y. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 435-445.
6. Weinges, K.; Dietz, U.; Oeser, T.; Irngartinger, H. *Angew. Chem. Int. Ed. Engl.*, **1990**, *29*, 680-682.
7. Giannetti, B.-M.; Steffan, B.; Steglich, W.; Kupka, J.; Anke, T. *Tetrahedron*, **1986**, *42*, 3587-3593.
8. Steglich, W. *Pure Appl. Chem.*, **1981**, *53*, 1233-1240.
9. Paquette, L. A.; Meister, P. G.; Friedrich, D.; Sauer, D. R. *J. Am. Chem. Soc.*, **1993**, *115*, 49-56.
10. Paquette, L. A.; Romine, J. L.; Lin, H.-S.; Wright, J. *J. Am. Chem. Soc.*, **1990**, *112*, 9284-9292.
11. Ramaiah, M. *Synthesis*, **1984**, 529-570.
12. Trost, B. M. *Angew. Chem. Int. Ed. Engl.*, **1986**, *25*, 1-20.
13. Hudlicky, T.; Price, S. D. *Chem. Rev.*, **1989**, *89*, 1467-1486.
14. Welker, M. E. *Chem. Rev.*, **1992**, *92*, 97-112.
15. Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.*, **1996**, *96*, 49-92.
16. Dieckmann, W. *Ber.*, **1894**, *27*, 103.
17. Miyaoka, H.; Honda, D.; Mitome, H.; Yamada, Y. *Tetrahedron Lett.*, **2002**, *43*, 7773-7775.
18. Nazarov, N. I. *Usp. Khim.*, **1949**, *18*, 377.
19. Nazarov, N. I.; Zaretskaya, I. I. *Zh. Obshch. Khim.*, **1957**, *27*, 693.
20. Denmark, S. E.; Wallace, M. A.; Walker, C. B. J. *J. Org. Chem.*, **1990**, *55*, 5543-5545.
21. Miesch, M.; Miesch-Gross, L.; Franck-Neumann, M. *Tetrahedron*, **1997**, *53*, 2111-2118.
22. Pridgen, L. N.; Huang, K.; Shilcrat, S.; Tickner-Eldridge, A.; DeBrosse, C.; Haltiwanger, R. C. *Synlett*, **1999**, 1612-1614.
23. Taura, Y.; Tanaka, M.; Wu, X.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron*, **1991**, *47*, 4879-4888.
24. Müller, P.; Fernandez, D. *Helv. Chim. Acta*, **1995**, *78*, 947-958.
25. Watanabe, N.; Ohtake, Y.; Hashimoto, S.; Shiro, M.; Ikegami, S. *Tetrahedron Lett.*, **1995**, *36*, 1491-1494.
26. Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc. Perkin Trans. 1*, **1973**, 977-981.
27. Bernardes, V.; Kann, N. R., A.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Org. Chem.*, **1995**, *60*, 6670-6671.
28. Bladon, P.; Pauson, P. L.; Brunner, H.; Eder, R. *J. Organomet. Chem.*, **1988**, *355*, 449-454.
29. Brunner, H.; Niedernhuber, A. *Tetrahedron Asymmetry*, **1990**, *1*, 711-714.
30. Verdaguer, X.; Moyano, A.; Pericàs, M. A.; Riera, A.; Maestro, M. A.; Mahía, J. *J. Am. Chem. Soc.*, **2000**, *122*, 10242-10243.
31. Shibata, T.; Toshida, N.; Takagi, K. *J. Org. Chem.*, **2002**, *67*, 7446-7450.
32. Greene, A. E.; Charbonnier, F.; Luche, M.-J.; Moyano, A. *J. Am. Chem. Soc.*, **1987**, *109*, 4752-4753.
33. Cagnon, R. *PhD-Thesis UCL-ORSY*, **1996**

34. Ghosez, L.; Chen, L.-Y.; Gobeaux, B.; Houge, C.; Markó, I. E.; Perry, M.; Saimoto, H., *Strain and its Implication in Organic Chemistry*; Kluwer Academic Publishers, 1989.
35. Ichikawa, Y.-i.; Narita, A.; Shiozawa, A.; Hayashi, Y.; Narasaka, K. *J. Chem. Soc., Chem. Commun.*, **1989**, 1919-1921.
