13. Synthesis and Odor of Chiral Partial Structures of Khusimone

Part 1

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Dedicated with best personal wishes to Prof. Dr. *W. Fleischhacker* on the occasion of his 65th birthday

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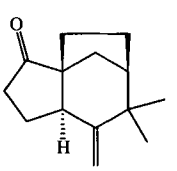
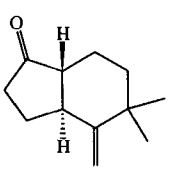
Khusimone (**1**), one of the main odor-donating compounds of vetiver oil is subject of the following study on structure/odor relationship. The omittance of the ethano bridge of the tricyclic khusimone leads to a bicyclic system. The stereoselective approach to this degraded structure is described, and the olfactory properties are studied. The key step of the synthesis of the hydrindane nucleus is based on a highly diastereoselective conjugate addition to a chiral oxo-cyclopentene-2-carboxylate.

Introduction. – Vetiver oil is widely used for high-quality, expensive perfumery compositions and soap perfumes. Though this natural product has a strong woody aroma, it is interesting to note that it is isolated not from wood but from the clean dried rootlets of the grass *Vetiveria zizanoides* by steam distillation. This grass originates from India and is cultivated also in Indonesia, Sri Lanka, Reunion, Haiti, and China. The odor of the oil has been described as heavy-sweet, woody, earthy, reminiscent of roots and wet soil with a rich undertone of precious wood [4]. To some extent, the olfactory properties of the main components α- and β-vetivone have been discussed controversially (see *Mookherjee et al.* [4] and *Maurer* [5]), but there is agreement that (−)-khusimone (**1**) is one of the main odor-donating compounds. Because of the pleasant odor of this tricyclic ketone, there were efforts to develop a short synthesis starting, for economic reasons, from the also naturally occurring (+)-zizanoic acid [5], but there are no structure/odor studies on (−)-khusimone (**1**) published. In the following, the first part of an examination of degraded structures of (−)-**1** is presented. In this study, we focused our interest to the olfactory consequences of degrading the tricyclic structure to the bicyclic structure (−)-**2**



(−)-**1**

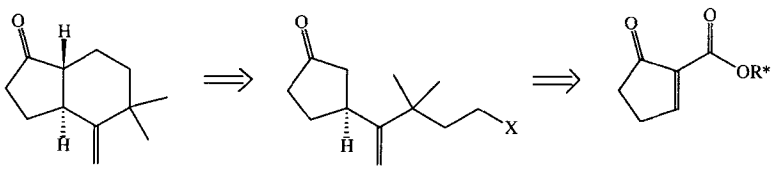


(−)-**2**

[1]) Part of the Ph.D. thesis [1].
[2]) Part of Diploma work [2].
[3]) Part of Diploma work [3].

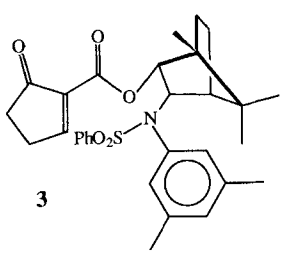
by omitting the ethano bridge. Furthermore, considering the fact that optical antipodes differ in many cases in their odorous properties, compound (−)-**2** has to be synthesized enantioselectively.

Scheme 1



(−)-**2**

Results and Discussion. – According to the retrosynthetic consideration depicted in *Scheme 1*, the key step of the route to (−)-**2** was the conjugate addition of an appropriate nucleophile to a chiral olefinic keto ester which should undergo at least intramolecular cyclization. As starting materials we used bromo compound **4** and the chiral olefinic keto ester **3** which is known to react with a great variety of organocopper compounds diastereoselectively with predictable configuration [6–8]. Moreover, the chiral auxiliary is commercially available and can be recovered in high yield [7] [8].



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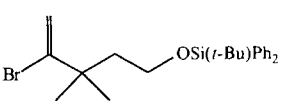

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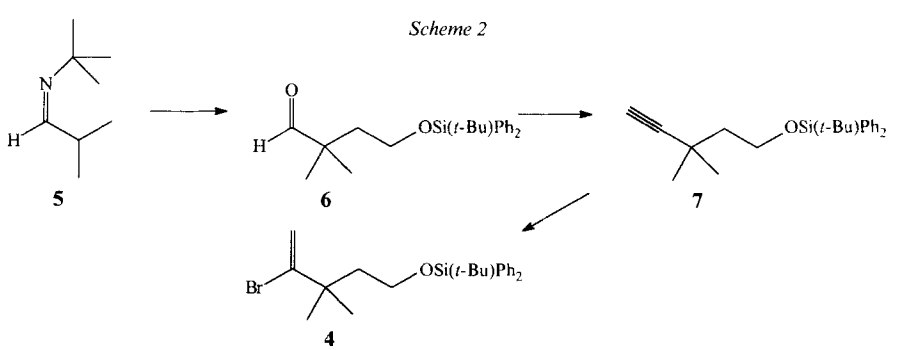
The synthesis of the necessary bromo compound **4** started from isobutyraldehyde which was alkylated after transforming it into the corresponding imino derivative **5** [9] [10], leading, after hydrolysis, to the protected hydroxy-butyraldehyde derivative **6** (*Scheme 2*). The C=O group was converted successfully by *Wittig* reaction with (chloro-

