Pheromones 80.[1] Synthesis of (*S*)-(+)-Manicone and (*S*)-(+)-Normanicone, Mandibular Gland Constituents of Myrmicine Ants

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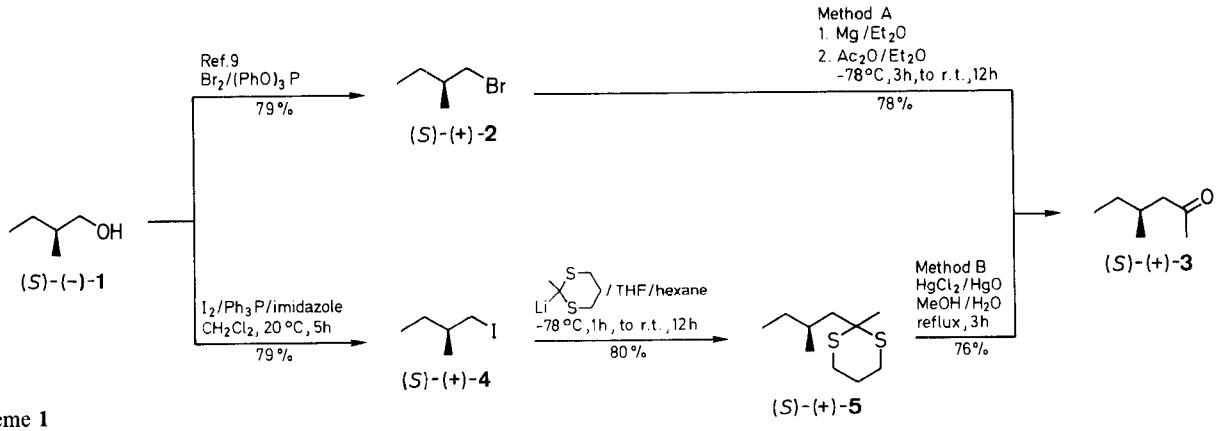
Optically active (4*E*,6*S*)-(+)-4,6-dimethyloct-4-en-3-one (**10a**), manicone, and (3*E*,5*S*)-(+)-3,5-dimethylhept-3-en-2-one (**10b**), normanicone, the biologically active stereoisomers of mandibular gland alarm pheromone components of Manica ants, were synthesized by three different routes starting from (*S*)-(−)-2-methylbutan-1-ol (**1**).