36. Houge, C.; Frisque-Hesbain, A.-M.; Mockel, A.; Ghosez, L. *J. Am. Chem. Soc.*, **1982**, *104*, 2920.
37. Chen, L.-y.; Ghosez, L. *Tetrahedron Lett.*, **1990**, *31*, 4467-4470.
38. Cordier, J.-F. *Master Degree UCL-ORSY*, **1991**
39. Genicot, C. *PhD-Thesis UCL-ORSY*, **1993**
40. Adam, J.-M. *PhD-Thesis UCL-ORSY*, **2000**
41. Ghosez, L.; Mahuteau-Betzer, F.; Genicot, C.; Vallribera, A.; Cordier, J.-F. *Chem. Eur. J.*, **2002**, *8*, 3411-3422.
42. Mahuteau-Betzer, F. *PhD-Thesis UCL-ORSY*, **2001**
43. Mahuteau-Betzer, F.; Ghosez, L. *Tetrahedron*, **2002**, *58*, 6991-7000.
44. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.*, **1979**, *101*, 6429-6432.
45. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.*, **1979**, *101*, 6432-6433.
46. Chaigne, F.; Gotteland, J.-P.; Malacria, M. *Tetrahedron Lett.*, **1989**, *30*, 1803-1806.
47. Trost, B. M.; Seoane, P.; Mignani, S.; Acemoglu, M. *J. Am. Chem. Soc.*, **1989**, *111*, 7487-7500.
48. Janson, M.; Kvarnström, I.; Svensson, S. C. T.; Classon, B.; Samuelsson, B. *Synthesis*, **1993**, 129-133.
49. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.*, **1983**, *105*, 2326-2335.
50. Yamamoto, A.; Ito, Y.; Hayashi, T. *Tetrahedron Lett.*, **1989**, *30*, 375-378.
51. Binger, P.; Brinkmann, A.; Richter, W. J. *Tetrahedron Lett.*, **1983**, *24*, 3599-3602.
52. Binger, P.; Schaefer, B. *Tetrahedron Lett.*, **1988**, *29*, 529-530.
53. Boger, D. L.; Wysocki, R. J. J. *J. Org. Chem.*, **1988**, *53*, 3408-3421.
54. Panek, J. S.; Jain, N. F. *J. Org. Chem.*, **1993**, *58*, 2345-2348.
55. Brengel, G. P.; Rithner, C.; Meyers, A. I. *J. Org. Chem.*, **1994**, *59*, 5144-5146.
56. Hua, D. H.; Venkataraman, S.; Coulter, M. J.; Sinai-Zingde, G. *J. Org. Chem.*, **1987**, *52*, 719-728.
57. Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.*, **1974**, *7*, 147-155.
58. Hua, D. H.; Venkataraman, S.; Ostrander, R. A.; Sinai-Zingde, G.; McCann, P. J.; Coulter, M. J.; Xu, M. R. *J. Org. Chem.*, **1988**, *53*, 507-515.
59. Hua, D. H. *J. Am. Chem. Soc.*, **1986**, *108*, 3835-3837.
60. Naasz, R.; Arnold, L. A.; Pineschi, M.; Keller, E.; Feringa, B. L. *J. Am. Chem. Soc.*, **1999**, *121*, 1104-1105.
61. Roekens, B. *Master Degree UCL-ORSY*, **1985**
62. Jung, M. E. *Tetrahedron*, **1976**, *32*, 3-31.
63. Demillequand, M. *PhD-Thesis UCL-ORSY*, **1993**
64. Nemery, I. *PhD-Thesis UCL-ORSY*, **1991**
65. Kallah, B. *On-going PhD-Thesis UCL-ORSY*,
66. Kagan, H. B., *Oxidation of hetero atoms: asymmetric oxidation of sulfides and selenides*, in *Asymmetric Oxidation Reactions (2001)*, Katsuki, T., Editor. Oxford University Press: Oxford, UK. 2001, p. 153-170.
67. Huart, C. *PhD-Thesis UCL-ORSY*, **1995**
68. Huart, C.; Ghosez, L. *Angew. Chem. Int. Ed. Engl.*, **1997**, *36*, 634-635.
69. Doub, M., in *Encyclopedia of Chemical Technology*, Grayson, M., Editor. Wiley: New York. 1983, p. 795.
70. Hoyle, J., *Preparation of sulphonic acids, esters, amides and halides*, in *The chemistry of sulphonic acids, esters and their derivatives*, Pataï, S. and Rappoport, Z., Editors. John Wiley & Sons: Chichester, England. 1991, p. 351-399.