Scheme 2



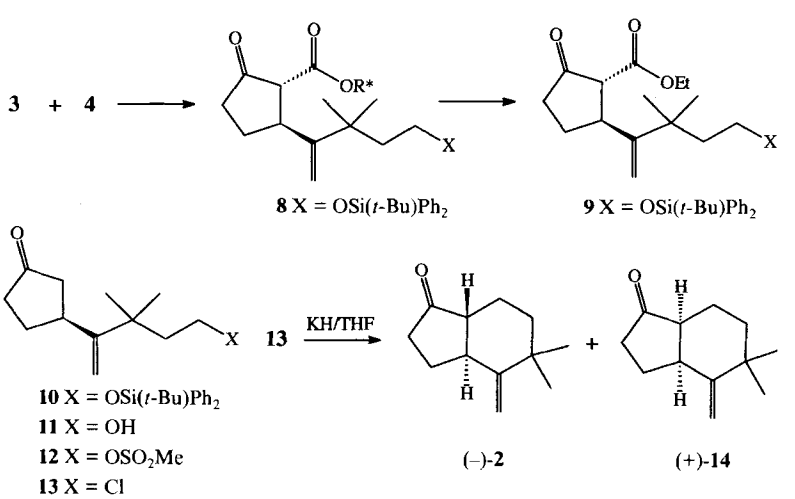
5 **6** **7**

4

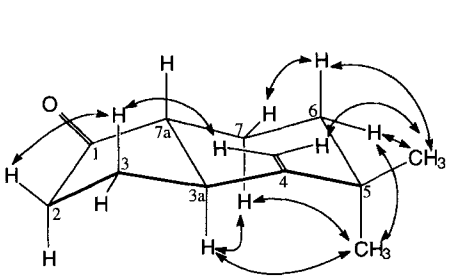
methyl)triphenylphosphonium chloride [11] and subsequent elimination with BuLi to the alkyne **7**. This new route to **7** is superior to previously published syntheses of the unprotected alcohol [12] [13]. Reaction of **7** with *B*-bromo-9-BBN (*B*-bromo-9-borabicyclo[3.3.1]nonane) [14] yielded **4**.

The following conjugate addition to the unsaturated keto ester **3** turned out to be difficult. Contrary to *Helmchen* and *Wenger* [6] [7], and *Urban et al.* [8], even the use of the highly reactive *Gilman*'s reagent (R_2CuLi) [15], derived from **4** by reaction with 2 equiv. of *t*-BuLi and addition of CuI, gave only poor yields of adduct **8** (less than 5%, *Scheme 3*). The yields could not be enhanced by increasing the reactivity of the organolithium cuprate by adding a *Lewis* acid like $BF_3 \cdot Et_2O$ [16] [17]. Presumably, the reason for the decreased reactivity was caused by the geminal dimethyl group adjacent to the exocyclic C=C bond. The stereochemical key step, however, was realized by the method of *Piers et al.* [18] by converting **4** into the organolithium compound by reaction with 2 equiv. *t*-BuLi, followed by $MgBr_2 \cdot Et_2O$ and $CuBr \cdot Me_2S$, $BF_3 \cdot Et_2O$ and subsequent conjugate addition to the chiral ester **3**. Moreover, this method is consuming only 1 equiv. of **4** like *Lipshutz*' reagent [19] which suffers of even lower reactivity than *Gilman*'s reagent. The yields of pure **8** were *ca.* 70%, and in accordance to [6–8] no diastereoisomeric impurities could be detected *via* ^1H- and ^{13}C-NMR. Transesterification of **8** with $Ti(EtO)_4$ [20] furnished the ethyl ester **9** which was submitted to decarbethoxylation [21] yielding the chiral ketone **10**. After deprotection of **10** with Bu_4NF, the resulting alcohol **11** was converted to the methanesulfonate **12** which unexpectedly did not undergo intramolecular cyclization. Neither the use of *t*-BuOK [22] nor $LiN(SiMe_3)_2$ [17] were successful. But after converting **12** to chloride **13**, smooth cyclization in the presence of KH/THF [18] occurred generating an epimeric mixture of (−)-**2** and (+)-**14** with a ratio of 1:1.8 determined by ^1H-NMR (GC conditions led to epimerization). Refluxing the epimers with NaOMe in MeOH had nearly no effect on the ratio: After refluxing for 18 h, the ratio has changed insignificantly to 1:1.6. Both epimers could be easily separated by TLC using $AgNO_3$-pretreated silica gel.