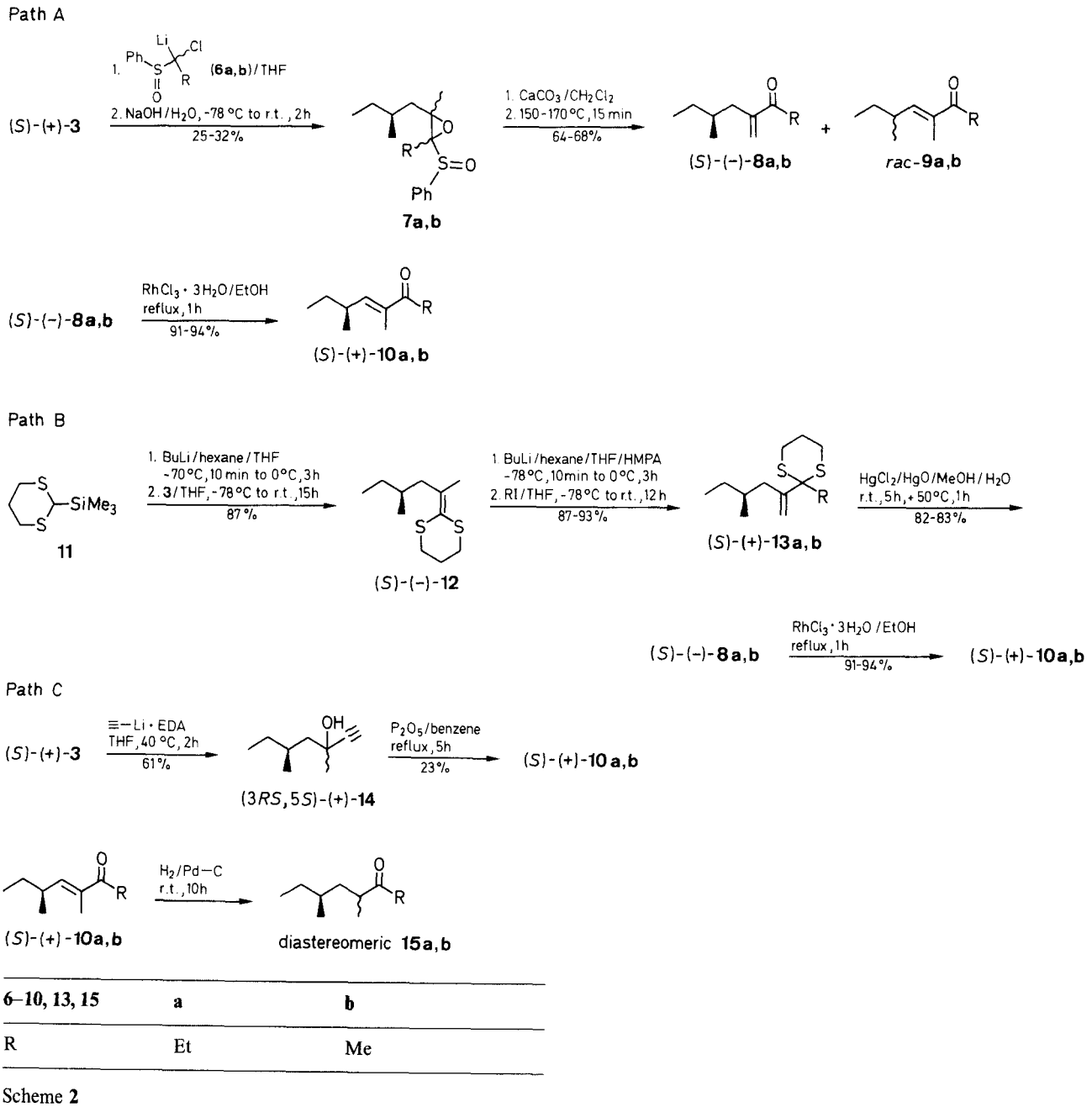
Manicone, (4*E*)-4,6-dimethyloct-4-en-3-one, was identified as the mandibular gland alarm pheromone of two North American ant species, *Manica mutica* and *Manica bradley* (Hymenoptera, Formicidae, Myrmicinae)[4] 18 years ago. Its absolute configuration was determined only recently by complexation gas chromatography as (6*S*)-(+) in *Manica rubida*, the only Eurasian Manica species.[5,6] Normanicone, (3*E*)-3,5-dimethylhept-3-en-2-one, is another major mandibular gland constituent[5,6] but revealed only weak biological activity in behavioral experiments with workers of the respective species.[7] Only one synthesis of optically active manicone has been described.[8] In the following, we report different syntheses for the optically active (*S*)-(+)-isomers of manicone and normanicone.

For all syntheses, (*S*)-(+)-4-methylhexan-2-one (**3**) was the key intermediate. It was obtained from commercially available (*S*)-(−)-2-methylbutan-1-ol (**1**) by two different routes according to Scheme **1**. Optically active **1** was originally converted into the bromo compound (*S*)-(+)-**2**[9] and its Grignard derivative subsequently reacted with acetic anhydride[10] to yield the chiral synthetic intermediate (*S*)-(+)-**3** in 61 % overall yield. Secondly, the optically active iodine compound **4**, obtained by reaction of **1** with iodine, triphenylphosphine and imidazole,[11] was converted into the (*S*)-(+)-dithiane **5** according to Seebach's method,[12] and the thioketal **5** cleaved to (*S*)-(+)-4-methylhexan-2-one **3** (Scheme **1**) with mercury(II) chloride/mercury(II) oxide/aqueous methanol.

The subsequent condensation of **3** with 1-chloroalkyl phenyl sulfoxide **6a** (R = Et) and **6b** (R = Me)[13] afforded the (*S*)-(+)-epoxides **7a** and **7b** as a mixture of diastereoisomers. By thermolysis of **7a** and **7b**, mixtures of (*S*)-(−)-enone **8a** and partially racemized manicone **9a**, and (*S*)-(−)-enone **8b** and partially racemized nor-



Scheme 1



6–10, 13, 15	a	b
R	Et	Me

Scheme 2

manicone **9b**, respectively, in a ratio of 5:3 each, were obtained. The mixtures were separated by silica gel column chromatography. Pure **8a** and **8b** thus obtained were smoothly isomerized to optically active (*S*)-(+)-manicone **10a** and (*S*)-(+)-normanicone **10b**, respectively, by refluxing with a catalytic amount of rhodium(III) chloride hydrate in ethanol[13] (Path A, Scheme 2).

Alternatively, **8a** and **8b** were also obtained by reaction of lithiated 2-trimethylsilyl-1,3-dithiane **11** with **3**, subsequent alkylation of the resulting ketene thioacetal (*S*)-(−)-**12** to (*S*)-(+)-**13**[14] and hydrolysis to **8a,b** with mercury(II) chloride/mercury(II) oxide in 63% overall yield. Finally, isomerization of **8a** and **8b** as above afforded optically active **10a** and **10b** according to Path B in Scheme 2. The optical purity of the target molecules **10a** and **10b** was determined as described below.