71. Tanaka, K., *Sulfonic acids, esters, amides and halides as synthons*, in *The chemistry of sulphonic acids, esters and their derivatives*, Patai, S. and

Rappoport, Z., Editors. John Wiley & Sons Ltd: Chichester, England. 1991, p. 401.
72. Bordwell, F. G. *Acc. Chem. Res.*, **1988**, 456-463.
73. Boche, G.; Lohrenz, J. C. W.; Cioslowski, J.; Koch, W., *Carbon acidity resulting from sulfur substituents*, in *The chemistry of sulphur-containing functional groups*, Patai, S. and Rappoport, Z., Editors. John Wiley & Sons Ltd. 1993, p. 339-362.
74. Cram, D. J.; Scott, D. A.; Nielsen, W. D. *J. Am. Chem. Soc.*, **1961**, *83*, 3696-3707.
75. Cram, D. J., *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965, p. 71-84.
76. Jordan, T.; Smith, H. W.; Lohr, L. L.; Lipscomb, W. N. *J. Am. Chem. Soc.*, **1963**, *85*, 846-851.
77. Kaiser, E. M.; Solter, L. E.; Schwarz, R. A.; Beard, R. D.; Hauser, C. R. *J. Am. Chem. Soc.*, **1971**, *93*, 4237-4242.
78. Schleyer, P. v. R.; Clark, T.; Kos, A. J.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.*, **1984**, *106*, 6467-6475.
79. Wolfe, S.; Stolow, A.; LaJohn, L. A. *Tetrahedron Lett.*, **1983**, *24*, 4071-4074.
80. Bors, D. A.; Streitwieser, A. J. *J. Am. Chem. Soc.*, **1986**, *108*, 1397-1404.
81. Corey, E. J.; Lowry, T. H. *Tetrahedron Lett.*, **1965**, 793-801.
82. Corey, E. J.; Lowry, T. H. *Tetrahedron Lett.*, **1965**, 803-809.
83. von E. Doering, W.; Levy, L. K. *J. Am. Chem. Soc.*, **1955**, *77*, 509-513.
84. Wolfe, S.; Rauk, A.; Csizmadia, I. G. *J. Am. Chem. Soc.*, **1969**, *91*, 1567-1569.
85. Lett, R.; Chassaing, G.; Marquet, A. *J. Organomet. Chem.*, **1976**, *11*, C17-C20.
86. Chassaing, G.; Marquet, A. *Tetrahedron*, **1978**, *34*, 1399-1404.
87. Boche, G. *Angew. Chem. Int. Ed. Engl.*, **1989**, *28*, 277-297.
88. Chassaing, G.; Marquet, A.; Corset, J.; Froment, F. *J. Organomet. Chem.*, **1982**, *232*, 293-313.
89. Gais, H. J.; Hellmann, G.; Günter, H.; Lopez, F.; Lindner, H. J.; Braun, S. *Angew. Chem. Int. Ed. Engl.*, **1989**, *28*, 1025.