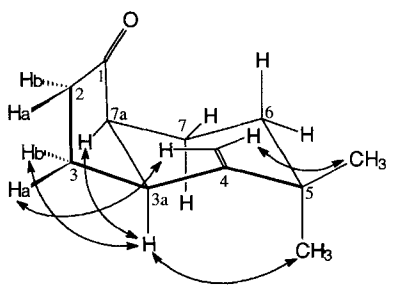
Scheme 3



The configuration of isomers (−)-**2** and (+)-**14** was mainly deduced by NOE experiments. Whereas irradiation of the H−C(3a) resonance in (+)-**14** gives a strong NOE to the signal of H−C(7a) (and thus indicating the *cis*-position of the involved protons), no such through-space connection could be observed with the corresponding protons H−C(3a) and H−C(7a) of (−)-**2** (giving a strong hint for *trans*-position). Moreover, the chemical shifts of H−C(3a) (3.19 ppm) and H−C(7a) (2.38 ppm) in (+)-**14** are in good accordance with those of its de(5,5-dimethyl)congener described as '*cis*-fused' in [18] (H-3a: 2.95 ppm, H-7a: 2.37–2.41 ppm). Unambiguous assignment for all ^{1}H and ^{13}C signals of (−)-**2** and (+)-**14** followed from APT, COSY, HMQC [23], and NOE experiments as well as from 1D-HETCOR [24] and long-range INEPT spectra [25] with selective excitation of suitable ^{1}H resonances. The most important through-space connections extracted from the NOE series are displayed below for structures (−)-**2** and (+)-**14**. It should be emphasized that the observed NOEs (*e.g.*, H−C(3a) ↔ (Me_{ax}−C(5) in (+)-**14**) support 'chair' conformation of the cyclohexane ring.



(−)-**2**



(+)-**14**

The odorous impression of (−)-**2** can be summarized as weak camphoraceous with a woody by-note. This means the degradation of the tricyclic khusimone (**1**) to the bicyclic structure (−)-**2** leads to the loss of the typical odor. The epimeric compound (+)-**14** exhibits an intense camphoraceous and fruity (reminiscent to strawberry and raspberry) odor.

We are indepted to Mr. *W. Höppner* and *V. Hausman*, perfumers of *Dragaco-Vienna*, for the organoleptic analyses of all new compounds.

Experimental Part

General. All reactions were carried out under Ar. THF and Et_2O: distilled over $LiAlH_4$. M.p. (uncorrected): *Kofler* apparatus. TLC: *Merck-F-254* (No. 5554) precoated sheets; visualization by anisaldehyde/H_2SO_4 or by UV. TLC: *Merck-F-254* (No. 5717) precoated plates; visualization by anisaldehyde/H_2SO_4 or by UV. Column chromatography (CC): *Merck KG 60 F 254*, 70–230 mesh ASTM (No. 7734). IR: *Perkin-Elmer* spectrophotometer *298*, ν_{max} in cm^{-1}. ^{1}H-NMR: *Bruker AC 80* (80 MHz) and *Varian Unityplus 300* (300 MHz); δ in ppm rel. to Me_4Si (= 0 ppm), J in Hz. ^{13}C-NMR: *Varian Unityplus 300* (75 MHz); δ rel. to Me_4Si (= 0 ppm). GC/MS: *Hewlett-Packard* spectrometer *5890/5970*.

*4-[(*tert*-Butyl)diphenylsilyloxy]-2,2-dimethylbutanal* (**6**). To a soln. of 5.7 ml (43.45 mmol) of abs. $(i\text{-}Pr)_2NH$ in 15 ml of THF were added at −40° slowly 27.2 ml (43.45 mmol) of a 1.6M soln. of BuLi in hexane. Then, the mixture was stirred for 20 min at 0°. Afterwards, the mixture was cooled to −10°, and a soln. of 3.67 g (28.93 mmol) of N-(*tert-butyl*)-*2-methylpropan-1-imine* (**5**) [9] in 15 ml of THF was added dropwise. After stirring for 7 h at 0°, a soln. of 10.5 g (28.93 mmol) of (2-bromoethoxy)(*tert*-butyl)diphenylsilane [26] in 30 ml of THF was added and the