Following a third synthetic route to optically active normanicone, (*S*)-(+)-**10b**, lithium acetylide was reacted with **3**[15] and the propargylic alcohol **14** formed as a mixture of diastereoisomers. Dehydration–hydration reaction (Rupe rearrangement)[16,17] of **14** with phosphorus pentoxide in refluxing benzene leads to (*S*)-(+)-normanicone **10b** as the major product isolated in moderate yield by column chromatography (Path C in Scheme 2). Under similar conditions, the 1-methyl derivative of **14** gave manicone **10a** only in a trace amount, thus testifying that in the case of disubstituted triple bonds the Rupe reaction is not the main process and that the same route is, therefore, inapplicable for the synthesis of the target molecule **10a**.

Since no satisfactory separation of the enantiomers of **10a** or **10b** was achieved with the chiral GC columns available, the double bonds of **10a** and **b** were hydrogen-

Table 1. Compounds **2–5, 7, 8, 10, 12–14** Prepared

Product	Yield (%)	bp (°C)/Torr	$[\alpha]_D^{20}$ (*c*, solvent)[a]	Molecular Formula[b] or Lit. bp (°C)/Torr
(*S*)-(+)-**2**	79	66–68/230		118–120/760[18]
(*S*)-(+)-**3**	78[c]	134–135/760	+4.94 (neat)	$C_7H_{14}O$ (114.2)
	78[d]	100–101[e]/230	+4.71 (10.2, $CHCl_3$)	
(*S*)-(+)-**4**	79	50–54[e]/20	+5.80 (7, CH_2Cl_2)	$C_5H_{11}I$ (198.1)
(*S*)-(+)-**5**	81	64–65[e]/0.2	+14.39 (neat)	$C_{10}H_{20}S_2$ (204.4)
(*S*)-(+)-**7a**[f]	25		+6.29 (14, CH_2Cl_2)	$C_{16}H_{24}O_2S$ (280.4)
(*S*)-(+)-**7b**[f]	32		+5.80 (10, CH_2Cl_2)	$C_{15}H_{22}O_2S$ (266.4)
(*S*)-(−)-**8a**	64[g], 83[h]	85–87[e]/35	−0.93 (7.5, EtOH)	$C_{10}H_{18}O$ (154.3)
(*S*)-(−)-**8b**	68[g], 82[h]	78–81[e]/35	−2.00 (7.5, EtOH)	$C_9H_{16}O$ (140.2)
(*S*)-(+)-**10a**	94[g,h]	83–84[e]/20	+43.80[k] (5, Et_2O)	$C_{10}H_{18}O$ (154.3)
(*S*)-(+)-**10b**	91[g,h]	78–80[e]/20	+37.60 (5, Et_2O)	$C_9H_{16}O$ (140.2)
	23[i,j]	78–80[e]/20	+36.13 (9.55, $CHCl_3$)	
(*S*)-(−)-**12**	87	87–88[e]/0.2	−1.36 (10, $CHCl_3$)	$C_{11}H_{20}S_2$ (216.4)
(*S*)-(+)-**13a**	87	90–91[e]/0.1	+16.20 (10, $CHCl_3$)	$C_{13}H_{24}S_2$ (244.5)
(*S*)-(+)-**13b**	93	90–93[e]/0.2	+16.70 (10, $CHCl_3$)	$C_{12}H_{22}S_2$ (230.4)
(3*RS*, 5*S*)-(+)-**14**	61[l]	70–71[e]/19	+7.94 (12.6, $CHCl_3$)	$C_9H_{16}O$ (140.2)

[a] Substance **9a** has $[\alpha]_D^{20}$ +35.30 (*c* = 5, Et_2O), 83% enantiomeric purity (GC determination); substance **9b** has $[\alpha]_D^{20}$ +28.50 (*c* = 5, Et_2O), 78% enantiomeric purity (GC determination).
[b] Satisfactory microanalysis obtained: C ±0.40, H ±0.30.
[c] Method A in Scheme **1**.
[d] Method B in Scheme **1**.
[e] Kugelrohr distillation, bath temperature.
[f] Substances **7a, b** are mixtures of four diastereoisomers.
[g] Path A in Scheme **2**.
[h] Path B in Scheme **2**.
[i] Path C in Scheme **2**.
[j] TLC (hexane/Et_2O, 9 : 1), R_f 0.38.
[k] Ref. 8, $[\alpha]_D^{20}$ +45.45 (*c* = 1.0, CH_2Cl_2).
[l] TLC (hexane/Et_2O, 7 : 3), R_f 0.50.