90. Boche, G.; Marsch, M.; Harms, K.; Sheldrick, G. M. *Angew. Chem. Int. Ed. Engl.*, **1985**, *24*, 573-575.
91. Gais, H.-J.; Lindner, H. J.; Vollhardt, J. *Angew. Chem. Int. Ed. Engl.*, **1985**, *24*, 859.
92. Dorie, J.; Gouesnard, J.-P. *J. Chem. Phys.*, **1984**, *81*, 15-19.
93. Jennings, W. B.; Spratt, R. *J. Chem. Soc. Chem. Commun.*, **1970**, 1418-1419.
94. Cram, D. J.; Trepka, R. D.; Janiak, P. S. *J. Am. Chem. Soc.*, **1964**, *86*, 2731-2733.
95. Goering, H. L.; Towns, D. L.; Dittmar, B. *J. Org. Chem.*, **1962**, 736-739.
96. Gais, H. J.; Hellmann, G. *J. Am. Chem. Soc.*, **1992**, *114*, 4439-4440.
97. Roitman, J. N.; Cram, D. J. *J. Am. Chem. Soc.*, **1971**, *93*, 2225-2231.
98. Krief, A. *Tetrahedron*, **1980**, *36*, 2531-2640.
99. Lucchetti, J.; Krief, A. *Tetrahedron Lett.*, **1978**, 2697-2700.
100. Lucchetti, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.*, **1979**, 2695-2696.
101. Anh, N. T. *Actual. Chim.*, **1974**, 9-19.
102. Kyriakakou, G.; Roux-Schmitt, M. C.; Seyden-Penne, J. *Tetrahedron*, **1975**, *31*, 1883-1888.
103. Cossentini, M.; Deschamps, B.; Anh, N. T.; Seyden-Penne, J. *Tetrahedron*, **1977**, *33*, 409-412.
104. Lefour, J.-M.; Loupy, A. *Tetrahedron*, **1978**, *34*, 2597-2605.
105. Christensen, L. W.; Seaman, J. M.; Truce, W. E. *J. Org. Chem.*, **1973**, *38*, 2243-2245.
106. Mladenova, M.; Biserkova, M.; Kaneti, J. *Phosphorus, Sulfur and Silicon*, **1995**, *104*, 151-159.
107. Hirama, M. *Tetrahedron*, **1981**, *22*, 1905-1908.

108. Binns, M. R.; Haynes, R. K.; Katsifis, A. G.; Schober, P. A.; Vonwiller, S. C. *J. Org. Chem.*, **1989**, *54*, 1960-1968.
109. Enders, D.; Kipphardt, H.; Gerdes, P.; Brena-Valle, L. J.; Bhushan, V. *Bull. Soc. Chim. Belg.*, **1988**, *97*, 691-704.
110. Kanth, J. V. B.; Periasamy, M. *Tetrahedron*, **1993**, *49*, 5127-5132.
111. Nakayama, K.; Thompson, W. J. *J. Am. Chem. Soc.*, **1990**, *112*, 6936-6942.
112. Douglass, I. B.; Johnson, T. B. *J. Am. Chem. Soc.*, **1938**, *60*, 1486-1489.
113. Goethals, E. J.; Verzele, M. *Bull. Soc. Chim. Belg.*, **1965**, *74*, 21.
114. Sheehan, J. C.; Tulis, R. W. *J. Org. Chem.*, **1974**, *39*, 2264-2267.
115. Atlani, M.; Corso, V.; Wakselman, C.; Loutaty, R.; Yacono, C. (Compagnie Française de Raffinage S. A., France), US 4170547, 1979
116. Aumaitre, G.; Chanet-Ray, J.; Durand, J.; Vessières, R.; Lonchambon, G. *Synthesis*, **1983**, 816-821.
117. King, J. F.; Lam, J. Y. L.; Ferrazzi, G. *J. Org. Chem.*, **1993**, *58*, 1128-1135.
118. Pinner, A. *Ber.*, **1883**, *16*, 325.
119. Mendez, J. M.; Flores, B.; Leon, F.; Martinez, M. E.; Vazquez, A.; Garcia, G. A.; Salmon, M. *Tetrahedron Lett.*, **1996**, *37*, 4099-4102.
120. Fry, J. L.; Ott, R. A. *J. Org. Chem.*, **1981**, *46*, 602-607.
121. Cunico, R. F.; Kuan, C. P. *J. Org. Chem.*, **1992**, *57*, 1202-1205.
122. Sanders, E. B.; Secor, H. V.; Seeman, J. I. *J. Org. Chem.*, **1978**, *43*, 324-330.
123. Büchi, G.; Liang, P. H.; Wüest, H. *Tetrahedron Lett.*, **1978**, *31*, 2763-2764.
124. Evans, D. A.; Carroll, G. L.; Truesdale, L. K. *J. Org. Chem.*, **1974**, *39*, 914-917.
125. Wakamatsu, T.; Hobara, S.; Ban, Y. *Heterocycles*, **1982**, *19*, 1395-1398.
126. Johnson, A. P.; Pelter, A. *J. Chem. Soc.*, **1964**, 520-522.
127. Jones, D. N.; Saeed, M. A. *J. Chem. Soc.*, **1963**, 4657-4663.
128. Williamson, A. *J. Chem. Soc.*, **1852**, *4*, 229.
129. Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.*, **1976**, *98*, 4887-4902.