mixture stirred for 4 d at r.t. The mixture was extracted with Et_2O/brine, the org. layer dried and concentrated *in vacuo*. The residue was dissolved in 30 ml of hexane and stirred under Ar with 77 ml of 1M AcOH/H_2O. The aq. layer was saturated with NaCl, extracted with Et_2O, the combined Et_2O extracts were washed with aq. $NaHCO_3$ and brine, dried, and concentrated: 9.73 g (95%) of **6**. IR (NaCl, liquid film): 1760. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.04 (*s*, 3 Me); 1.06 (*s*, 2 Me); 1.78 (*m*, CH_2); 3.63 (*m*, CH_2O); 7.41 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.66 (*m*, 4 H, H–C(2), H–C(6) of Ph); 9.54 (*s*, CHO). ^{13}C-NMR (20 MHz, $CDCl_3$): 205.3 (C=O); 135.5 (arom. C(2), C(6)); 133.3 (arom. C(1)); 129.6 (arom. C(4)); 127.60 (arom. C(3), C(5)); 60.1 (C(4)); 44.5, 40.6 (C(2), C(3)); 26.7 (*Me*$_3$C); 21.5 (*Me*$_2$C); 19.0 (Me$_3$*C*). MS: 298 (22), 297 (92), 219 (42), 199 (100), 189 (32), 183 (11), 181 (15), 139 (25), 77 (10).

*5-[(*tert*-Butyl)diphenylsilyloxy]-3,3-dimethylpent-1-yne* (**7**). 1. *(E/Z)-5-[(*tert*-Butyl)diphenylsilyloxy]-1-chloro-3,3-dimethylpent-1-ene*. To a suspension of 10.85 g (31.25 mmol) of (chloromethyl)triphenylphosphonium chloride in 50 ml of abs. Et_2O and 3.1 ml (31.25 mmol) of abs. piperidine were added, under Ar, 19.53 ml (31.25 mmol) of 1.6M BuLi in hexane. After 2 h of stirring, a soln. of 9.73 g (27.4 mmol) of **6** dissolved in 25 ml of abs. Et_2O was added and the mixture stirred for further 12 h at r.t. The precipitate was filtered off and the filtrate washed with 1N HCl and H_2O, dried, and concentrated *in vacuo*: 7.94 g (75%) of **7**. IR (NaCl, liquid film): 1620. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.96 (*s*, 3 Me); 0.90, 1.08 (2*s*, 2 Me); 1.52, 1.75 (2*t*, J = 6.9, CH_2); 3.60 (*m*, CH_2O); 5.45–5.74 (*m*, CH=CH); 7.31 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.58 (*m*, 4 H, H–C(2), H–C(6) of Ph). MS: 329 (52), 247 (28), 219 (42), 217 (100), 199 (25), 181 (27), 105 (28), 95 (28).

2. The obtained residue (7.94 g, 20.51 mmol) was dissolved in 60 ml of abs. Et_2O, and 25.64 ml (41.03 mmol) of 1.6M BuLi in hexane were added dropwise at 0°. After stirring for 3 h at 0°, H_2O was added cautiously, the mixture was extracted with Et_2O, the org. phases were dried and concentrated *in vacuo*. The residue was subjected to CC (petroleum ether/AcOEt 10:0.4): 4.52 g (63%) of **7**. IR (NaCl, liquid film): 3300. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*s*, 3 Me); 1.12 (*s*, 2 Me); 1.66 (*t*, J = 7.05, CH_2); 1.94 (*s*, HC≡C); 3.81 (*t*, J = 7.05, CH_2O); 7.33 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.62 (*m*, 4 H, H–C(2), H–C(6) of Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 135.6 (arom. C(2), C(6)); 133.9 (arom. C(1)); 129.5 (arom. C(4)); 127.6 (arom. C(3), C(5)); 91.2 (C(2)); 68.0 (C(1)); 61.5 (C(5)); 45.0 (C(3)); 29.7 (*Me*$_2$C); 29.6 (CH_2); 26.8 (*Me*$_3$C); 19.1 (Me$_3$*C*). MS: 293 (30), 216 (21), 215 (100), 199 (11), 197 (16), 185 (10), 183 (9), 137 (11).

*2-Bromo-5-[(*tert*-butyl)diphenylsilyloxy]-3,3-dimethylpent-1-ene* (**4**). To a soln. of 10.6 ml (10.6 mmol) of *B*-bromo-9-BBN in CH_2Cl_2 were added, under Ar, 3.37 g (9.64 mmol) of **7** dissolved in 20 ml of abs. CH_2Cl_2. After stirring for 2.5 h at 0°, again 10.6 ml (10.6 mmol) of *B*-bromo-9-BBN (= *B*-bromo-9-barabicyclo[3.3.1]nonane) in CH_2Cl_2 were added dropwise. After stirring for additional 2.5 h at 0°, 1.3 ml of AcOH were added slowly, stirring was continued for 1 h at 0°, and the mixture was then poured into H_2O and extracted with hexane. The combined hexane extracts were washed with H_2O, aq. $NaHCO_3$ and again H_2O, dried, and concentrated *in vacuo*. The residue was subjected to CC (petroleum ether/AcOEt 10:0.4): 2.83 g (68%) of **4**. IR (NaCl, liquid film): 1625, 1590. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.04 (*s*, 3 Me); 1.15 (*s*, 2 Me); 1.8 (*t*, J = 7.2, CH_2); 3.64 (*t*, J = 7.2, CH_2O); 5.37 (*d*, J = 1.65, 1 H, CH_2=C); 5.49 (*d*, J = 1.65, 1 H, CH_2=C); 7.40 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.67 (*m*, 4 H, H–C(2), H–C(6) of Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 145.1 (C(2)); 135.6 (arom. C(2), C(6)); 133.9 (arom. C(1)); 129.5 (arom. C(4)); 127.6 (arom. C(3), C(5)); 115.6 (C(1)); 60.8 (C(5)); 43.0, 41.6 (C(3), C(4)); 27.6 (*Me*$_2$C); 26.8 (*Me*$_3$C); 19.1 (Me$_3$*C*). MS: 375 (51), 373 (49), 263 (93), 262 (19), 261 (100), 211 (35), 181 (22), 95 (20).

