141. Preparation of Optically Active Flowery and Woody-Like Odorant Ketones *via Corey-Chaykovsky* Oxiranylation: Irones and Analogues[1])

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α-, β-, and γ-Irones and analogues have been prepared from optically active ketones (+)-**1**, (+)-**6a,b**, and (+)-**17**, *via* a *Corey-Chaykovsky* oxiranylation (Me_2S, Me_2SO_4, Me_2SO, NaOH) followed by isomerisation ($SnCl_4$ or $MgBr_2$). (+)-Dihydrocyclocitral (**19a**), obtained from (−)-citronellal, and analogue (+)-**19b**, were condensed with various ketones to afford (+)-**21a–f**, and after hydrogenation (+)-**22a–f**. A mild oxidative degradation of aldehydes (+)-*trans*- and (−)-*cis*-**8a,b** to ketones (−)-**16a,b**, as well as olfactive evaluations, ^{13}C-NMR assignments, and absolute configurations of the intermediate epoxides, aldehydes, and alcohols are presented.

Introduction. – Irones are responsible for the powerful and pleasant violet-like scent of the precious *Iris* essential oil. First isolated from *Iris* rhizomes in 1893 [1], their correct molecular formula was established only forty years later [2] and their constitutional structure recognised in 1947 by *Ruzicka et al.* [3] and *Naves et al.* [4], after an extended and controversial study[2]). The complete relative configurational features were reviewed in 1963 [6] but, it was not until 1971 that *Rautenstrauch* and *Ohloff* published the absolute configuration [7]. Irones, also found in oak moss [8], are naturally occurring in both antipodal series, depending on the geographical origin of the *Iris* plant [9]. This was recently systematically confirmed by using chiral GC analysis [10]. Enzymes are believed to be responsible for the cyclisation of a common precursor [9b] [11]. For a long time, optically active irones have been derived exclusively from natural sources [12], and only a few examples of synthesis based on optical resolution [13a] or using starting material from the chiral pool [13b–e] have been reported[3]).

After recent publications describing the synthesis of optically active cyclohexenones [15] derived from campholenal analogues [16], we now present the preparation of various irones and irone analogues [17], which possess particularly intense and precious odorant properties.

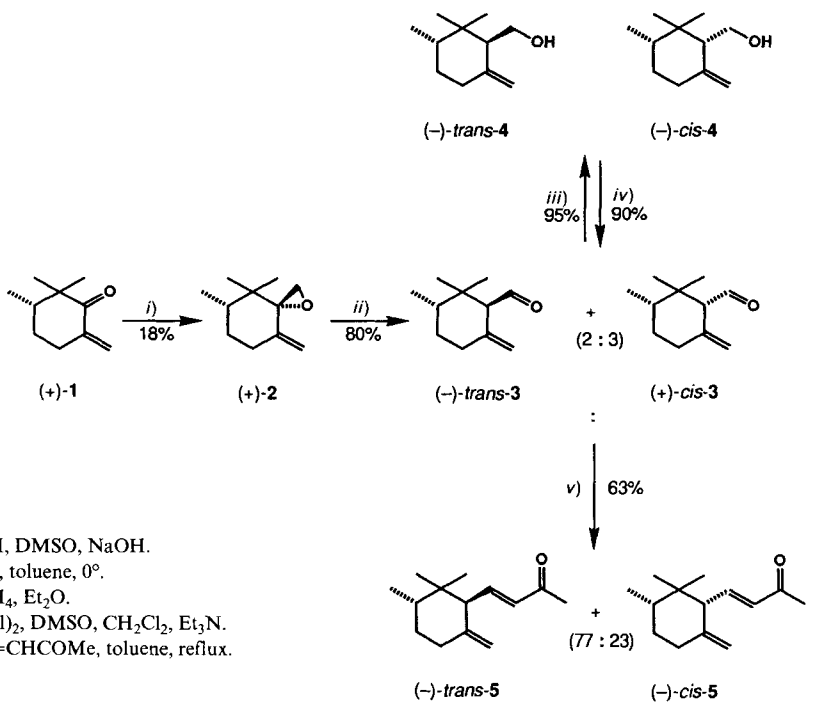
Results and Discussion. – *trans*- or *cis*-γ-Aldehydes **3** [18] are direct precursors for *trans*- [19] or *cis*-γ-irones [20]. With enone (+)-**1** (76% ee [15b]) in hand, a *Corey-Chaykovsky* oxiranylation [21] followed by isomerisation seemed to be a promising approach. Unfortunately, competitive dimerisation of (+)-**1** is a serious side reaction, and epoxide (+)-**2** was isolated as a single diastereoisomer in only 18% yield (*Scheme 1*). Of

[1]) Presented at the 'XVth International Conference on Organometallic Chemistry', 9–14 August 1992, Warsaw.

[2]) For two points of view of this controversy, see [5].

[3]) For a recent synthesis of racemic irones and references or earlier work, see [14].

Scheme 1



i) Me_3SI, DMSO, NaOH.
ii) $SnCl_4$, toluene, 0°.
iii) $LiAlH_4$, Et_2O.
iv) $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N.
v) $Ph_3P{=}CHCOMe$, toluene, reflux.

several *Lewis* acids (*e.g.* $TiCl_4$, $BF_3 \cdot OEt_2$, $ZnBr_2$, $EtAlCl_2$), $SnCl_4$ (0.02 mol-equiv., toluene, 0° [17]) then gave the best yield (80%) of a 2:3 (–)-*trans*/(+)-*cis*-**3** mixture[4]), without isomerisation to the *β*-isomer (–)-**11a** (*cf. Scheme 3*). Attempted separation of this mixture by distillation, chromatography or preparative GC failed, due to ready isomerisation to aldehyde (–)-**11a** and autoxidation. Only by reduction ($LiAlH_4$, Et_2O, 95%), separation of the corresponding alcohols (–)-*trans*-**4** and (–)-*cis*-**4** (for racemic material, see [24]) by preparative GC, and reoxidation (*Swern*'s method [25]: $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N, 90%) were we able to prepare pure (–)-*trans*-**3** and (+)-*cis*-**3**. The known *Wittig* condensation ($Ph_3P{=}CHCOMe$, toluene, 110°, 63% [26]) of the 2:3 (–)-*trans*/(+)-*cis*-**3** mixture gave a 77:23 mixture of *γ*-irones (–)-*trans*-**5**[5])/(–)-*cis*-**5**[6]), separable by preparative GC.

Fortunately, the more stable cyclohexenones (+)-**6a,b** (86% ee and 90% ee, respectively [15b]) gave, under modified *Corey-Chaykovsky* conditions (Me_2S, Me_2SO_4, Me_2SO,

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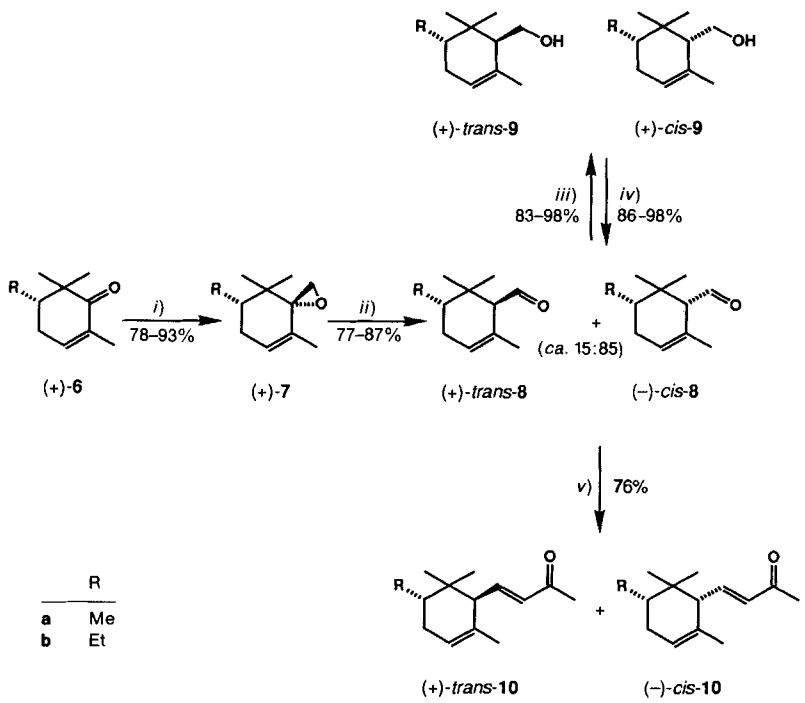
[4]) Aldehydes (+)-*cis*-**3** and (–)-*cis*-**8a,b** were first kinetically obtained *via* a stereospecific, in plane 1,2-H shift [22] from epoxide (+)-**2** and (+)-**7a,b**, respectively. Under the $SnCl_4$-catalyzed conditions, partial epimerisation to the more stable aldehydes (–)-*trans*-**3** and (+)-*trans*-**8a,b** occurred. For a similar example, see [23].

[5]) $[\alpha]_D^{20} = -53.4$ ($c = 2.34$, $CHCl_3$, 76% ee, typically irone, green scent). [13b]: $[\alpha]_D^{20} = -43.3$ ($c = 0.8$, CH_2Cl_2, 70% ee). (+)-*trans*-**5** has an irone, rooty odor, $[\alpha]_D^{20} = +57.0$ ($c = 0.33$, CH_2Cl_2, 80% ee [13d]).

[6]) $[\alpha]_D^{20} = -5.4$ ($c = 1.66$, $CHCl_3$, 76% ee, irone, violet). [27]: $[\alpha]_D^{20} = -5.3$ ($c = 0.7$, CH_2Cl_2). (+)-*cis*-**5** $[\alpha]_D^{20} = +2.0$ ($c = 0.443$, CH_2Cl_2 [7], orris, rooty).