130. Zoretic, P. A.; Soja, P. *J. Heterocyclic Chem.*, **1977**, *14*, 681-682.
131. Sharpless, K. B.; Young, M. W.; Lauer, R. F. *Tetrahedron Lett.*, **1973**, 1979-1982.
132. Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.*, **1973**, *95*, 6137-6139.
133. Zoretic, P. A.; Soja, P. *J. Org. Chem.*, **1976**, *41*, 3587-3589.
134. Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem.*, **1974**, *39*, 3459-3460.
135. Donnay, G.; Gryder, J. W. *J. Chem. Educ.*, **1965**, *42*, 223.
136. Wuepper, J. L.; Popov, A. I. *J. Am. Chem. Soc.*, **1969**, *91*, 4352-4356.
137. Yeager, H. L.; Fedyk, J. D.; Parker, R. J. *J. Phys. Chem.*, **1973**, *77*, 2407-2410.
138. Matsubara, K.; Kaneuchi, R.; Maekita, N. *J. Chem. Soc., Faraday Trans.*, **1998**, *94*, 3601-3605.
139. Seebach, D. *Angew. Chem. Int. Ed. Engl.*, **1988**, *27*, 1624-1654.
140. Sun, X.; Collum, D. B. *J. Am. Chem. Soc.*, **2000**, *122*, 2459-2463.
141. Normant, J. F. *Bull. Soc. Chim. Fr.*, **1968**, 761.
142. House, H. O., *Modern Synthetic Reactions*; 2nd ed; W.A. Benjamin, Inc.: Menlo Park, CA, 1972 527-530.
143. Sauvetre, R.; Seyden-Penne, J. *Tetrahedron Lett.*, **1976**, *44*, 3949-3952.
144. Sauvetre, R.; Roux-Schmitt, M. C.; Seyden-Penne, J. *Tetrahedron*, **1978**, *34*, 2135-2140.
145. Wartski, L.; El Bouz, M.; Seyden-Penne, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.*, **1979**, *17*, 1543-1546.
146. Reich, H. J.; Borst, J. P.; Dykstra, R. R. *Tetrahedron*, **1994**, *50*, 5869-5880.
147. Cohen, T.; Abraham, W. D.; Myers, M. *J. Am. Chem. Soc.*, **1987**, *109*, 7923-7924.
148. Jackman, L. M.; Chen, X. *J. Am. Chem. Soc.*, **1992**, *114*, 403-411.
149. Reich, H. J.; Borst, J. P.; Dykstra, R. R.; Green, D. P. *J. Am. Chem. Soc.*, **1993**, *115*, 8728-8741.

150. Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.*, **1990**, *112*, 8008-8014.
151. Masamune, S.; Ali, S. K.; Snitman, D. L.; Garvey, D. S. *Angew. Chem. Int. Ed. Engl.*, **1980**, *19*, 557-558.
152. Nemery, I. *Master Degree UCL-ORSY*, **1986**
153. Hanawa, H.; Maekawara, N.; Maruoka, K. *Tetrahedron Lett.*, **1999**, *40*, 8379-8382.
154. Pindur, U., *Preparation and chemistry of ortho acids, ortho esters and ortho amides*, in *Supplement B: The Chemistry of Acids Derivatives*, Patai, S., Editor. John Wiley & Sons, Inc.: New York. 1992, p. 967-1005.
155. Sikorski, W. H.; Reich, H. J. *J. Am. Chem. Soc.*, **2001**, *123*, 6527-6535.
156. Hoppe, D.; Hense, T. *Angew. Chem. Int. Ed. Engl.*, **1997**, *36*, 2283-2316.
157. Hammond, G. S., *Steric Effects on Equilibrated Systems*, in *Steric Effects in Organic Chemistry*, Newman, M. S., Editor. John Wiley & Sons, Inc.: New York. 1956, p. 462-465.
158. Anet, F. A.; Haq, M. Z. *J. Am. Chem. Soc.*, **1965**, *87*, 3147-3150.
159. Pitzer, K. S. *J. Chem. Phys.*, **1944**, *12*, 310-314.
160. Riviere, H.; Tostain, J. *Bull. Soc. Chim. Fr.*, **1969**, 568-576.
161. Toromanoff, E. *Bull. Soc. Chim. Fr.*, **1962**, 708-712.
162. Karpf, M.; Huguet, J.; Dreiding, A. S. *Helv. Chim. Acta*, **1982**, *65*, 13-25.
163. Yoshikawa, N.; Yamada, Y. M. A.; Das, J.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.*, **1999**, *121*, 4168-4178.