*(1R,2S,3R,4S)-3-[*N*-(3,5-Dimethylphenyl)-*N*-(phenylsulfonyl)amino-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl (1R,2S)-2-{4-[(*tert*-Butyl)diphenylsilyloxy]-2,2-dimethyl-1-methylidenebutyl}-5-oxocyclopentane-1-carboxylate* (**8**). 2.27 g (5.26 mmol) of **4** were dissolved in 20 ml of abs. Et_2O and treated afterwards with 7.0 ml (10.52 mmol) of 1.5N soln. of *t*-BuLi in pentane at −78°. After stirring for additional 90 min, to the soln. of the *in situ* formed Li compound, 1.63 g (6.31 mmol) of $MgBr_2 \cdot Et_2O$ were added. After stirring for 10 min, 40 ml of abs. Et_2O were added, and the stirring was continued for additional 10 min. Subsequently, 271 mg (1.32 mmol) $CuBr \cdot Me_2S$, a soln. of 2.74 g (5.26 mmol) of **3** in 50 ml of abs. THF, and 0.78 ml (6.31 mmol) of freshly distilled $BF_3 \cdot Et_2O$ were added, and the mixture was stirred for additional 3 h at −78°. After addition of 30 ml aq. NH_4Cl at −78°, the mixture was allowed to warm up to r.t. under vigorous stirring (open to atmosphere!) and subsequently extracted with CH_2Cl_2, dried, and concentrated. The residue was purified by CC (petroleum ether/AcOEt 9:1): 3.2 g (70%) of **8**. Colorless crystals. M.p. 119°. IR (KBr): 1760, 1735, 1640, 1615, 1600, 1170, 1090. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.58 (*s*, Me); 0.90 (*s*, Me); 0.97 (*s*, Me); 1.02 (*s*, *t*-Bu); 1.06 (*s*, Me); 1.12 (*s*, Me); 1.27–1.87 (*m*, 8 H); 1.97 (br. *s*, *Me*C_6H_3); 2.16–2.62 (*m*, *Me*C_6H_3, 3 aliph. H); 3.29–3.80 (*m*, 4 H, CH_2O, H–C(1), H–C(2)); 3.84 (*d*, J = 6.9, H–C(3′)); 4.97 (*s*, 1 H, C=CH_2); 5.02 (*s*, 1 H, C=CH_2); 5.27 (*d*, J = 6.9, H–C(2′)); 5.58 (*s*, H–C(2) of $Me_2C_6H_3$); 6.83 (*s*, H–C(4) of $Me_2C_6H_3$); 7.13 (*s*, H–C(6) of $Me_2C_6H_3$); 7.22–7.56 (*m*, 11 arom. H); 7.57–7.80 (*m*, 4 H, H–C(2), H–C(6) of Ph_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 211.1 (C(5)); 167.1 (COO); 155.9 (=*C*CMe_2); 138.1 (C(1) of $PhSO_2$); 136.9 (C(1) of $Me_2C_6H_3$); 135.1 (C(2), C(6) of Ph_2Si); 133.7 (C(1) of Ph_2Si); 131.8 (C(4) of

$PhSO_2$); 129.0, 128.9, 127.8, 127.5, 127.1, 127.0 (arom. C); 108.9 (CH_2=); 82.1 (C(2')); 66.9 (C(3')); 62.0 (C(1)); 60.8 (CH_2O); 50.3 (C(1')); 48.0 (C(4')); 46.9 (C(7')); 42.7 (Me_2C); 40.1 (C(2)); 38.3, 38.1 (C(CH_2CH_2O) or C(4)); 31.7, 30.8, 27.4 (C(3), C(5'), C(6')); 27.3, 26.8 (Me_2C); 26.4 (Me_3C); 21.0, 20.6, 20.3 (arom. Me, 2 Me); 18.7 (Me_3C); 10.9 (Me). MS: 875 (3, M^+), 820 (26), 786 (30), 403 (100), 396 (58), 377 (28), 328 (53), 272 (58), 160 (35), 132 (34). Anal. calc. for $C_{53}H_{67}NO_6SSi$ (874.26): C 72.81, H 7.72, N 1.60; found: C 72.53, H 7.88, N 1.56.