Scheme 2



i) Me_2S, Me_2SO_4, DMSO, NaOH. *ii*) $SnCl_4$, toluene, 0°. *iii*) $LiAlH_4$, Et_2O. *iv*) $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N. *v*) acetone, EtONa, EtOH.

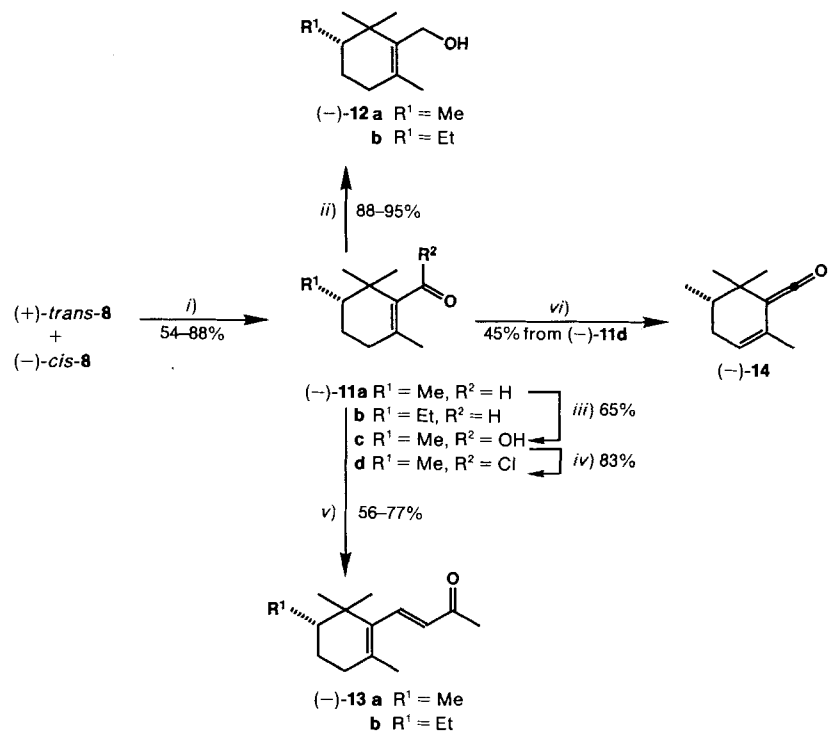
NaOH[7])), the stereochemically pure epoxides (+)-**7a** (93%) and (+)-**7b** (78%), respectively (*Scheme 2*). Subsequent catalytic $SnCl_4$ isomerisation gave 14:86 (+)-*trans*/(−)-*cis*-**8a** (77%; for racemic material, *cf.* [29]) and 16:84 (+)-*trans*/(−)-*cis*-**8b** (87%) mixtures[4]), respectively, without any trace of (−)-**11a,b** (*cf. Scheme 3*).

Once again, as for **3**, stereochemically pure samples of (+)-*trans*-**8a,b** and (−)-*cis*-**8a,b** were obtained by reduction ($LiAlH_4$, Et_2O, 83–98%) to the corresponding (+)-*trans*/(+)-*cis*-**9a**[8]), **9b** mixtures (for racemic material, see [30]), followed by preparative GC separation and *Swern* oxidation (86–98%). The (+)-*trans*/(−)-*cis*-**8a**[8]) mixture was condensed with acetone (EtONa (1 mol-equiv.), EtOH, 76%) to give a 38:7:55 equilibrated

[7]) Our initial conditions (Me_2S, Me_2SO_4, Me_2SO, NaH 1.3 mol-equiv.) gave 75–90% yield. We then successfully applied the industrial conditions developed by Dr. *C. Margot* [17] using an excess of NaOH (7 mol-equiv., 78–93%), since, unexpectedly, these conditions were found to be far superior to those previously reported (NaOH, 1.5 mol-equiv. [28]) when applied to such sterically hindered ketones.

[8]) *cis*-**8a** and **11a** of undetermined absolute configuration were found in *Iris* essential oil [27] [31]. Although unpublished [32], the absolute configurations of (+)-*trans*-**8a** ($\alpha_D^{20} = +35.8$), (+)-*trans*-**9a** ($\alpha_D^{20} = +4.5$), (−)-**11a** ($\alpha_D^{20} = -2.6$), and (−)-**12a** ($\alpha_D^{20} = -5.4$), based on substantially racemised material, were already determined in 1982.

Scheme 3



i) EtONa, EtOH, reflux. *ii*) $LiAlH_4$, Et_2O. *iii*) O_2, Et_2O. *iv*) $(COCl)_2$, toluene. *v*) Acetone, EtONa, EtOH. *vi*) Et_3N, toluene, 140°.

mixture of irones (+)-*trans*-**10a**[9])/(−)-*cis*-**10a**[10])/(−)-**13a** (*Scheme 3*) separable by preparative GC.

The same (+)-*trans*/(−)-*cis*-**8a,b** mixtures were readily isomerised to the β-isomers (−)-**11a**[8]) (88%; for racemic material, *cf.* [33]) and (−)-**11b** (54%) in the presence of a trace of base (EtONa, 0.1 mol-equiv., EtOH), prior to reduction ($LiAlH_4$, Et_2O, 88–95%) to allylic alcohols (−)-**12a**[8]),**b**.

When the isomerisation was performed in the presence of acetone, (−)-β-irone ((−)-**13a**[11]), 77%) and its analogue (−)-**13b** (56%) could be isolated by distillation from the crude 8:2:90 (+)-*trans*-**10a**/(−)-*cis*-**10a**/(−)-**13a** and 13:4:83 (+)-*trans*-**10b**/(−)-*cis*-**10b**/

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[9]) $[\alpha]_D^{20} = +432.8$ ($c = 2.85$, CH_2Cl_2, 86% ee). [13c]: $[\alpha]_D^{20} = +306.0$ ($c = 0.98$, CCl_4, 73% ee); [13b]: $[\alpha]_D^{20} = +297.0$ ($c = 1.1$, $CHCl_3$). (−)-*trans*-**10a**: [13d]: $[\alpha]_D^{20} = -318.0$ ($c = 0.33$, CH_2Cl_2, 80% ee); [7]: $[\alpha]_{578}^{20} = -385$ ($c = 0.976$, CH_2Cl_2). Our optical purities are based on ^{1}H-NMR analysis of the starting materials [15] in presence of Eu(hfbc)$_3$. The ee reported in the literature were mainly calculated by comparison with the previously reported highest α_D values for irones.

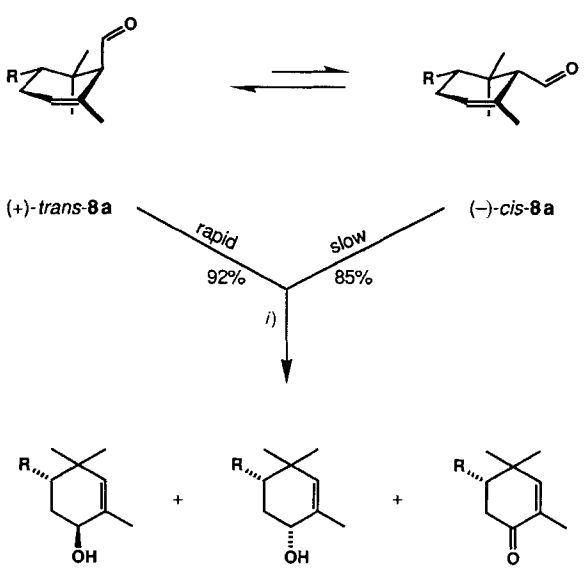
[10]) $[\alpha]_D^{20} = -103.7$ ($c = 0.65$, $CHCl_3$, 86% ee); [13a]: $[\alpha]_D^{20} = -119.2$ ($c = 0.25$, CH_2Cl_2); [9b]: $[\alpha]_{578}^{20} = -115.0$ ($c = 0.65$, CH_2Cl_2); [27]: $[\alpha]_D^{20} = -96.0$ ($c = 1.0$, $CHCl_3$). (+)-*cis*-**10a**: [13a]: $[\alpha]_D^{20} = +111.4$ ($c = 1.21$, CH_2Cl_2); [7]: $[\alpha]_D^{20} = +109.0$ ($c = 0.92$, CH_2Cl_2); [13c]: $[\alpha]_D^{20} = +55.0$ ($c = 0.879$, CH_2Cl_2).

[11]) $[\alpha]_D^{20} = -65.0$ ($c = 1.8$, CH_2Cl_2, 86% ee), (+)-**13a**: [7]: $[\alpha]_D^{20} = +33.0$ ($c = 1.097$, CH_2Cl_2).

(−)-**13b** aldol mixtures. In contrast to (−)-**13a**, (−)-**13b** has merely an ionone rather than an irone-like scent. We took advantage of the rapid autoxidation of (−)-**11a** to transform acid (−)-**11c** (O_2, 65%) thus obtained, into its acid chloride (−)-**11d** ($(COCl)_2$, toluene, 83% [34]). This precursor of labile ketene (−)-**14** (Et_3N, toluene, 140°, 45% [35]), is a potential chiron for the preparation of naturally occurring α-iris-furans [27] according to a recently proposed synthesis [36].