164. Ishihara, K.; Kondo, S.; Yamamoto, H. *J. Org. Chem.*, **2000**, *65*, 9125-9128.
165. Kobayashi, Y.; Murugesh, M. G.; Nakano, M.; Takahisa, E.; Usmani, S. B.; Ainai, T. *J. Org. Chem.*, **2002**, *67*, 7110-7123.
166. O'Donnell, M. J., *Asymmetric Phase Transfer Reactions*, in *Catalytic Asymmetric Synthesis*, Ojima, I., Editor. VCH Publishers, Inc.: New York. 1993, p. 389-411.
167. Weber, W. P.; Gokel, G. W., *Phase Transfer Catalysis in Organic Synthesis*; Springer-Verlag: Berlin, 1977.
168. Colonna, S.; Hiemstra, H.; Wynberg, H. *J. Chem. Soc. Chem. Commun.*, **1978**, 238-239.
169. Colonna, S.; Re, A.; Wynberg, H. *J. Chem. Soc. Perkin Trans. 1*, **1981**, 547-552.
170. Cram, D. J.; Sogah, G. D. Y. *J. Chem. Soc. Chem. Commun.*, **1981**, 625-628.
171. Conn, R. S. E.; Lovell, A. V.; Karady, S.; Weinstock, L. M. *J. Org. Chem.*, **1986**, *51*, 4710-4711.
172. Corey, E. J.; Noe, M. C.; Xu, F. *Tetrahedron Lett.*, **1998**, *39*, 5347-5350.
173. Perrard, T.; Plaquevent, J.-C.; Desmurs, J.-R.; Hébrault, D. *Org. Lett.*, **2000**, *2*, 2959-2962.
174. Perrard, T. *PhD-Thesis Faculté des Sciences et Techniques de l'Université de Rouen*, **1999**
175. Cardillo, G.; Savoia, D.; Umani-Ronchi, A. *Synthesis*, **1975**, 453-455.
176. Jonczyk, A.; Banko, K.; Makosza, M. *J. Org. Chem.*, **1975**, *40*, 266-267.
177. Jonczyk, A.; Radwan-Pytlewski, T. *Polish J. Chem.*, **1995**, *69*, 1161-1167.
178. Liu, G.-J.; Zhang, Z.; Sun, Y.-P.; Wang, Y.-L.; Cai, S.-C. *Youji Huaxue*, **1990**, *10*, 217-222.
179. Liu, G.-J.; Zhang, Z.; Wang, Y.-L.; Sun, Y.-P.; Bai, Y.-L. *Youji Huaxue*, **1995**, *15*, 590-594.
180. Wladislaw, B.; Marzorati, L.; Claro, N. F.; DiVitta, C. *Synthesis*, **1997**, 420-422.
181. Miesch, M.; Mislin, G.; Franck-Neumann, M. *Tetrahedron Lett.*, **1998**, *39*, 6873-6876.
182. Rosini, G.; Ballini, R. *Synthesis*, **1988**, 833-847.
183. Mikló, K.; Jaszberenyi, J. C.; Kádas, I.; Árvai, G.; Töke, L. *Tetrahedron Lett.*, **1996**, *37*, 3491-3494.
184. Kádas, I.; Árvai, G.; Töke, L. *Monatsh. Chem.*, **1996**, *127*, 887-893.
185. Nowitzki, O.; Münnich, I.; Stucke, H.; Hoffmann, H. M. R. *Tetrahedron*, **1996**, *52*, 11799-11810.
186. Corey, E. J.; Zhang, F.-Y. *Org. Lett.*, **2000**, *2*, 4257-4259.

187. Novak, T.; Tatai, J.; Bako, P.; Czugler, M.; Kegelvich, G.; Töke, L. *Synlett*, **2001**, 424-426.
188. Öhrlein, R.; Schwab, W.; Ehrler, R.; Jäger, V. *Synthesis*, **1986**, 535-538.