*Ethyl (1R,2S)-2-{4-[(*tert*-Butyl)diphenylsilyloxy]-2,2-dimethyl-1-methylidenebutyl}-5-oxocyclopentanecarboxylate* (**9**). 5.38 g (6.15 mmol) of **8** and 1.29 ml (6.15 mmol) of $Ti(OEt)_4$ dissolved in 150 ml of abs. EtOH were refluxed for 115 h. After evaporation of the solvent, the residue was dissolved in 150 ml of CH_2Cl_2, 150 ml of 1N HCl were added, and the mixture was stirred for 1 h at r.t. Afterwards, the layers were separated, and the org. layer was dried and the solvent distilled off under reduced pressure. The residue (6.38 g) was purified by CC ($CHCl_3$/pentane 3:1). R_f (**9**) 0.31. Yield: 2.64 g (85%). Recovered chiral auxiliary alcohol (R*OH, R_f(R*OH) 0.25): 2.11 g (83%). IR (NaCl, liquid film): 1760, 1730, 1660, 1635, 1590, 1110. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.00 (*s*, Me); 1.04 (*s*, Me, *t*-Bu); 1.20 (*t*, *J* = 7.2, Me); 1.33–1.60 (*m*, 1 H, CH_2CH_2C=O); 1.71 (*t*, *J* = 7.5, CH_2CH_2O); 1.97–2.64 (*m*, 3 H, CH_2C=O, CH_2CH_2C=O); 3.07–3.33 (*m*, H–C(1), H–C(2)); 3.42–3.76 (*m*, CH_2OSi); 3.89–4.20 (*m*, CH_2OC=O); 4.93 (*s*, 1 H, CH_2=C); 4.98 (*s*, 1 H, CH_2=C); 7.29–7.53 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.54–7.82 (*m*, 4 H, H–C(2), H–C(6) of Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 211.5 (C(5)); 169.0 (COO); 157.3 (C(2')); 135.5 (arom. C(2), C(6)); 133.9 (arom. C(1)); 129.5 (arom. C(4)); 127.5 (arom. C(3), C(5)); 108.9 (C(1')); 63.2 (C(1)); 61.3, 61.0 (C(5'), CH_2O); 42.5 (C(3')); 41.9 (C(2)); 38.9, 38.5 (C(4), C(4')); 31.9 (C(3)); 27.3, 27.0 (Me_2C); 26.8 (Me_3C); 19.0 (Me_3C); 14.1 (Me). MS: 378 (24), 377 (87), 347 (31), 295 (13), 225 (17), 200 (18), 199 (100), 183 (21), 181 (13), 135 (12). HR-MS: calc. for $C_{31}H_{42}O_4Si^+$: 506.2852; found: 506.2858 ± 0.005.

*(3S)-3-{4-[(*tert*-Butyl)diphenylsilyloxy]-2,2-dimethyl-1-methylidenebutyl}cyclopentanone* (**10**). A soln. of 2.48 g (4.89 mmol) of **9** in 10 ml of abs. DMSO was added dropwise at 120° to a soln. of 1.96 g (17.47 mmol) of 1,4-diazabicyclo[2.2.2]octane in 40 ml of abs. DMSO. After addition, stirring was continued for 6 h. The mixture was allowed to cool to r.t. and diluted subsequently with 150 ml of pentane and 100 ml of Et_2O. The mixture was treated with 100 ml of 1N HCl. After separation of the layers, the aq. layer was extracted with Et_2O. The combined org. layers were dried and concentrated *in vacuo*: 1.86 g (88%) of **10**. Purification for spectroscopic purposes by TLC (CH_2Cl_2). IR (NaCl, liquid film): 1745, 1635, 1590, 1110. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*s*, Me); 1.03 (*s*, Me, *t*-Bu); 1.53–1.67 (*m*, 2 H); 1.71 (*t*, *J* = 7.8, CH_2CH_2O); 1.84–2.44 (*m*, 4 H); 2.66 (*m*, 1 H); 3.56 (*dt*, *J* = 3.3, 5.9, CH_2O); 4.84 (*s*, 1 H, CH_2=C); 4.89 (*s*, 1 H, CH_2=C); 7.29–7.53 (*m*, 6 H, H–C(3), H–C(4), H–C(5) of Ph); 7.58–7.78 (*m*, 4 H, H–C(2), H–C(6) of Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 219.0 (C(1)); 158.5 (C(1')); 135.5 (arom. C(2), C(6)); 133.9 (arom. C(1)); 129.6 (arom. C(4)); 127.6 (arom. C(3), C(5)); 107.9 (CH_2=); 61.1 (C(4')); 48.0 (C(2)); 42.9 (C(2')); 39.1, 38.5 (C(5), C(3')); 37.6 (C(3)); 32.2 (C(4)); 27.5, 27.4 (Me_2C); 26.8 (Me_3C); 19.1 (Me_3C). MS: 378 (32), 377 (100), 347 (32), 295 (15), 225 (15), 200 (17), 199 (87), 183 (21), 181 (14), 135 (13). Anal. calc. for $C_{28}H_{38}O_2Si$ (434.69): C 77.37, H 8.81; found: C 77.16, H 9.00.