ated using palladium on carbon as catalyst to convert the unsaturated ketones, which have one chiral centre only, to the diastereoisomeric ketones **15a** and **15b**, respectively, which were readily separated.[6] With these diastereoisomers under similar GC conditions, [Lipodex C and manganese(II)-bis(heptafluorobutyryl-1(*R*)-campherate)], the enantiomeric purity of the (6*S*)- and (5*S*)-isomers, respectively, could be determined by gas chromatography. The intensity of signals generated by stereoisomers derived from the corresponding (6*R*)- and (5*R*)-isomers of **10a** and **b**, respectively, was below 1.5%, as determined by co-chromatography of all four isomers each obtained from hydrogenation of racemic manicone and normanicone, thus giving optical purities of 97% ee.

Gas chromatographic analyses were carried out on a Hewlett-Packard 5890A and a Packard United Technologies 438A gas chromatograph equipped with a flame-ionization detector and fused-silica capillary columns SE-54, chiral Lipodex C and Mn(II)-bis(heptafluorobutyryl-1(R)-campherate) 0.25 mm × 25 m each. TLC was performed on silica gel plates Kieselgel 60 F_{254} and visualized by sat. aq $KMnO_4$. Column chromatography was carried out on a glass column with Merck silica gel (70–230 mesh). $[\alpha]_D$-Values were measured at 20°C with a Polartronic E polarimeter, mass spectra recorded on a Varian MAT CH-4B mass spectrometer with EI ionization. IR spectra were obtained using Beckman Acculab 8 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained from a Jeol JNM-GX400 FT spectrometer at 400 and 100 MHz, respectively. Elementary analyses were performed with a Heraeus CHN-Rapid. Melting and boiling points are not corrected. Yields, physical data and formulae of the compounds prepared are given in Table 1, IR, ^{1}H- and ^{13}C-NMR spectra in Table 2. (*S*)-(−)-2-Methylbutan-1-ol was purchased from Fluka (FRG), chemical purity > 99% (GC), $[\alpha]_D^{20} = -6.6 \pm 0.3°$ (*c* = 10, EtOH). 2-Methyl-1,3-dithiane, chloroalkyl phenyl sulfoxides **6a,b** and 2-trimethylsilyl-1,3-dithiane **(11)** were prepared according to known methods.[12–14]

(*S*)-(+)-2-Methyl-1-bromobutane (2):
Prepared by the procedure described in Ref. 9 from **1** (17.6 g, 200 mmol), Br_2 (32.0 g, 200 mmol) and $(PhO)_3P$ (62.0 g, 200 mmol).

(*S*)-(+)-2-Methyl-1-iodobutane (4):
I_2 (31.8 g, 125 mmol) is added at r.t. to a solution of (*S*)-(−)-2-methylbutan-1-ol (**1**; 8.8 g, 100 mmol), Ph_3P (40.6 g, 155 mmol) and imidazole[11] (10.2 g, 150 mmol) in CH_2Cl_2 (200 mL). After 5 h at 20°C, the solution is treated with MeOH (5 mL). The mixture is stirred for 1 h, filtered and concentrated on a rotavapor at r.t. The residue after distillation gives (*S*)-(+)-**4** as a colorless liquid.

(*S*)-(+)-2-(2-Methylbutyl)-2-methyl-1,3-dithiane (5):
A 1.6 M solution of BuLi in hexane (47.5 mL, 76 mmol) is added over 15 min under N_2 to a stirred solution of 2-methyl-1,3-dithiane (9.4 g, 70 mmol) at −70°C in THF (80 mL) and stirring is continued for 3 h while heating to 0°C. The yellow solution is recooled to −78°C and **4** (15.0 g, 76 mmol) in THF is added over 10 min. The resulting mixture is stirred at −78°C for 1 h and then at r.t. overnight (12 h), quenched with ice-cold H_2O (300 mL), and extracted with petroleum ether (2 × 50 mL). The petroleum ether extract is washed with H_2O (3 × 10 mL), dried ($MgSO_4$), the solvent is evaporated and the residue distilled at reduced pressure.

(*S*)-(+)-4-Methyl-2-hexanone (3):
Method A: According to procedure,[10] the Grignard reagent obtained from **2** (15.1 g, 100 mmol) and Mg (2.64 g, 110 mmol) in Et_2O (100 mL), is added dropwise to a solution of freshly distilled Ac_2O (9.18 g, 90 mmol) in Et_2O (100 mL) at −78°C under N_2 atmosphere. After the addition is complete (1 h), the mixture is stirred for additional 2 h at −78°C, afterwards at r.t. overnight. The mixture is treated at 0°C with sat. aq NH_4Cl until the precipitate dissolves, the Et_2O layer is separated, washed with a diluted solution of NaOH (2 × 20 mL) and dried (Na_2SO_4). The Et_2O is distilled off under atmospheric pressure, the residue is fractionated under reduced pressure to give (*S*)-(+)-**3**.