In the course of our reduction, separation and re-oxidation procedures on alcohols (+)-*trans*-**9a,b** and (+)-*cis*-**9a,b**, we had initially used pyridinium chlorochromate as oxidant [37]. Although the oxidation itself proceeded efficiently, we observed during a simple extractive workup of residual pyridine (5% aqueous solution $CuSO_4 \cdot 5\ H_2O$) a rapid and pratically complete decomposition of aldehyde (+)-*trans*-**8a**. Similarly, (−)-*cis*-**8a** partially decomposed during extraction. The decomposition products were identified as (−)-*trans*-**15a**, (−)-*cis*-**15a** [15b], and (−)-**16a** [15b]. The transformation of (−)-*cis*-**8a** could be completed by bubbling O_2 into an ethereal solution in the presence of pyridine and aqueous $CuSO_4 \cdot 5\ H_2O$, to give a 28:4:68 mixture of (−)-*trans*-**15a**/(−)-*cis*-**15a**/(−)-**16a** in 85% yield (*Scheme 4*).

Scheme 4



	R	*trans*-**15**		*cis*-**15**		(−)-**16**
a	Me	28	:	4	:	68
b	Et	28	:	12	:	60

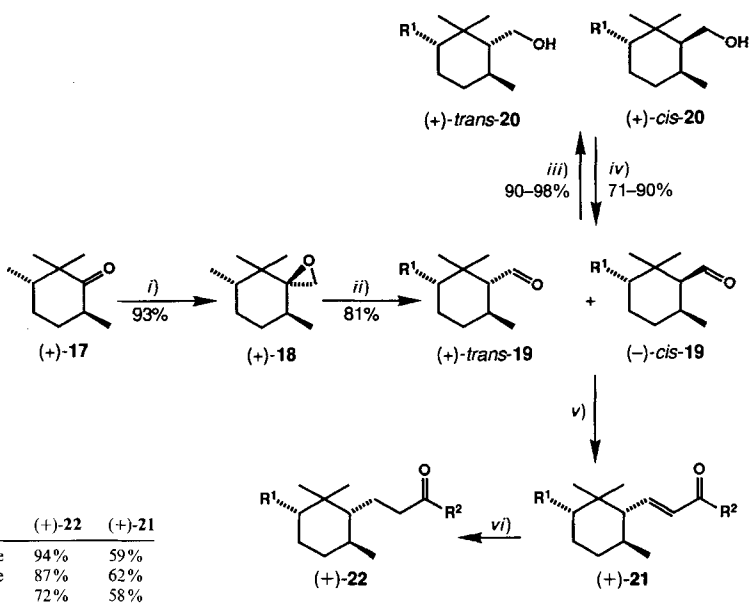
i) $CuSO_4 \cdot 5H_2O$, Py, O_2, H_2O, Et_2O.

The same mixture (92% yield) was obtained from (+)-*trans*-**8a** under the same conditions. The reaction does not proceed under careful exclusion of O_2 or pyridine, but works perfectly in the dark and slowly in the presence of a catalytic amount (0.1 mol-equiv.) of $CuSO_4 \cdot 5\ H_2O$ and an excess of pyridine or NaCN (2.0 mol-equiv.). Based

on the similarity of the product ratios from both (+)-*trans*-**8a** or (−)-*cis*-**8a**, we postulate that the more stable (+)-*trans*-**8a** (12.7 Kcal/mol [38]) is the common reactive intermediate, under the assumption that continuous epimerisation of the less stable diastereoisomer (−)-*cis*-**8a** (13.4 Kcal/mol [38]) is taking place under the reaction conditions. Such an oxidative degradation has precedent under more drastic conditions (CrO_3) on drimenol [39], or *via* hydroperoxides in the presence of a basic solution of Cu^{2+} for the autoxidation of linear alcohols [40][12]). These new, surprisingly mild conditions, may be considered to be 'biomimetic' and may well explain the absence of *trans*-**8a** in *Iris* essential oils [27].

Two of the four possible diastereoisomers of endocyclic dihydroirone have already been described in the literature[13]). The 1,3-*cis*;1,6-*trans* diastereoisomer **21b** has never been fully assigned and characterised [42]. By successive epimerisation of cyclohexanone **17** and aldehyde **19**, our methodology allows control of the three equatorial substituents of **21b** with greater than 94% stereoselectivity (*Scheme 5*).

Scheme 5



	R^1	R^2	(+)-**22**	(+)-**21**
a	H	Me	94%	59%
b	Me	Me	87%	62%
c	H	Et	72%	58%
d	Me	Et	98%	70%
e	H	Pr	70%	51%
f	Me	Pr	96%	50%

i) Me_2S, Me_2SO_4, DMSO, NaOH. *ii*) $MgBr_2$, toluene reflux. *iii*) $LiAlH_4$, Et_2O. *iv*) $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N. *v*) R_2COMe, EtONa, EtOH reflux. *vi*) H_2, 5% Pd/C, AcOEt.

[12]) For an alternative *Baeyer-Villiger* oxidation and formate rearrangement process, see [41], although no traces of formates were detected in our case. Under the same conditions (see *Exper. Part*) a 16:84 mixture of (+)-*trans*-**8b**/(−)-*cis*-**8b** gave a 28:12:60 mixture of *trans*-**15b**/*cis*-**15b**/(−)-**16b** in 91% yield. Similarly, *rac*-2,6,6-trimethylcyclohex-2-ene-1-carbaldehyde gave a 32:68 mixture of 2,4,4-trimethylcyclohex-2-en-1-ol/2,4,4-trimethylcyclohex-2-en-1-one in 95% yield. The 2:3 (−)-*trans*-**3**/(+)-*cis*-**3** mixture was mostly isomerised to (−)-**11a,c** under those conditions.

[13]) Namely *rac*-1,3-*cis*;1,6-*cis*-**21b** [42] and *rac*-1,3-*trans*;1,6-*trans*-**21b** (nicely irone, myrrh, elegant [17]).

Accordingly, under *Corey-Chaykovsky* conditions (Me_2S, Me_2SO_4, Me_2SO, NaOH, 93%), the optically pure *trans*-ketone (+)-**17** (98% ee [15a]) reacts faster than its *cis*-diastereoisomer, and by continuous epimerisation, epoxide (+)-**18** was obtained as a 3:32:65 (3*R*,5*S*,8*R*)-**18**/(3*R*,5*S*,8*S*)-**18**/(3*S*,5*S*,8*S*)-**18**[14]) mixture. Isomerisation of (+)-**18** ($MgBr_2$, toluene, 110°, 81% [17a] [44]) gave a 53:47 (+)-*trans*/(−)-*cis*-**19b** mixture whose reduction ($LiAlH_4$, Et_2O, 90%) afforded the corresponding (+)-*trans*/(+)*cis*-**20b** primary alcohols, separated by preparative GC and individually re-oxidised ($(COCl)_2$, DMSO, CH_2Cl_2, Et_3N, 71–90%) to the pure aldehydes. This mixture can also be epimerised (EtONa, 0.1 mol-equiv., EtOH, reflux) to a 90:10 (+)-*trans*/(−)-*cis*-**19b** mixture and condensed with diverse ketones, with *in situ* epimerisation favouring (+)-*trans*-**19b**, to afford (+)-**21b**[15]) (acetone, 62%), (+)-**21d** (ethyl methyl ketone, 70%) and (+)-**21f** [45] (methyl propyl ketone, 50%). Hydrogenation (H_2, 5% Pd/C, AcOEt) furnished (+)-**22b** (87%), exhibiting inverse optical properties compared with a previously reported value[16]), (+)-**22d** (98%), and (+)-**22f** (96%; for racemic material, see [47]), an important precursor [48] for the preparation of *(+)-Limbanol*®[17]) [45], an extremely powerful woody fragrance.

Table 1. *Olfactive Properties of Compounds* **21a–f** *and* **22a–f**

Compound	α_D^{20}	Olfactive properties of (−)-compound	Olfactive properties of (+)-compound	Olfactive properties of *rac*-compound
21a	−31.6	woody, ionone, leather, camphor, weak	aromatic, carvone, woody, humus, powdery, ionone, myrrh, violet, strong	woody, ionone
21b	−32.5	woody, powdery, incence	nicely orris, irone, balsamic, myrrh	orris, powdery, violet, myrrh
21c	−25.6	saffron, woody, floral	oily	floral, fruity, methyl ionone
21d	−29.2	woody	woody, orris, powdery, myrrh, balsamic	mouldy, humus, earthy
21e	−24.1	woody, dry	liquor, quince, violet, woody, powdery	woody, vague
21f	−23.0			orris, violet, ionone, tobacco
22a	−10.7	woody, cedar, powdery	woody, powdery, amber, ionone	woody
22b	−6.7	unpleasant	woody, powdery, ambergris	woody, amber, myrrh, pleasant
22c	−9.3	amber, woody, saffron	woody, irone, weak	woody
22d	−4.9	woody	woody, weak, irone	woody, weak, vague
22e	−8.8	ionone, woody	myroxyde, lavender, woody, ionone	vaguely woody, camphor
22f	−8.6			pepper, tobacco, weak

[14]) This mixture is only partially separable by GC but can be readily analysed by ^{1}H-NMR: (3*R*,5*S*,8*R*)-**18**: 2.45 (*d*, *J* = 5, 1 H); 2.51 (*d*, *J* = 5, 1 H); (3*R*,5*S*,8*S*)-**18**: 2.59 (*d*, *J* = 5, 1 H); 2.66 (*d*, *J* = 5, 1 H); (3*S*,5*S*,8*S*)-**18**: 2.61 (*d*, *J* = 4, 1 H); 2.70 (*d*, *J* = 4, 1 H); (3*S*,5*S*,8*R*)-**18**: 2.64 (*d*, *J* = 4, 1 H); 2.74 (*d*, *J* = 4, 1 H). The reverse diastereoselectivity was observed after peracetic acid epoxidation (93%) of the (+)-**17** methylenic *Wittig* product (Ph_3P^+–CH_3Br^-, *t*-BuOK, toluene, 110°, 78%) [43].