189. Rohrer, A.; Ocampo, R.; Callot, H. J. *Synthesis*, **1994**, 923-925.
190. Movsumzade, E. M.; Kulieva, D. A.; Mamedov, M. G.; Nasirov, Y. F. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, **1985**, *28*, 12-16.
191. Kornblum, N., *The Synthesis of Aliphatic and Alicyclic Nitro Compounds*, in *Organic Reactions*. John Wiley & Sons, Inc.: New York. 1962, p. 101-156.
192. Lucet, D.; Sabelle, S.; Kostelitz, O.; Le Gall, T.; Mioskowski, C. *Eur. J. Org. Chem.*, **1999**, 2583-2591.
193. Desmaële, D.; Louvet, J. M. *Tetrahedron Lett.*, **1994**, *35*, 2549-2552.
194. Solladié-Cavallo, A.; Bonne, F. *Tetrahedron Asymmetry*, **1996**, *7*, 171-180.
195. Fernandez, R.; Gasch, C.; Lassaletta, J. M.; Llera, J. M.; Vazquez, J. *Tetrahedron Lett.*, **1993**, *34*, 141-144.
196. Keinan, E.; Sinha, S. C.; Singh, S. P. *Tetrahedron*, **1991**, *47*, 4631-4638.
197. Keller, W. E., *Phase-Transfer Reactions. Fluka Compendium*. Vol. 3; Thieme: Stuttgart, 1990.
198. Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.*, **1997**, *119*, 12414-12415.
199. Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.*, **1997**, *38*, 8595-8598.
200. Jew, S.-S.; Jeong, B.-S.; Yoo, M.-S.; Huh, H.; Park, H.-G. *Chem. Comm.*, **2001**, 1244-1245.
201. O'Donnell, M. J.; Wu, S.; Huffman, J. C. *Tetrahedron*, **1994**, *50*, 4507-4518.
202. Corey, E. J.; Zhang, F.-Y. *Angew. Chem. Int. Ed. Engl.*, **1999**, *38*, 1931-1934.
203. Clark, J. H. *Chem. Rev.*, **1980**, *80*, 429-452.
204. Landini, D.; Maia, A.; Rampoldi, A. *J. Org. Chem.*, **1989**, *54*, 328-332.
205. Torssell, K.; Zeuthen, O. *Acta Chem. Scand., Ser. B*, **1978**, *32*, 118-124.
206. Colvin, E. W.; Seebach, D. *J. Chem. Soc. Chem. Commun.*, **1978**, 689-691.
207. Martin, O. R.; Khamis, F. E.; El-Shenawy, H. A.; Rao, S. P. *Tetrahedron Lett.*, **1989**, *30*, 6139-6142.
208. Menzel, A.; Öhrlein, R.; Griesser, H.; Wehner, V.; Jäger, V. *Synthesis*, **1999**, 1691-1702.
209. Knudsen, K. R.; Risgaard, T.; Nishiwaki, N.; Gothelf, K. V.; Jørgensen, K. A. *J. Am. Chem. Soc.*, **2001**, *123*, 5843-5844.
210. Aizpurua, J. M.; Oiarbide, M.; Palomo, C. *Tetrahedron Lett.*, **1987**, *28*, 5361-5364.
211. Ooi, T.; Doda, K.; Maruoka, K. *J. Am. Chem. Soc.*, **2003**, *125*, to be published.
212. Bluet, G.; Campagne, J.-M. *J. Org. Chem.*, **2001**, *66*, 4293-4298.
213. Hayami, J.; Ono, N.; Kaji, A. *Tetrahedron Lett.*, **1968**, *11*, 1385-1386.
214. Yamada, K.-i.; Moll, G.; Shibasaki, M. *Synlett*, **2001**, 980-982.
215. Xu, Y.; Ohori, K.; Ohshima, T.; Shibasaki, M. *Tetrahedron*, **2002**, *58*, 2585-2588.
216. Takita, R.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.*, **2002**, *43*, 4661-4665.
217. Johnson, J. S.; Evans, D. A. *Acc. Chem. Res.*, **2000**, *33*, 325-335.
218. Pfaltz, A. *Acc. Chem. Res.*, **1993**, *26*, 339-345.
219. Christensen, C.; Juhl, K.; Jørgensen, K. A. *Chem. Comm.*, **2001**, 2222-2223.
220. Nishiwaki, N.; Knudsen, K. R.; Gothelf, K. V.; Jørgensen, K. A. *Angew. Chem. Int. Ed. Engl.*, **2001**, *40*, 2992-2995.