Method B: (*S*)-(+)-Dithiane **5** (12.2 g, 60 mmol) is added to an efficiently stirred suspension of $HgCl_2$ (35.9 g, 132 mmol) and HgO (14.3 g, 66 mmol) in 85% aq MeOH (800 mL). The mixture is stirred and heated at reflux under N_2 for 3 h, cooled and filtered. The filtrate is diluted with 10% aq NaCl (800 mL) and thoroughly extracted

Table 2. Spectral Data of Compounds **3, 5, 7, 8, 10, 12–14**

Compound	IR (neat) ν (cm^{-1})	^{1}H-NMR (400 MHz, $CDCl_3$/TMS) δ, J (Hz)	^{13}C-NMR (100 MHz, $CDCl_3$/TMS) δ
3	1714	0.86 (t, 3H, 7.4), 0.87 (d, 3H, 6.8), 1.14–1.25 (m, 1H), 1.28–1.38 (m, 1H), 1.88–1.96 (m, 1H), 2.22 (dd, 1H, J_1 = 8.2, J_2 = 15.9), 2.42 (dd, 1H, J_1 = 5.8, J_2 = 15.9), 3.13 (s, 3H)	11.32 (CH_3), 19.35 (CH_3), 29.51 (CH_2), 30.40 (CH_3), 30.89 (CH), 50.89 (CH_2), 209.23 (CO)
5	1275	0.90 (t, 3H, 7.3), 1.01 (d, 3H, 6.7), 1.20–1.28 (m, 1H), 1.40–1.47 (m, 1H), 1.62–1.78 (m, 2H), 1.67 (s, 3H), 1.91–1.99 (m, 3H), 2.80–2.91 (m, 4H)	11.42 (CH_3), 21.75 (CH_3), 25.36 (CH_2), 26.67 (CH_2) 26.67 (CH_2), 28.83 (CH_3), 31.18 (CH), 31.50 (CH_2), 48.54 (CH_2), 49.67 (C)
7a[a]	1080, 1046	0.67–2.15 (m, 19H), 7.49–7.68 (m, 5H)	10.23–11.60 (4 × 2CH_3 for four diastereoisomers), 16.91–18.20 (4 × CH_2), 18.43–20.04 (4 × 2CH_3), 28.54–30.72 (4 × CH_2), 31.22–32.36 (4 × CH), 40.60–41.06 (4 × CH_2), 66.15–66.97 (4 × C), 83.20–84.73 (4 × C), 124.18–131.13 (4 × CH_{arom}), 141.24–141.38 (4 × C_{arom})
7b[a]	1087, 1050	0.87–1.08 (m, 6H), 1.10–1.23 (m, 1H), 1.27–1.53 (m, 1H), 1.30–1.82 (eight s, 6H), 1.63–1.82 (m, 1H), 1.88–2.17 (m, 2H), 7.49–7.67 (m, 5H)	8.23–8.64 (4 × CH_3 for four diastereoisomers), 11.29–11.70 (4 × CH_3), 18.46–19.54 (4 × 2CH_3), 29.36–29.84 (4 × CH_2), 31.68–32.30 (4 × CH), 40.09–41.42 (4 × CH_2), 68.14–68.61 (4 × C), 78.54–79.40 (4 × C), 125.02–130.87 (4 × CH_{arom}), 139.89–139.92 (4 × C_{arom})
8a	1680, 1624	0.81 (d, 3H, 6.7), 0.88 (t, 3H, 7.5), 1.08–1.17 (m, 1H), 1.09 (t, 3H, 7.3), 1.30–1.40 (m, 1H), 1.44–1.52 (m, 1H), 2.01 (dd, 1H, J_1 = 8.2, J_2 = 13.4), 2.35 (dd, 1H, J_1 = 5.8, J_2 = 13.4), 2.71 (q, 2H, 7.3), 5.66 (s, 1H), 6.00 (s, 1H)	8.50 (CH_3), 11.38 (CH_3), 18.88 (CH_3), 29.46 (CH_2), 31.04 (CH_2), 33.56 (CH), 38.54 (CH_2), 124.35 (CH_2), 147.86 (C), 202.71 (CO)
8b	1674, 1621	0.81 (d, 3H, 6.7), 0.86 (t, 3H, 7.5), 1.08–1.20 (m, 1H), 1.26–1.40 (m, 1H), 1.45–1.54 (m, 1H), 2.01 (dd, 1H, J_1 = 8.2, J_2 = 13.4), 2.32 (dd, 1H, J_1 = 6.1, J_2 = 13.4), 2.33 (s, 3H), 5.72 (s, 1H), 6.03 (s, 1H)	11.20 (CH_3), 18.70 (CH_3), 25.82 (CH_3), 29.25 (CH_2), 33.38 (CH), 37.93 (CH_2), 125.62 (CH_2), 148.16 (C), 199.68 (CO)