[15]) *rac*-**21b** is a powerful captive odorant produced by *Firmenich SA*.

[16]) (1*S*,3*R*,6*R*)-**22b**: $[\alpha]_D^{20} = -3.8$ (*c* = 2.23, EtOH). [46]: $[\alpha]_D^{20} = +0.94$ (*c* = 2.24, EtOH; contaminated by 4% of (+)-*cis*-dihydro-γ-irone).

[17]) *Limbanol*® is a registered trade name of *Firmenich SA* for (1′*RS*,3′*SR*,6′*SR*)-1-(2′,2′,3′,6′-tetramethyl-1′-cyclohexyl)hexan-3-ol.

Dihydrocyclocitral, a 3-demethyl analogue, was obtained as a 90:10 (+)-*trans*/(−)-*cis*-**19a**[18]) (78% [50]) mixture from optically pure (−)-citronellal, using the same methodology as developed for the racemate [51]. The alcohols (+)-*trans*/(+)*cis*-**20a** [52], obtained by reduction ($LiAlH_4$, Et_2O, 98%), were separated by preparative GC and re-oxidised ($(COCl)_2$, DMSO, CH_2Cl_2, Et_3N, 90%) to (+)-*trans*-**19a**[18]). Condensation with diverse ketones gave enones (+)-**21a**[19]) [54] (for racemic material, see [55]) (acetone, 59%), (+)-**21c** (ethyl methyl ketone, 58%), and (+)-**21e** [47] (methyl propyl ketone, 51%). Subsequent hydrogenation (H_2, 5% Pd/C, AcOEt) gave the ketones (+)-**22a**[20]) (94%), (+)-**22c** (72%), and (+)-**22e** (70%), a strategic precursor of *(+)-Norlimbanol*®[21]) [45] [47] [50b]. Generally, the ketones (+)-**21** and (+)-**22** were olfactively superior to their antipodes, due to their organoleptic properties and strength.

The synthesis of damascone-like analogues, as well as the application of this *Corey-Chaykovsky* methodology towards the preparation of an optically active taxane skeleton [16] will be presented in due course.

We are indebted to Dr. *K.H. Schulte-Elte* for stimulating discussions, Drs. *P.-A. Blanc* and *D. Kastner* for olfactive evaluations, Mrs. *B. Baer*, Miss *C. Cantatore*, and Mr. *M. Barthe* for their experimental skill, as well as *Takasago Perf. Int. Co.* for a generous gift of (−)- and (+)-citronellal.

Experimental Part

General. See [16]. t_R for GC in min. FT-IR: *Hewlett-Packard 5965 B* coupled with a *Hewlett-Packard 5890* GLC instrument.

Starting Materials. [15]: (+)-**1**: $[\alpha]_D^{20} = +6.7$ ($c = 5.01$, $CHCl_3$, 76% ee); (−)-**1**: $[\alpha]_D^{20} = -10.9$ ($c = 1.4$, CCl_4, 88% ee); (+)-**6a**: $[\alpha]_D^{20} = +79.5$ ($c = 2.2$, $CHCl_3$, 86% ee); (+)-**6b**: $[\alpha]_D^{20} = +89.4$ ($c = 1.9$, $CHCl_3$, 90% ee); (+)-**17**: $[\alpha]_D^{20} = +52.2$ ($c = 1.78$, $CHCl_3$, 86% ee); $\alpha_D^{20} = +50.5$ (98% ee); (−)-**17**: $[\alpha]_D^{20} = -54.7$ ($c = 3.1$, $CHCl_3$, 88% ee); $\alpha_D^{20} = -50.7$ (99% ee); (−)-citronellal: $\alpha_D^{20} = -13.6$ (98% ee, *Takasago*); (+)-citronellal: $\alpha_D^{20} = +13.7$ (99% ee, *Takasago*).

General Procedure A for the Corey-Chaykovsky *Oxiranylation.* In a three-necked vessel equipped with a dry-ice condenser, under Ar, a soln. of Me_2SO_4 (340 g, 2.7 mol) and Me_2S (185 g, 3.0 mol) in DMSO (1.3 l) was stirred mechanically and the temp. maintained at 50°. When the exothermic reaction was exhausted, the cooling bath was removed and the soln. stirred, until it reached 20°. NaOH in small beads (660 g, 16.5 mol, 1–2-mm diam.) was added, followed by the appropriate ketone (2.3 mol) at 20°. The mixture was stirred at r.t. for 6–40 h and monitored by GC. After disappearance of the starting material, the mixture was diluted with petroleum ether (1 l) and poured at 0° into H_2O (3 l). Extraction of the H_2O phase was carried out with petroleum ether (2 × 500 ml) and AcOEt (2 × 500 ml). The combined org. layers were washed with brine (3 × 500 ml), H_2O (500 ml), dried (Na_2SO_4), filtered, and evaporated. The crude material was distilled to give the desired epoxide as a colourless oil.

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[18]) For a non-granted Japanese patent, due to our priority [45], see [49]. Japanese authors found inverse optical properties for (1*R*,6*S*)-**19a** $[\alpha]_D^{25} = -0.56$ and for (1*S*,6*R*)-**19a** $[\alpha]_D^{25} = +0.54$ in comparison with our observations: $\alpha_D^{20} = +1.2$ (minty, pine) and $\alpha_D^{20} = -0.78$ (sulfury, cassis, minty camphoraceous), respectively. (1*S*,6*R*)-**19a** exhibits $\alpha_D^{20} = -6.4$, when exempt of traces of (1*R*,6*R*)-**19a**.

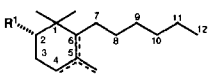
[19]) Compound **21a** of unknown absolute configuration was found in volatile leaf oils of *Juniperus jaliscana* [53].

[20]) For the optically active *cis*-diastereoisomer, see [52]. Perhydroionone of unknown absolute configuration was found in *Boronia megastigma* [56], a southern *Tasmania* flower, and *Satureja hortensis linnaeus* [57], a plant of Italian Piémont origin.

[21]) *Norlimbanol*® is a registered trade name for (1′*RS*,6′*SR*)-1-(2′,2′,6′-trimethyl-1′-cyclohexyl)hexan-3-ol, a strong woody, captive fragrance produced by *Firmenich SA*.

Table 2. *^{13}C-NMR Data of Compounds* **3**, **8a**,**b**, *(−)-*__11a–d__, *and* **19a**, **b**

Compound	R^1		C(1)[a]	C(2)	C(3)	C(4)	C(5)	C(6)	Me_{trans}–C(1)[b]	Me_{cis}–C(1)[b]	Me–C(5)	C(7)
(+)-*cis*-**3**[c]		14.9	38.0	41.7	31.5	36.1	145.2	65.3	27.2	15.3	109.5	205.2
(−)-*trans*-**3**[c]		15.5	37.7	37.1	31.3	32.7	143.1	69.3	26.5	21.0	113.3	202.5
(−)-*cis*-**8a**[c]		14.7	35.6	37.6	31.7	125.0	128.4	64.2	27.1	16.1	22.0	205.1
(+)-*trans*-**8a**[c]		14.9	34.6	33.5	32.3	126.0	127.4	66.2	25.7	20.7	22.4	202.5
(−)-*cis*-**8b**[d]	12.7	21.6	35.9	44.8	27.8	125.0	128.1	64.4	27.4	17.6	22.1	206.0
(+)-*trans*-**8b**	12.3	22.0	34.9	40.7	28.9	126.0	127.2	66.7	25.9	21.6	22.3	202.4
(−)-**11a**		15.6	36.1	39.9	26.3	34.7	155.2	140.9	26.3	20.9	19.4	192.8
(−)-**11b**[d]	12.9	21.7[e]	36.5	47.8	22.1[e]	35.1	155.4	141.1	26.0	21.0	19.4	192.9
(−)-**11c**[c]		15.8	36.0	38.3	26.5	30.7	135.1	134.8	27.0	21.8	21.5	176.2
(−)-**11d**		15.6	36.9	38.2	26.2	30.2	141.4	134.1	27.2	21.9	21.3	170.7
(−)-*cis*-**19a**[d]			33.2	35.7	22.2	30.7	30.2	62.5	27.3[f]	29.8[f]	20.1	207.7
(+)-*trans*-**19a**[c]			33.8	41.6	21.7	34.4	27.8	66.2	31.0[f]	21.0[f]	20.8	207.2
(−)-*cis*-**19b**[c]		15.8	36.3	37.1	31.3[e]	31.4[e]	30.5	65.1	27.6	20.1[e]	21.1[e]	207.2
(+)-*trans*-**19b**[c]		15.0[f]	36.7	41.8	30.6	34.7	28.1	67.6	27.7	15.2[f]	20.7	207.7

[a]) Carotenoid numbering:  : for systematic names, see *Exper. Part.*

[b]) Relative to R^1.

[c]) 2D Experiments: COSY and C,H correlation.

[d]) Deduced from a mixture.

[e]) Interchangeable.

[f]) Relative to CHO.