221. Yamaguchi, M.; Igarashi, Y.; Reddy, R. S.; Shiraishi, T.; Hirama, M. *Tetrahedron*, **1997**, *53*, 11223-11236.
222. Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.*, **1996**, *61*, 3520-3530.
223. Bui, T.; Barbas III, C. F. *Tetrahedron Lett.*, **2000**, *41*, 6951-6954.
224. List, B. *Tetrahedron*, **2002**, *58*, 5573.
225. Betancourt, J. M.; Sakthivel, K.; Thayumanavan, R.; Barbas III, C. F. *Tetrahedron Lett.*, **2001**, *42*, 4441-4444.
226. Melchiorre, P.; Jørgensen, K. A. *J. Org. Chem.*, **2003**, *68*, 4151-4157.
227. Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.*, **2003**, *125*, 1192-1194.

228. Hanessian, S.; Pham, V. *Org. Lett.*, **2000**, *2*, 2975-2978.
229. Kádas, I.; Árvai, G.; Töke, L.; Toth, G.; Szollosy, A.; Bihari, M. *Tetrahedron*, **1994**, *50*, 2895-2906.
230. Barco, A.; Benetti, S.; Bianchi, A.; Casolari, A.; Pollini, G. P.; Romagnoli, R.; Spalluto, G.; Zanirato, V. *Tetrahedron*, **1994**, *50*, 11743-11754.
231. Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.*, **1982**, *47*, 5045-5050.
232. Ding, P.; Ghosez, L. *Tetrahedron*, **2002**, *58*, 1565-1571.
233. Venkatachalam, M.; Deshpande, M. N.; Jawdosiuk, M.; Kubiak, G.; Wehrli, S.; Cook, J. M.; Weiss, U. *Tetrahedron*, **1986**, *42*, 1597-1605.
234. Momose, T.; Yoshizawa, E.; Muraoka, O. *Synth. Commun*, **1985**, *15*, 17-25.
235. Evans, D. A.; Urpi, F.; Somers, T. C.; Clark, J. S.; Bilodeau, M. T. *J. Am. Chem. Soc.*, **1990**, *112*, 8215-8216.
236. Nef, J. U. *Liebigs Ann. Chem.*, **1894**, *280*, 264.
237. Shechter, H.; Williams Jr., F. T. *J. Org. Chem.*, **1962**, *27*, 3699.
238. Kornblum, N.; Erickson, A. S.; Kelly, W. J.; Henggeler, B. *J. Org. Chem.*, **1982**, *47*, 4534.
239. Clark, J. H.; Cork, D. G. *J. Chem. Soc. Perkin Trans. 1* , **1983**, 2253-2258.
240. Vankar, P. S.; Rathore, R.; Chandrasekaran, S. *Synth. Commun*, **1987**, *17*, 195.
241. Bartlett, P. A.; Green III, F. R.; Webb, T. R. *Tetrahedron Lett.*, **1977**, 331.
242. Narayana, C.; Reddy, N. K.; Kabalka, G. W. *Synth. Commun*, **1992**, *22*, 2587.
243. Adam, W.; Makosza, M.; SahaMoller, C. R.; Zhao, C. G. *Synlett*, **1998**, 1335.
244. McMurry, J. E.; Melton, J. *J. Org. Chem.*, **1973**, *38*, 4367.
245. Kalita, D.; Khan, A. T.; Barua, N. C.; Bez, G. *Tetrahedron*, **1999**, *55*, 5177.
246. Akita, Y.; Inaba, M.; Uchida, H.; Ohta, A. *Synthesis*, **1977**, 792.
247. Barton, D. H. R.; Motherwell, W. B.; Simon, E. S.; Zard, S. Z. *J. Chem. Soc. Perkin Trans. 1*, **1986**, 2243-2252.
248. Jonsson, S. Y.; Löfström, C. M. G.; Bäckvall, J.-E. *J. Org. Chem.*, **2000**, *65*, 8454-8457.
249. Farhat, S.; Marek, I. *Angew. Chem. Int. Ed. Engl.*, **2002**, *41*, 1410-1413.
250. Marek, I., *Conference*, Louvain-la-Neuve, 2002.