10a	1671, 1640	0.87 (t, 3H, 7.5), 1.02 (d, 3H, 6.4), 1.10 (t, 3H, 7.3), 1.26–1.51 (m, 2H), 1.79 (d, 3H, 1.5), 2.43–2.52 (m, 1H), 2.69 (q, 2H, 7.3), 6.38 (dd, 1H, J_1 = 1.5, J_2 = 9.8)	8.91 (CH_3), 11.63 (CH_3), 11.95 (CH_3), 19.76 (CH_3), 29.43 (CH_2), 29.82 (CH_2), 35.25 (CH), 135.69 (C), 147.74 (CH), 202.81 (CO)
10b	1662, 1635	0.88 (t, 3H, 7.3), 1.03 (d, 3H, 6.4), 1.32–1.50 (m, 2H), 1.77 (d, 3H, 1.5), 2.31 (s, 3H), 2.45–2.51 (m, 1H), 6.38 (dd, 1H, J_1 = 1.5, J_2 = 9.8)	11.37 (CH_3), 11.93 (CH_3), 19.73 (CH_3), 25.49 (CH_3), 29.75 (CH_2), 35.75 (CH), 135.44 (C), 149.38 (CH), 200.20 (CO)
12	1580, 1271	0.83 (d, 3H, 6.7), 0.89 (t, 3H, 7.5), 1.09–1.20 (m, 1H), 1.29–1.38 (m, 1H), 1.53–1.59 (m, 1H), 1.88 (s, 3H), 2.08–2.14 (m, 2H), 2.24–2.33 (m, 2H), 2.81–2.88 (m, 4H)	11.58 (CH_3), 18.88 (CH_3), 20.51 (CH_3), 25.08 (CH_2), 29.42 (CH_2), 30.22 (CH_2), 30.55 (CH_2), 33.83 (CH), 43.03 (CH_2), 119.98 (C), 140.15 (C)
13a	1621, 1270	0.89 (t, 3H, 7.3), 0.91 (t, 3H, 7.3), 0.92 (d, 3H, 6.7), 1.11–1.21 (m, 1H), 1.41–1.51 (m, 1H), 1.65–1.75 (m, 1H), 1.84– 2.04 (m, 3H), 1.90 (q, 2H, 7.3), 2.15 (dd, 1H, J_1 = 5.8, J_2 = 16.2), 2.62–2.67 (m, 2H), 2.78–2.85 (m, 2H), 5.29 (d, 1H, 1.2), 5.69 (s, 1H)	8.39 (CH_3), 11.58 (CH_3), 19.25 (CH_3), 25.56 (CH_2), 27.40 (CH_2), 27.49 (CH_2), 29.61 (CH_2), 32.45 (CH_2), 33.17 (CH), 38.52 (CH_2), 60.35 (C), 116.76 (CH_2), 144.64 (C)
13b	1620, 1270	0.90 (d, 3H, 6.4), 0.91 (t, 3H, 7.5), 1.10–1.19 (m, 1H), 1.40–1.48 (m, 1H), 1.59–1.71 (m, 1H), 1.62 (s, 3H), 1.84–2.04 (m, 3H), 2.23 (dd, 1H, J_1 = 6.1, J_2 = 15.9), 2.67–2.85 (m, 4H), 5.16 (s, 1H), 5.71 (s, 1H)	11.60 (CH_3), 19.07 (CH_3), 24.91 (CH_2), 27.82 (CH_2), 27.89 (CH_2), 28.78 (CH_3), 29.49 (CH_2), 33.53 (CH), 39.04 (CH_2), 54.87 (C), 114.77 (CH_2), 147.72 (C)
14	3380 (br), 3300, 2100	0.89 (t, 3H, 7.5), 1.01 (d, 3H, 5.8), 1.03 (d, 3H, 5.5), 1.20–1.27 (m, 1H), 1.41–1.55 (m, 2H), 1.50 (s, 3H), 1.51 (s, 3H), 1.67–1.75 (m, 2H), 1.97 (s br, 1H), 2.450 (s, 1H), 2.453 (s, 1H)	11.11, 11.14 (C-7), 20.70 (5-CH_3), 30.58, 30.63, 30.66, 30.77, 30.96, 31.31, 49.41, 49.61 (C-4, C-5, C-6, 3-CH_3), 67.74, 68.06 (C-3), 71.28, 71.37 (C-1), 88.14, 88.31 (C-2)

[a] Substances **7a** and **7b** are mixtures of diastereoisomers.

with pentane (5 × 100 mL). The organic phase of the filtrate is washed with H_2O (100 mL), brine (50 mL), and dried ($MgSO_4$). The solvent is distilled off over a Vigreux column and the residue distilled at atmospheric pressure.