Table 3. *^{13}C-NMR Data of Alcohols (−)-*__4__, *(+)-*__9a,b__, *(−)-*__12a,b__, *and (+)-*__20a,b__

Compound	R^1		C(1)[a]	C(2)	C(3)	C(4)	C(5)	C(6)	Me_{trans}–C(1)[b]	Me_{cis}–C(1)[b]	Me–C(5)	C(7)
(−)-*cis*-**4**[c]		15.8	38.2	42.1	33.0	37.0	148.1	56.6	26.6	15.0	106.6	59.6
(−)-*trans*-**4**		15.7	36.2	35.7	30.8[d]	31.5[d]	147.4	58.9	26.5	21.8	112.9	59.2
(+)-*cis*-**9a**		15.3	35.1	38.6	31.8	124.2	133.6	53.3	26.8	15.2	22.2	61.3
(+)-*trans*-**9a**[c]		15.3	34.8	33.0	32.5	124.9	132.2	54.8	25.8	21.3	22.8	61.3
(+)-*cis*-**9b**[c]	12.8	21.9	35.5	45.9	27.8	124.2	133.3	53.4	27.0	16.5	22.2	61.4
(+)-*trans*-**9b**[c]	12.4	22.4	35.0	40.0	29.0	124.7	131.9	55.2.	26.1	22.2	22.7	61.3
(−)-**12a**[c]		16.4	37.3	39.2	27.1	31.8	133.3	138.2	26.8	21.8	19.7	59.2
(−)-**12b**	13.0	22.5[d]	37.7	47.0	22.8[d]	32.1	133.6	138.4	26.4	22.0	19.7	59.3
(+)-*cis*-**20a**			33.4	36.7	21.2	31.1	29.6	52.8	28.6[d]	28.5[d]	19.1	60.3
(+)-*trans*-**20a**[c]			33.5	42.7	22.2	36.5	30.7	55.7	31.2[e]	21.3[e]	20.9	62.3
(+)-*cis*-**20b**[c]		15.9	36.4	36.1	30.9	31.2	30.1	56.1	27.7	21.6	20.2	59.6
(+)-*trans*-**20b**[c]		16.3	36.6	42.5	31.0	36.2	31.1	57.3	27.2	15.0	21.1	62.7

[a]) Carotenoid numbering, see *Table 2*; for systematic names, see *Exper. Part.*

[b]) Relative to R^1.

[c]) 2D Experiments: COSY and C,H correlation.

[d]) Interchangeable.

[e]) Relative to CH_2OH.

Table 4. *^{13}C-NMR Data of Compounds (−)-***5***, **10a,b**, (−)-**13a,b**, (+)-**21a–f**, and (+)-**22a–f***

	R^1		C(1)[a]	C(2)	C(3)	C(4)	C(5)	C(6)	Me_{trans}–C(1)[b]	Me_{cis}–C(1)[b]	Me–C(5)	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)
(−)-*cis*-**5**[c])[d])		15.8	38.8	42.0	32.0	36.3	148.8	57.8	27.7	14.4	108.7	146.9	133.6	197.8	27.2		
(−)-*trans*-**5**[d])		15.6	37.7	36.4	31.5	31.5	148.0	59.6	27.0	21.5	110.5	147.3	132.0	198.3	27.3		
(−)-*cis*-**10a**[d])		15.4	35.8	37.9	31.8	123.0	132.0	56.0	26.6	15.1	22.9	149.2	134.3	198.0	26.9		
(+)-*trans*-**10a**[c])[d])		15.1	35.4	32.0	32.4	123.2	132.1	56.5	26.5	20.8	22.6	148.5	132.5	198.2	26.9		
(+)-*trans*-**10b**	12.3	22.1	35.6	39.0	28.9	123.1	131.8	57.1	26.8	21.7	22.5	148.7	132.4	198.6	27.0		
(−)-**13a**[c])		16.2	37.2	39.1	26.7	32.2	134.0	136.3	27.6	22.2	21.8	144.1	132.5	198.5	27.1		
(−)-**13b**	12.9	22.4	37.6	46.8	22.4	32.6	134.3	136.5	27.4	22.3	21.8	144.2	132.6	198.7	27.1		
(+)-**21a**[c])			34.0	41.3	21.9	35.2	31.4	58.6	31.5[e])	20.6[e])	21.5	149.9	133.2	198.1	27.0		
(+)-**21b**[c])		16.1	36.9	41.9	30.7	35.4	31.5	59.9	27.9	14.5	21.7	150.0	133.5	198.0	27.0		
(+)-**21c**			33.9	41.3	21.8	35.2	31.4	58.5	31.4[e])	20.5[e])	21.5	148.6	132.0	200.7	33.3	8.3	
(+)-**21d**		16.2	36.8	41.9	30.7	35.4	31.4	59.9	27.9	14.5	21.7	148.8	132.3	200.7	33.3	8.3	
(+)-**21e**			33.9	41.3	21.8	35.2	31.4	58.6	31.4[e])	20.6[e])	21.5	148.8	132.4	200.4	42.0	18.0	13.8
(+)-**21f**		16.1	36.8	41.8	30.7	35.3	31.4	59.9	27.9	14.4	21.7	148.9	132.6	200.3	42.1	17.9	13.8
(+)-**22a**[c])			34.5	42.3	22.1	36.6	34.4	53.1	30.8[e])	20.0[e])	21.1	23.5	46.1	208.9	29.8		
(+)-**22b**[c])		16.7	37.7	42.5	30.8	36.2	34.6	54.3	26.8	13.7	21.3	23.8	46.5	209.1	29.8		
(+)-**22c**			34.5	42.3	22.1	36.6	34.4	53.1	30.8[e])	20.0[e])	21.1	23.6	44.7	211.7	35.8	7.9	
(+)-**22d**[c])		16.7	37.7	42.6	30.8	36.3	34.7	54.4	26.8	13.7	21.3	24.0	45.1	211.7	35.8	7.9	
(+)-**22e**			34.6	42.3	22.1	36.6	34.4	53.1	30.8[e])	20.0[e])	21.2	23.5	44.7	211.4	45.1	17.4	13.8
(+)-**22f**		16.7	37.7	42.6	30.8	36.3	34.6	54.4	26.8	13.7	21.3	23.8	45.5	211.4	44.7	17.4	13.8

[a]) Carotenoid numbering, see *Table 2*; for systematic names, see *Exper. Part.*

[b]) Relative to R^1.

[c]) 2D Experiments: COSY and C,H correlation.

[d]) The known spectra of the irones are added for comparison [13b] [13c] [25].

[e]) Relative to the side chain.

General Procedure B for Epoxide Isomerisation. To a soln. of the appropriate epoxide (43.4 mmol), in toluene (66 ml) at 0° and under N_2, was added $SnCl_4$ (0.1 ml, 0.85 mmol). After 20 min of stirring, a few drops of sat. aq. $NaHCO_3$ were added, then H_2O (20 ml). The aq. phase was extracted with toluene (3 × 20 ml) and the org. phase was washed with H_2O (2 × 20 ml). After drying ($MgSO_4$) and evaporation, the desired aldehyde was purified by distillation.

General Procedure C for Reduction. To a suspension of $LiAlH_4$ (4.0 g, 0.092 mol) in Et_2O (300 ml) at 0° was added dropwise a soln. of the appropriate aldehyde (0.24 mol) in Et_2O (100 ml). After 1 h at r.t., H_2O (4 ml), 15% aq. NaOH (4 ml), then H_2O (12 ml) were added. After 30 min, the mixture was filtered through *Celite* and evaporated to give a crude oil, purified by distillation.

General Procedure D for Oxidation. A soln. of oxalyl chloride (0.11 ml, 1.2 mmol) in CH_2Cl_2 (2 ml) was cooled to −70° and DMSO (0.2 ml, 2.4 mmol) was added dropwise, followed by a soln. of the appropriate alcohol (1.1 mmol) in CH_2Cl_2 (1 ml). After 15 min at −70°, Et_3N (0.8 ml, 5.5 mmol) was added and the temp. raised to r.t. After 30 min at r.t., Et_2O (20 ml) was added, and the org. phase was washed with H_2O until neutral, dried (Na_2SO_4), concentrated, and purified by bulb-to-bulb distillation.

General Procedure E for the Aldol Condensation. A soln. of the appropriate aldehyde (52 mmol), the appropriate ketone (140 mmol), and EtONa (5.2 mmol) in EtOH (52 ml) was refluxed and the reaction was monitored by GC until complete disappearance of the aldehyde. The EtOH was partially evaporated and Et_2O (100 ml) was added. The org. phase was washed with H_2O until neutral, dried (Na_2SO_4), concentrated, and purified by distillation.

General Procedure F for Isomerisation. A soln. of the appropriate aldehyde (18 mmol) in EtONa/EtOH (36 ml, 0.05M, 1.8 mmol) was stirred at r.t. and monitored by GC. When the α-isomer was no longer detected, the reaction mixture was concentrated, Et_2O (50 ml) was added, and the org. phase was washed with H_2O, brine, then dried (Na_2SO_4), and evaporated. The crude oil was purified by distillation.

General Procedure G for Hydrogenation. A soln. of the appropriate enone (+)-**21** (0.32 mol) in AcOEt (500 ml) was hydrogenated at r.t. and ambiant pressure over 5% Pd/C (3.0 g). The soln. was filtered through *Celite*, concentrated and distilled.

(+)-(3R,5S)-4,4,5-Trimethyl-8-methylidene-1-oxaspiro[2.5]octane ((+)-**2**). Obtained in 18% yield from (+)-**1** using Me_3SI (1.4 mol-equiv.) and NaOH (5 mol-equiv.) following *Procedure A*. B.p. 58°/0.9 Torr, 47°/0.25 Torr. $[\alpha]_D^{20} = +22.8$ ($c = 5.2$, $CHCl_3$). IR: 2990, 2950, 1660, 1460, 1400, 1200, 1100, 920, 910. ^{1}H-NMR: 0.77 (*s*, 3 H); 0.83 (*s*, 3 H); 0.9 (*d*, $J = 7$, 3 H); 1.41 (*dq*, $J = 4$, 13, 1 H); 1.60 (*m*, 2 H); 2.16 (*m*, 1 H); 2.33 (*d*, $J = 7$, 1 H); 2.43 (*m*, 1 H); 2.90 (*d*, $J = 7$, 1 H); 4.69 (*t*, $J = 2$, 1 H); 4.92 (*t*, $J = 2$, 1 H). ^{13}C-NMR: 15.6 (Me–C(5)); 16.7 (Me_{cis}–C(4)); 21.3 (Me_{trans}–C(4)); 31.0 (C(6)); 34.0 (C(7)); 37.8 (C(4)); 41.3 (C(5)); 52.8 (C(2)); 65.3 (C(3)); 106.4 (CH_2=); 146.5 (C(8)). MS: 166 (8, $M^{+\cdot}$), 151 (50), 137 (21), 123 (33), 109 (60), 95 (100), 81 (70), 67 (39), 55 (40), 41 (18).