(3S)-3-(4-Hydroxy-2,2-dimethyl-1-methylidenebutyl)cyclopentanone (**11**). A soln. of 1.94 g (4.46 mmol) of **10** in 30 ml of abs. THF was treated under Ar with 8.9 ml (8.92 mmol) of 1M soln. of Bu_4NF in THF. After 2.5 h of stirring at r.t., the mixture was worked up by extraction with H_2O/AcOEt. The crude product was purified by CC (petroleum ether/AcOEt 1:1): 613 mg (70%) of **11**. IR (NaCl, liquid film): 3440, 1750, 1640. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.11 (*s*, Me); 1.13 (*s*, Me); 1.73 (*t*, *J* = 7.2, CH_2CH_2O); 1.77–1.93 (*m*, 2 H); 2.00–2.36 (*m*, 3 H); 2.37–2.62 (*m*, 2 H); 2.82 (*m*, 1 H); 3.57 (*t*, *J* = 7.2, CH_2O); 4.99 (*s*, 1 H, CH_2=C); 5.04 (*s*, 1 H, CH_2=C). ^{13}C-NMR (75 MHz, $CDCl_3$): 219.0 (C(1)); 159.0 (C(1')); 108.0 (CH_2=); 59.8 (C(4')); 48.1 (C(2)); 42.9 (C(2')); 39.0, 38.6 (C(5) or C(3')); 37.6 (C(3)); 32.2 (C(4)); 27.34, 27.27 (Me_2C). MS: 196 (5, M^+), 152 (88), 137 (45), 110 (100), 109 (45), 96 (66), 95 (47), 83 (56), 67 (57), 55 (62). HR-MS: calc. for $C_{12}H_{20}O_2^+$: 196.1463; found: 196.1453 ± 0.0019.

3,3-Dimethyl-4-[(1S)-3-oxocyclopentyl]pent-4-enyl Methanesulfonate (**12**). A soln. of 994 mg (5.06 mmol) of **11** and 1.1 ml (7.76 mmol) of abs. Et_3N in 45 ml of abs. CH_2Cl_2 was treated between 0° and −10° with 0.48 ml (6.19 mmol) of freshly distilled CH_3SO_2Cl. After separation of the CH_2Cl_2 layer, the latter was washed twice with aq. $CuSO_4$ and H_2O, dried, and the solvent was distilled off under reduced pressure. The resulting residue was used without further purification for the next step. Yield: 1.3 g (96%). Purification for spectroscopic purposes by TLC (petroleum ether/AcOEt 1:1). IR (NaCl, liquid film): 1745, 1640, 1360, 1175, 960. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.14 (*s*, 2 Me); 1.81–2.44 (*m*, 9 H); 2.97 (*s*, $MeSO_3$); 4.14 (*t*, *J* = 7.5, CH_2O); 5.05 (*s*, CH_2=C). MS: 274 (11, M^+), 152 (23), 151 (100), 110 (32), 109 (23), 107 (23), 95 (31), 79 (39), 67 (25), 55 (24).

(3S)-3-(4-Chloro-2,2-dimethyl-1-methylidenebutyl)cyclopentanone (**13**). 1.34 g (4.88 mmol) of **12** and 2.22 g (52.2 mmol) of LiCl (dried for 18 h over P_2O_5 at 100° at 7 Torr) were dissolved in 75 ml of abs. acetone and stirred at 60–65° for 9 d. After cooling to r.t., the precipitate was filtered off and the filtrate evaporated. The residue was extracted with Et_2O/H_2O, and the Et_2O layers were dried and concentrated *in vacuo*. The crude product (1.08 g) was purified by preparative TLC (petroleum ether/AcOEt 85:15). Yield: 599 mg (57%). IR (NaCl, liquid film): 1750, 1640, 1155, 905. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.11 (*s*, Me); 1.13 (*s*, Me); 1.72–2.32 (*m*, 6 H); 2.41–2.52 (*m*,

2 H); 2.80 (*m*, 1 H); 3.36 (*dt*, J = 3.6, 6.5, CH_2Cl); 5.04 (*s*, CH_2=C). ^{13}C-NMR (75 MHz, $CDCl_3$): 218.4 (C(1)); 157.4 (C(1′)); 109.0 (CH_2=); 48.0 (C(2)); 43.6, 41.0, 39.8, 39.0 (C(5), C(2′), C(3′), C(4′)); 37.6 (C(3)); 32.3 (C(4)); 27.0, 26.9 (Me_2C). MS: 214 (3, M^+), 152 (100), 110 (42), 109 (30), 107 (28), 95 (49), 83 (60), 79 (29), 67 (37), 55 (41).