(*S*)-(+)-3,4-Epoxy-4,6-dimethyl-3-(phenylsulfinyl)octane (7a) and (*S*)-(+)-2,3-Epoxy-3,5-dimethyl-2-(phenylsulfinyl)heptane (7b):
Diastereoisomeric 1-chloropropyl phenyl sulfoxide (**6a**) and 1-chloroethyl phenyl sulfoxide (**6b**), respectively, (3 mmol) in THF (1 mL) are added over 1 min to a magnetically stirred solution of lithium diisopropylamide (LDA, 4.2 mmol) in THF (15 mL) under N_2 at −78 °C to give a clear pale yellow solution. A solution of (*S*)-(+)-**3** (800 mg, 7 mmol) in THF (1.5 mL) is added over 1 min to give a clear colorless solution. The cooling bath is removed, and the mixture is stirred and allowed to warm to r.t. Aq NaOH (50%, 3 mL) is added and the mixture stirred rapidly at r.t. for 1 h. The mixture is diluted with 5% aq HCl (50 mL), extracted with CH_2Cl_2 (2 × 25 mL), washed with H_2O (20 mL), dried (K_2CO_3), evaporated, and chromatographed on Kieselgel 60 (40 g, 30% EtOAc/hexane) to give **7a** (R_f 0.35) and **7b** (R_f 0.35), respectively, as colorless oils.

Thermolysis of Epoxides 7a,b to 8a,b and 9a,b:
A solution of **7a,b** (1.5 mmol) in CH_2Cl_2 (3 mL) is distilled bulb-to-bulb over $CaCO_3$ (0.5 g) at 30 Torr and oven temperature 150–170 °C. The distillate is chromatographed on Kieselgel 60 (40 g, 7.5% Et_2O/petroleum ether) to give after distillation (*S*)-(+)-**8a** (R_f 0.73), (*S*)-(+)-**8b** (R_f 0.53), and racemized **9a** (R_f 0.56) and **9b** (R_f 0.35).

(*S*)-(−)-2-(1,3-Dimethylpentylidene)-1,3-dithiane (12):
A 1.6 M solution of BuLi in hexane (24 mL, 38.4 mmol) is added over 10 min under N_2 to a stirred solution of 2-trimethylsilyl-1,3-

dithiane (**11**; 6.7 g, 35 mmol) at −70 °C in THF (75 mL). After raising the temperature to 0 °C within 3 h the resulting yellow solution is cooled again to −78 °C. A solution of **3** (4.0 g, 35 mmol) in THF (5 mL) is added over 10 min and stirring is continued for 1 h at this temperature and then at r.t. overnight. The mixture is quenched with ice-water (200 mL), extracted with pentane (2 × 100 mL), washed with H_2O (3 × 30 mL) and dried ($MgSO_4$). After evaporation of the solvent, the residue is distilled in vacuum.

(*S*)-(+)-2-(4-Methylhex-1-en-2-yl)-1,3-dithiane 13a,b:
A 1.6 M solution of BuLi in hexane (8.5 mL, 13.6 mmol) is added over 10 min under N_2 to a stirred at −78 °C solution of **12** (2.5 g, 11.6 mmol) in THF/HMPA (hexamethylphosphoric triamide) (25:10 mL) mixture. After raising the temperature to 20 °C within 3 h the resulting dark red solution is cooled again to −78 °C. EtI or MeI (15 mmol each) is added over 10 min, and stirring is continued for 1 h at this temperature and then overnight. Further workup is analogous to the isolation of **12**.

Hydrolysis of (*S*)-(+)-13a,b to (*S*)-(−)-8a,b:
(*S*)-(+)-Dithiane **13a** and **13b** (10 mmol), respectively, is added to an efficiently stirred suspension of $HgCl_2$ (6.0 g, 22 mmol) and HgO (2.4 g, 11 mmol) in 85% aq MeOH (130 mL). The mixture is stirred at r.t. for 5 h, at 50 °C for 1 h, then cooled and filtered. Further workup is analogous to isolation of **3**, Path B.