(−)-(1S,3S)-2,2,3-Trimethyl-6-methylidenecyclohexane-1-carbaldehyde ((−)-*trans*-**3**). Obtained in 90% yield from (−)-*trans*-**4** following *Procedure D*. t_R (*DB-1*, 80–110°) 2.09. B.p. 58°/0.3 Torr. $[\alpha]_D^{20} = -82.6$ ($c = 1.1$, CCl_4). IR: 3100, 2960, 2750, 1730, 1650, 1460, 1400, 1375, 900. ^{1}H-NMR: 0.61 (*s*, 3 H); 0.65 (*d*, $J = 7$, 3 H); 0.91 (*s*, 3 H); 1.10 (*m*, 1 H); 1.30 (*m*, 1 H); 1.66 (*m*, 1 H); 2.07 (*m*, 2 H); 2.48 (*d*, $J = 4$, 1 H); 4.60 (br. *s*, 1 H); 4.78 (br. *s*, 1 H); 9.60 (*d*, $J = 4$, 1 H). ^{13}C-NMR: *Table 2*. MS: 166 (3, $M^{+\cdot}$), 151 (7), 137 (29), 123 (20), 109 (31), 95 (100), 81 (57), 67 (28), 55 (36), 41 (12).

(+)-(1R,3S)-2,2,3-Trimethyl-6-methylidenecyclohexane-1-carbaldehyde ((+)-*cis*-**3**). Obtained in 80% yield from (+)-**2** as a 2:3 (−)-*trans*-**3**/(+)-*cis*-**3** mixture ($[\alpha]_D^{20} = -18.9$ ($c = 5.7$, $CHCl_3$)) following *Procedure B*. Also obtained in 90% yield from (−)-*cis*-**4** following *Procedure D*. t_R (*DB-1*, 80–110°) 2.57. B.p. 50°/0.3 Torr. $[\alpha]_D^{20} = +24.8$ ($c = 1.15$, CCl_4). IR: 3100, 2960, 2750, 1730, 1650, 1460, 1400, 1375, 900. ^{1}H-NMR: 0.61 (*d*, $J = 7$, 3 H); 0.80 (*s*, 3 H); 0.84 (*s*, 3 H); 0.96 (*m*, 1 H); 1.11 (*m*, 1 H); 1.20 (*m*, 1 H); 1.78 (br. *dt*, $J = 5$, 11, 1 H); 2.05 (*ddd*, $J = 4$, 5, 15, 1 H); 2.40 (*m*, 1 H); 4.48 (br. *s*, 1 H); 4.77 (br. *s*, 1 H); 9.78 (*d*, $J = 5$, 1 H). ^{13}C-NMR: *Table 2*. MS: 166 (6, $M^{+\cdot}$), 151 (23), 123 (32), 109 (47), 95 (100), 83 (70), 67 (32), 55 (49).

(−)-(1S,3S)-2,2,3-Trimethyl-6-methylidenecyclohexane-1-methanol ((−)-*trans*-**4**). Pure material for analysis was obtained by prep. GC from a 2:3 (−)-*trans*-**3**/(+)-*cis*-**3** mixture. t_R (*DB-Wax*, 80–110°) 3.49. M.p. 34–38°. $[\alpha]_D^{20} = -34.0$ ($c = 0.95$, $CHCl_3$). IR: 3600, 3075, 2990, 2940, 1640, 1460, 1380, 1050, 900. ^{1}H-NMR: 0.80 (*s*, 3 H); 0.81 (*d*, $J = 7$, 3 H); 0.93 (*s*, 3 H); 1.27 (*m*, 2 H); 1.54 (*m*, 1 H); 1.56 (*s*, OH); 2.02 (*dd*, $J = 6$, 11, 1 H); 2.18 (*dd*, $J = 3$, 7, 2 H); 3.66 (*m*, 2 H); 4.77 (br. *s*, 1 H); 4.93 (br. *s*, 1 H). ^{13}C-NMR: *Table 3*. MS: 168 (3, $M^{+\cdot}$), 150 (22), 137 (41), 123 (30), 107 (66), 95 (84), 83 (100), 67 (58), 55 (91), 41 (78).

(−)-(1R,3S)-2,2,3-Trimethyl-6-methylidenecyclohexane-1-methanol ((−)-*cis*-**4**). Obtained as a 2:3 (−)-*trans*-**4**/(−)-*cis*-**4** mixture in 95% yield from a (−)-*trans*-**3**/(+)-*cis*-**3** mixture following *Procedure C*. Pure (−)-*cis*-**4** for

analysis was obtained by prep. GC. t_R (*DB-Wax*, 80–110°). 5.18. M.p. 34–40°. $[\alpha]_D^{20} = -28.5$ ($c = 1.0$, $CHCl_3$). IR: 3660, 2990, 2940, 2870, 1640, 1460, 1380, 1190, 1040, 900. ^{1}H-NMR: 0.57 (*s*, 3 H); 0.83 (*d*, $J = 7$, 3 H); 1.03 (*s*, 3 H); 1.26 (*dq*, $J = 4$, 12, 1 H); 1.45 (*m*, 2 H); 1.60 (*m*, 1 H); 2.05 (*m*, 2 H); 2.33 (*dt*, $J = 3$, 12, 1 H); 3.86 (*m*, 2 H); 4.67 (*d*, $J = 2$, 1 H); 4.96 (*d*, $J = 2$, 1 H). ^{13}C-NMR: *Table 3*. MS: 168 (1, M^+), 150 (22), 135 (31), 123 (26), 107 (50), 83 (100), 55 (71), 41 (34).

*(–)-*trans-*γ-Irone* ((–)-*trans*-**5**). A sample was purified by prep. GC from the 77:23 (–)-*trans*-**5**/(–)-*cis*-**5** mixture for analysis. t_R (*DB-1*, 110–150°) 3.54. B.p. 50°/0.004 Torr. $[\alpha]_D^{20} = -53.4$; $[\alpha]_{578}^{20} = -55.9$; $[\alpha]_{546}^{20} = -65.8$; $[\alpha]_{436}^{20} = -134.1$ ($c = 2.34$, $CHCl_3$). IR: 2960, 2940, 1680, 1620, 1360, 1250, 980, 890. ^{1}H-NMR: 0.81 (*s*, 3 H); 0.86 (*d*, $J = 7$, 3 H); 0.90 (*s*, 3 H); 1.32 (*m*, 1 H); 1.63 (*m*, 2 H); 2.22 (*m*, 2 H); 2.25 (*s*, 3 H); 2.64 (*d*, $J = 8$, 1 H); 4.67 (br. *s*, 1 H); 4.76 (br. *s*, 1 H); 6.09 (*d*, $J = 15$, 1 H); 7.07 (*dd*, $J = 8$, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 206 (4, M^+), 163 (27), 149 (20), 121 (60), 109 (25), 81 (36), 55 (42), 43 (100).

*(–)-*cis-*γ-Irone* ((–)-*cis*-**5**). A soln. of (–)-*trans*-**3**/(+)-*cis*-**3** (2:3 mixture, 10.4 g, 63 mmol) and (acetylmethylene)triphenylphosphorane (39.8 g, 125 mmol) in toluene (630 ml) was refluxed for 24 h, then cooled to 0° and filtrated to give a 23:77 mixture of (–)-*cis*-**5**/(–)-*trans*-**5** ($\alpha_D^{20} = -33.7$) in 63% yield after bulb-to-bulb distillation. A sample was purified by prep. GC for analysis. t_R (*DB-1*, 110–150°) 3.76. B.p. 50°/0.004 Torr. $[\alpha]_D^{20} = -5.4$; $[\alpha]_{578}^{20} = -5.4$; $[\alpha]_{546}^{20} = -7.8$; $[\alpha]_{436}^{20} = -30.1$ ($c = 1.66$, $CHCl_3$). IR: 2990, 2940, 2860, 1680, 1650, 1630, 1360, 1250, 1000, 890. ^{1}H-NMR: 0.73 (*s*, 3 H); 0.87 (*d*, $J = 7$, 3 H); 0.88 (*s*, 3 H); 1.32 (*dq*, $J = 5$, 11, 1 H); 1.43 (*m*, 1 H); 1.56 (*m*, 1 H); 2.10 (br. *dt*, $J = 5$, 11, 1 H); 2.29 (*s*, 3 H); 2.35 (*m*, 1 H); 2.55 (br. *d*, $J = 11$, 1 H); 4.43 (*d*, $J = 2$, 1 H); 4.80 (*d*, $J = 2$, 1 H); 6.09 (*d*, $J = 15$, 1 H); 6.94 (*dd*, $J = 9$, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 206 (3, M^+), 191 (7), 163 (22), 149 (29), 121 (80), 109 (24), 81 (29), 55 (41), 43 (100).