(3aS,7aR)-5,5-Dimethyl-4-methylideneoctahydro-1H-inden-1-one ((−)-**2**) *and (3aS,7aS)-5,5-Dimethyl-4-methylideneoctahydro-1H-inden-1-one* ((+)-**14**). To a suspension of 279 mg (6.97 mmol) of KH (prepared from 799 mg of a 35% suspension in mineral oil) in 10 ml of abs. THF were added dropwise 599 mg (2.79 mmol) of **13** dissolved in 15 ml of THF at −30°. The mixture was heated up slowly to 40°, and the temp. was maintained for additional 2 h. After cooling to 0°, aq. NH_4Cl and Et_2O were added, and the org. layer was washed with brine, dried, and concentrated *in vacuo*. Yield: 430 mg crude product ((−)-**2**/(+)-**14** 1:1.8). Separation of the epimers was performed by TLC (CH_2Cl_2/AcOEt 98:2; plates pretreated with aq. 10% $AgNO_3$ soln.) yielding 64.5 mg of (−)-**2** and 223.6 mg of (+)-**14** (total yield 58%; 13% (−)-**2** and 45% (+)-**14**); R_f ((−)-**2**) 0.26; R_f ((+)-**14**) 0.48.

*Data of (−)-***2**: $[\alpha]_D = -112.37$ (c = 0.76 in EtOH). IR (NaCl, liquid film): 1750, 1635, 895. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.06 (*s*, Me_{ax}); 1.15 (*s*, Me_{eq}); 1.31 (*m*, H_{ax}–C(6)); 1.46 (*m*, H_{ax}–C(7)); 1.59 (*m*, H–C(7a)); 1.61 (*m*, H_{eq}–C(6)); 1.77 (*m*, H_{eq}–C(3)); 1.95 (*m*, H_{eq}–C(7)); 2.10 (*m*, H_{ax}–C(3)); 2.22 (*m*, H_{ax}–C(2)); 2.37 (*m*, H–C(3a)); 2.43 (*m*, H_{eq}–C(2)); 4.68 (*s*, 1 H, CH_2=C (*E*)); 4.82 (*s*, 1 H, CH_2=C (*Z*)). ^{13}C-NMR (75 MHz, $CDCl_3$): 217.7 (C(1)); 157.6 (C(4)); 102.8 (=CH_2); 57.4 (C(7a)); 43.8 (C(3a)); 41.2 (C(6)); 37.8 (C(2)); 37.1 (C(5)); 28.7 (Me_{eq}); 27.1 (Me_{ax}); 24.2 (C(3)); 21.5 (C(7)). MS: 178 (60, M^+), 163 (37), 122 (52), 121 (57), 109 (84), 107 (69), 96 (77), 93 (69), 91 (67), 79 (100). HR-MS: calc. for $C_{12}H_{18}O^+$: 178.1358; found: 178.1364 ● 0.0018.

*Data of (+)-***14**: $[\alpha]_D = +161.13$ (c = 2.6 in EtOH). IR (NaCl, liquid film): 1750, 1635, 895. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.06 (*s*, Me_{eq}); 1.07 (*s*, Me_{ax}); 1.16 (*m*, H_{eq}–C(6)); 1.30 (*m*, H_{ax}–C(6)); 1.78 (*m*, H_{eq}–C(7)); 1.90 (*m*, H–C(3)); 1.93 (*m*, H_{ax}–C(7)); 2.14–2.19 (*m*, 2 H–C(2)); 2.31 (*m*, H–C(3)); 2.38 (*m*, H–C(7a)); 3.19 (*m*, H–C(3a)); 4.80 (*d*, J = 2.0, 1 H, CH_2=C (*E*)); 4.92 (*d*, J = 2.0, 1 H, CH_2=C (*Z*)). ^{13}C-NMR (75 MHz, $CDCl_3$): 219.0 (C(1)); 153.2 (C(4)); 106.3 (=CH_2); 52.0 (C(7a)); 39.3 (C(3a)); 3.81 (C(6)); 36.0 (C(5)); 35.0 (C(2)); 29.5 (Me_{eq}); 25.9 (Me_{ax}); 24.2 (C(3)); 18.8 (C(7)). MS: 178 (73, M^+), 163 (44), 122 (62), 109 (100), 107 (75), 93 (55), 91 (70), 83 (59), 79 (90), 77 (51). HR-MS: calc. for $C_{12}H_{18}O^+$: 178.1358; found: 178.1365 ± 0.0018.

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