(3*RS*,5*S*)-(+)-3,5-Dimethyl-1-heptyn-3-ol (14):
To a stirred suspension[15] of lithium acetylide, ethylenediamine complex (EDA) (9.2 g, 100 mmol) in freshly distilled THF (80 mL), a solution of **3** (5.7 g, 50 mmol) in THF (20 mL) is dropped at 40 °C under N_2 atmosphere (20 min). The mixture is heated at 40 °C for additional 2 h, neutralized at 0 °C with H_2O (40 mL), sat. aq NH_4Cl (100 mL) and extracted with Et_2O (3 × 80 mL). The combined etheral extracts are dried ($NaSO_4$), Et_2O is evaporated on a rotavapor at r.t. and the residue distilled bulb-to-bulb to give **14**.

(*S*)-(+)-Manicone 10a and (*S*)-(+)-Normanicone 10b:
From Path A and B: To a solution of (*S*)-(−)-**8a** or **8b** (150 mg) in 95% EtOH (15 mL) is added $RhCl_3 \cdot 3H_2O$ (15 mg, 10 wt%) and the mixture is refluxed under a N_2 atmosphere for 1 h. The mixture is diluted with H_2O (50 mL), extracted with Et_2O (3 × 20 mL), washed with H_2O (15 mL), dried ($MgSO_4$) and distilled under reduced pressure.

From Path C: To a solution of (*S*)-(+)-**14** (1.26 g, 9 mmol) in benzene (25 mL) P_2O_5 (248 mg, 2 mmol) is added and the mixture refluxed under N_2 atmosphere for 5 h. The course of the reaction is monitored by TLC and during the heating more P_2O_5 (284 mg, 2 mmol) is added in two portions. At the end of the reaction, the benzene solution is decanted, washed with 5% aq $NaHCO_3$ (2 × 5 mL), H_2O (5 mL) and dried (Na_2SO_4). The benzene is removed on a rotavapor at r.t., and the residue was chromatographed on Kieselgel 60 (30 g) using as eluent hexane/Et_2O (15:1) to give 26% of **10b**. The product is additionally distilled *in vacuo* (Kugelrohr).

Hydrogenation of 9, 10:
Compounds **10a,b** as well as **9a,b** (5 mg each) are hydrogenized at atmospheric pressure in the presence of 10% Pd-C (1 mg) in Et_2O (1 mL) for 10 h, filtered and analysed gas chromatographically[6] on a chiral Lipodex C and a Mn(II)-bis(heptafluorobutyryl-1(*R*)-campherate) column.

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(1) Pheromones, 79: Bestmann, H.J.; Erler, J.; Garbe, W.; Kern, F.; Martischonok, V.; Vostrowsky, O.; Wasserthal, L. *Experientia*, in press.
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(4) Fales, H.M.; Blum, M.S.; Crewe, R.M.; Brand, J.M. *J. Insect Physiol.* **1972**, *18*, 1077.
(5) Bestmann, H.J.; Attygalle, A.B.; Glasbrenner, J.; Riemer, R.; Vostrowsky, O. *Angew. Chem.* **1987**, *99*, 784; *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 784.
(6) Bestmann, H.J.; Attygalle, A.B.; Glasbrenner, J.; Riemer, R.; Vostrowsky, O.; Constantino, M.G.; Melikyan, G.; Morgan, E.D. *Liebigs Ann. Chem.* **1988**, 55.
(7) Cammaerts, M.C.; Attygalle, A.B.; Vostrowsky, O.; Bestmann, H.J. *J. Insect. Physiol.* **1988**, *34*, 347.
(8) Banno, K.; Mukaiyama, T. *Chem. Lett.* **1976**, 279.
(9) Coe, D.G.; Landauer, S.R.; Rydon, H.N. *J. Chem. Soc.* **1954**, 2281.
(10) Newman, M.S.; Smith, A.S. *J. Org. Chem.* **1948**, *13*, 592.
(11) Giese, B.; Pupaner, R. *Synthesis* **1988**, 219.
(12) Seebach, D.; Steinmüller, D. *Angew. Chem.* **1968**, *80*, 617; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 619.
(13) Taber, D.F.; Gunn, B.P. *J. Org. Chem.* **1979**, *44*, 450.
(14) Seebach, D.; Kolb, M.; Gröbel, B.-T. *Tetrahedron Lett.* **1974**, 3171.
(15) Smith, W.N.; Kuehn, E.D. *J. Org. Chem.* **1973**, *38*, 3588.
(16) Saunders, J.H. *Organic Synthesis Coll. Vol. III*, 22.
(17) Swaminathan, S.; Narayanan, K.Y. *Chem. Rev.* **1971**, *71* 429.
(18) Crombie, L.; Harper, S.H. *J. Chem. Soc.* **1950**, *3*, 2685.