*(+)-(3*R,*7*S*)-4,7,8,8-Tetramethyl-1-oxaspiro[2.5]oct-4-ene* ((+)-**7a**). Obtained in 93% yield from (+)-**6a** following *Procedure A*. B.p. 67°/4 Torr. $\alpha_D^{20} = +53$. IR: 2960, 2880, 1670, 1440, 1360, 1200, 1060, 930, 910, 840. ^{1}H-NMR: 0.78 (*s*, 3 H); 0.86 (*s*, 3 H); 0.90 (*d*, $J = 7$, 3 H); 1.50 (*d*, $J = 2$, 3 H); 1.78 (*m*, 2 H); 2.10 (*m*, 1 H); 2.70 (*d*, $J = 4$, 1 H); 2.85 (*d*, $J = 4$, 1 H); 5.66 (br. *s*, 1 H). ^{13}C-NMR: 15.5 (*Me*–C(6)); 16.7 (*Me*–C(3)); 16.7 (Me_{cis}–C(7)); 22.0 (Me_{trans}–C(7)); 32.0 (C(5)); 35.5 (C(7)); 37.7 (C(6)); 47.6 (C(1)); 63.3 (C(2)); 127.0 (C(4)); 132.6 (C(3)). MS: 166 (10, M^+), 151 (35), 137 (30), 124 (100), 121 (50), 109 (32), 105 (40), 95 (40), 91 (35), 79 (35), 41 (55).

*(+)-(3*S,*7*S*)-7-Ethyl-4,8,8-trimethyl-1-oxaspiro[2.5]oct-4-ene* ((+)-**7b**). Obtained in 78% yield from (+)-**6b** following *Procedure A*. B.p. 75°/7.2 Torr. $\alpha_D^{20} = +54$. IR: 2940, 2860, 1670, 1450, 1380, 1200, 1300, 920. ^{1}H-NMR: 0.80 (*s*, 3 H); 0.87 (*s*, 3 H); 0.88 (*t*, $J = 7$, 3 H); 1.10 (*m*, 1 H); 1.45 (*m*, 1 H); 1.51 (*d*, $J = 2$, 3 H); 1.60 (*m*, 1 H); 1.77 (*m*, 1 H); 2.25 (*m*, 1 H); 2.70 (*d*, $J = 4$, 1 H); 2.84 (*d*, $J = 4$, 1 H); 5.69 (br. *s*, 1 H). MS: 180 (5, M^+), 165 (24), 151 (30), 137 (22), 124 (100), 105 (31), 91 (24), 41 (56).

*(+)-(1*S,*5*S*)-2,5,6,6-Tetramethylcyclohex-2-ene-1-carbaldehyde* ((+)-*trans*-**8a**). Obtained in 98% yield from (+)-*trans*-**9a** following *Procedure D*. t_R (*DB-1*, 80–110°) 5.22. B.p. 45°/0.4 Torr. $[\alpha]_D^{20} = +297$ ($c = 1.27$, $CHCl_3$). IR: 2960, 1720, 1680, 1450, 1370, 1060, 810. ^{1}H-NMR: 0.80 (*s*, 3 H); 0.89 (*d*, 3 H); 1.00 (*s*, 3 H); 1.58 (br. *s*, 3 H); 1.75 (*m*, 1 H); 1.88 (*m*, 1 H); 2.16 (*m*, 1 H); 2.36 (*d*, $J = 5$, 1 H); 5.70 (br. *s*, 1 H); 9.56 (*d*, $J = 5$, 1 H). ^{13}C-NMR: *Table 2*. MS: 166 (15, M^+), 137 (60), 108 (52), 95 (100), 81 (61), 67 (34), 55 (50), 41 (84).

*(–)-(1*R,*5*S*)-2,5,6,6-Tetramethylcyclohex-2-ene-1-carbaldehyde* ((–)-*cis*-**8a**). Obtained in 77% yield from (+)-**7a** as a 14:86 (+)-*trans*-**8a**/(–)-*cis*-**8a** mixture following *Procedure B*. Also obtained in 98% yield from (+)-*cis*-**9a** following *Procedure D*. t_R (*DB-1*, 80–110°) 5.83. B.p. 90°/3 Torr. $[\alpha]_D^{20} = -54.5$ ($c = 1.62$, $CHCl_3$). IR: 2960, 1720, 1680, 1450, 1370, 1060, 810. ^{1}H-NMR: 0.88 (*d*, $J = 7$, 3 H); 0.91 (*s*, 3 H); 0.99 (*s*, 3 H); 1.43 (*m*, 1 H); 1.63 (*d*, $J = 2$, 3 H); 1.80 (*m*, 1 H); 2.04 (*m*, 1 H); 2.57 (*m*, 1 H); 5.67 (br. *s*, 1 H); 9.65 (*d*, $J = 5$, 1 H). ^{13}C-NMR: *Table 2*. MS: 166 (11, M^+), 137 (57), 121 (18), 108 (50), 95 (100), 81 (57), 70 (39), 55 (53), 41 (82).

*(+)-(1*S,*5*S*)-5-Ethyl-2,6,6-trimethylcyclohex-2-ene-1-carbaldehyde* ((+)-*trans*-**8b**). Obtained in 87% yield from (+)-**7b** as a 16:84 (+)-*trans*-**8b**/(–)-*cis*-**8b** mixture ($\alpha_D^{20} = +29.2$) following *Procedure B*. Also obtained in 75% yield from (+)-*trans*-**9b** following *Procedure D*. t_R (*DB-1*, 100–140°) 3.93. B.p. 70°/0.4 Torr. $[\alpha]_D^{20} = +503.8$ ($c = 1.3$, $CHCl_3$). IR: 2960, 2860, 1720, 1670, 1460, 1380, 1370, 1200, 1070, 805. ^{1}H-NMR: 0.76 (*s*, 3 H); 0.92 (*t*, $J = 7$, 3 H); 1.02 (*s*, 3 H); 0.85–1.1 (*m*, 2 H); 1.59 (br. *s*, 3 H); 1.63 (*m*, 3 H); 2.34 (br. *d*, $J = 5$, 1 H); 5.74 (br. *s*, 1 H); 9.56 (*d*, $J = 5$, 1 H). ^{13}C-NMR: *Table 2*. MS: 180 (19, M^+), 151 (72), 133 (18), 122 (43), 109 (78), 95 (87), 81 (35), 67 (46), 55 (41), 41 (100).

*(–)-(1*R,*5*S*)-5-Ethyl-2,6,6-trimethylcyclohex-2-ene-1-carbaldehyde* ((–)-*cis*-**8b**). Obtained in 86% yield from (+)-*cis*-**9b** following *Procedure D*. t_R (*DB-1*, 100–140°) 4.25. B.p. 70°/0.4 Torr. $[\alpha]_D^{20} = -57.2$ ($c = 2.6$, $CHCl_3$). IR: 2965, 1720, 1460, 1370, 1075, 810. ^{1}H-NMR: 0.89 (*t*, $J = 7$, 3 H); 0.99 (*s*, 3 H); 1.01 (*s*, 3 H); 1.12 (*m*, 1 H); 1.30 (*m*, 1 H); 1.63 (br. *s*, 3 H); 1.76 (*m*, 2 H); 2.20 (*m*, 1 H); 2.55 (br. *s*, 1 H); 5.68 (br. *s*, 1 H); 9.62 (*d*, $J = 5$, 1 H). ^{13}C-NMR: *Table 2*. MS: 180 (21, M^+), 151 (69), 133 (16), 122 (42), 109 (84), 95 (86), 69 (76), 55 (39), 41 (100).

*(+)-(1*S,*5*S*)-2,5,6,6-Tetramethylcyclohex-2-ene-1-methanol* ((+)-*trans*-**9a**). A sample of the material prepared following *Procedure C* (14:86 (+)-*trans*-**9a**/(+)-*cis*-**9a** mixture) was purified by prep. GC. t_R (*DB-Wax*,

80–110°) 4.56. M.p. 36–39°. $[\alpha]_D^{20} = +127.7$ ($c = 1.06$, $CHCl_3$). IR: 3270, 2990, 2960, 1430, 1210, 1130, 1010, 820. ^{1}H-NMR: 0.77 (*s*, 3 H); 0.82 (*d*, $J = 7$, 3 H); 1.02 (*s*, 3 H); 1.20 (*t*, $J = 6$, OH); 1.60 (br. *s*, 1 H); 1.65 (*m*, 1 H); 1.73 (*d*, $J = 2$, 3 H); 1.85 (*m*, 1 H); 2.00 (*m*, 1 H); 3.77 (*d*, $J = 5$, 2 H); 5.57 (br. *s*, 1 H). ^{13}C-NMR: *Table 3*. MS: 168 (9, M^+), 150 (12), 137 (73), 121 (17), 107 (37), 95 (100), 81 (49), 70 (50), 55 (38), 41 (35).

(+)-(1R,5S)-2,5,6,6-Tetramethylcyclohex-2-ene-1-methanol ((+)-*cis*-**9a**). Obtained in 98% yield from a 14:86 (+)-*trans*-**8a**/(−)-*cis*-**8a** mixture following *Procedure C*. Pure material for analysis was obtained by prep. GC. t_R (*DB-Wax*, 80–110°) 7.46. M.p. 57–60°. $[\alpha]_D^{20} = +20.9$ ($c = 1.8$, $CHCl_3$). IR: 3270, 2990, 1430, 1210, 1130, 1010, 820. ^{1}H-NMR: 0.73 (*s*, 3 H); 0.85 (*d*, $J = 7$, 3 H); 1.00 (*s*, 3 H); 1.28 (br. *s*, OH); 1.47 (*m*, 1 H); 1.72 (*m*, 1 H); 1.80 (*s*, 3 H); 1.86 (*m*, 2 H); 3.78 (*dd*, $J = 4$, 11, 1 H); 3.91 (*dd*, $J = 4$, 11, 1 H); 5.51 (br. *s*, 1 H). ^{13}C-NMR: *Table 3*. MS: 168 (8, M^+), 150 (16), 137 (76), 107 (37), 95 (96), 81 (51), 70 (100), 55 (60), 41 (46).

(+)-(1S,5S)-5-Ethyl-2,6,6-trimethylcyclohex-2-ene-1-methanol ((+)-*trans*-**9b**). A sample of the material prepared following *Procedure C* (16:84 (+)-*trans*-**9b**/(+)-*cis*-**9b** mixture) was purified by prep. GC. t_R (*DB-1*, 100–140°) 4.78. B.p. 110°/0.7 Torr. $[\alpha]_D^{20} = +28.4$ ($c = 2.15$, $CHCl_3$). IR: 3270, 2970, 1430, 1210, 1030, 1010, 820. ^{1}H-NMR: 0.77 (*s*, 3 H); 0.86 (*t*, $J = 7$, 3 H); 0.95 (*m*, 1 H); 1.04 (*s*, 3 H); 1.20 (br. *s*, OH); 1.50 (*m*, 1 H); 1.60 (*m*, 3 H); 1.74 (*d*, $J = 2$, 3 H); 2.20 (*m*, 1 H); 3.75 (*d*, $J = 3$, 2 H); 5.60 (br. *s*, 1 H). ^{13}C-NMR: *Table 3*. MS: 182 (7, M^+), 164 (7), 151 (41), 135 (20), 121 (30), 109 (64), 95 (89), 84 (66), 69 (100), 55 (44), 41 (53).

(+)-(1R,5S)-5-Ethyl-2,6,6-trimethylcyclohex-2-ene-1-methanol ((+)-*cis*-**9b**). Obtained in 83% yield from a 16:84 (+)-*trans*-**8b**/(−)-*cis*-**8b** mixture following *Procedure C*. Pure material for analysis was obtained by prep. GC. t_R (*DB-1*, 100–140°) 5.68. M.p. 57–59°. $[\alpha]_D^{20} = +43.2$ ($c = 1.7$, $CHCl_3$). IR: 3270, 2970, 1430, 1210, 1030, 1010, 820. ^{1}H-NMR: 0.76 (*s*, 3 H); 0.87 (*t*, $J = 7$, 3 H); 0.96 (*m*, 1 H); 1.02 (*s*, 3 H); 1.13 (*m*, 1 H); 1.17 (*t*, $J = 6$, OH); 1.60 (*m*, 2 H); 1.80 (*d*, $J = 2$, 3 H); 1.86 (br. *s*, 1 H); 2.10 (*m*, 1 H); 3.79 (*dd*, $J = 4$, 11, 1 H); 3.91 (*dd*, $J = 4$, 11, 1 H); 5.55 (br. *s*, 1 H). ^{13}C-NMR: *Table 3*. MS: 182 (4, M^+), 164 (7), 151 (23), 109 (36), 95 (47), 84 (67), 69 (100), 55 (33), 41 (40).

*(+)-*trans-α-*Irone* ((+)-*trans*-**10a**). (+)-*trans*-**10a** was purified for analysis by prep. GC from the 5:28:67 (−)-*cis*-**10a**/(+)-*trans*-**10a**/(−)-**13a** mixture obtained after distillation of the reaction mixture generated by performing *Procedure E* on a 14:86 (+)-*trans*/(−)-*cis*-**8a** mixture. t_R (*DB-1*, 130–180°) 3.68. B.p. 62°/0.06 Torr. $[\alpha]_D^{20} = +432.8$ ($c = 2.85$, CH_2Cl_2). IR: 2940, 1670, 1600, 1440, 1425, 1355, 1250, 980. ^{1}H-NMR: 0.82 (*s*, 3 H); 0.85 (*d*, $J = 7$, 3 H); 0.88 (*s*, 3 H); 1.55 (*d*, $J = 2$, 3 H); 1.65 (*m*, 1 H); 1.70 (*m*, 1 H); 2.05 (*m*, 1 H); 2.27 (*s*, 3 H); 2.29 (*m*, 1 H); 5.47 (br. *s*, 1 H); 6.03 (*d*, $J = 15$, 1 H); 6.68 (*dd*, $J = 10$, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 206 (7, M^+), 191 (4), 136 (51), 121 (100), 109 (13), 93 (68), 43 (60).

*(−)-*cis-α-*Irone* ((−)-*cis*-**10a**). Obtained in 76% yield from a 14:86 (+)-*trans*-**8a**/(−)-*cis*-**8a** mixture as a 7:38:55 (−)-*cis*-**10a**/(+)-*trans*-**10a**/(−)-**13a** following *Procedure E* using 1 mol-equiv. of EtONa. Purified by prep. GC for analysis. t_R (*DB-1*, 130–180°) 3.89. B.p. 69°/0.06 Torr. $[\alpha]_D^{20} = -103.7$ ($c = 0.65$, $CHCl_3$). IR: 2900, 1660, 1605, 1440, 1425, 1355, 1250, 980. ^{1}H-NMR: 0.71 (*s*, 3 H); 0.87 (*s*, 3 H); 0.88 (*d*, $J = 7$, 3 H); 1.48 (*m*, 1 H); 1.53 (*d*, $J = 2$, 3 H); 1.75 (*m*, 1 H); 1.96 (*m*, 1 H); 2.27 (*s*, 3 H); 2.55 (*m*, 1 H); 5.52 (br. *s*, 1 H); 6.12 (*d*, $J = 15$, 1 H); 6.65 (*dd*, $J = 10$, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 206 (8, M^+), 191 (4), 136 (50), 121 (100), 109 (12), 93 (68), 43 (53).

(+)-(1′S,5′S,E)-4-(5′-Ethyl-2′,6′,6′-trimethylcyclohex-2′-enyl)but-3-en-2-one ((+)-*trans*-**10b**). Compound (+)-*trans*-**10b** was purified for analysis by prep. GC from the 4:13:83 (−)-*cis*-**10b**/(+)-*trans*-**10b**/(−)-**13b** mixture obtained after distillation of the reaction mixture generated by performing *Procedure E* on (−)-**11b**. t_R (*DB-Wax*, 100–140°) 4.08. B.p. 77°/0.03 Torr. $[\alpha]_D^{20} = +408.7$ ($c = 1.1$, $CHCl_3$). IR: 2960, 1675, 1600, 1440, 1420, 1360, 1250, 980. ^{1}H-NMR: 0.82 (*s*, 3 H); 0.87 (*s*, 3 H); 0.88 (*t*, $J = 7$, 3 H); 0.97 (*m*, 2 H); 1.35 (*m*, 1 H); 1.57 (*s*, 3 H); 1.57 (*m*, 2 H); 2.22 (*m*, 1 H); 2.26 (*s*, 3 H); 5.50 (br. *s*, 1 H); 6.03 (*d*, $J = 16$, 1 H); 6.68 (*dd*, $J = 11$, 16, 1 H). ^{13}C-NMR: *Table 4*. MS: 220 (21, M^+), 136 (69), 121 (100), 109 (12), 93 (78), 77 (13), 69 (14), 55 (18), 43 (99).

(−)-(1′R,5′S,E)-4-(5′-Ethyl-2′,6′,6′-trimethylcyclohex-2′-enyl)but-3-en-2-one ((−)-*cis*-**10b**). Compound (−)-*cis*-**10b** was obtained pure *via* prep. GC of the reaction mixture described above. t_R (*DB-Wax*, 100–140°) 4.56. B.p. 80°/0.03 Torr. $[\alpha]_D^{20} = -65.2$ ($c = 0.8$, $CHCl_3$). IR: 2960, 2920, 1675, 1600, 1440, 1420, 1360, 1250, 980. ^{1}H-NMR: 0.74 (*s*, 3 H); 0.89 (*s*, 3 H); 0.89 (*t*, $J = 7$, 3 H); 1.00 (*m*, 1 H); 1.16 (*m*, 1 H); 1.52 (*s*, 3 H); 1.60 (*m*, 2 H); 2.20 (*m*, 1 H); 2.28 (*s*, 3 H); 2.54 (*m*, 1 H); 5.56 (br. *s*, 1 H); 6.13 (*d*, $J = 16$, 1 H); 6.64 (*dd*, $J = 11$, 16, 1 H). ^{13}C-NMR: *Table 4*. MS: 220 (21, M^+), 136 (100), 121 (99), 93 (68), 43 (60).

(−)-(5S)-2,5,6,6-Tetramethylcyclohex-1-ene-1-carbaldehyde ((−)-**11a**). Obtained in 88% yield from a 14:86 (+)-*trans*-**8a**/(−)-*cis*-**8a** mixture following *Procedure F*. t_R (*DB-1*, 80–110°) 8.80. B.p. 90°/3 Torr, 79°/4.4 Torr. M.p. 52°. $\alpha_D^{20} = -48.2$. IR: 2960, 1660, 1375, 1280. ^{1}H-NMR: 0.90 (*d*, $J = 7$, 3 H); 1.06 (*s*, 3 H); 1.22 (*s*, 3 H); 1.42 (*m*, 2 H); 1.58 (*m*, 1 H); 2.09 (*s*, 3 H); 2.20 (*m*, 2 H); 10.13 (*s*, 1 H). ^{13}C-NMR: *Table 2*. MS: 160 (70, M^+), 151 (63), 148 (35), 133 (40), 123 (48), 109 (77), 95 (53), 81 (100), 41 (91).

(−)-(5S)-5-Ethyl-2,6,6-trimethylcyclohex-1-ene-1-carbaldehyde ((−)-**11b**). Obtained in 54% yield from a 16:84 (+)-*trans*-**8b**/(−)-*cis*-**8b** mixture following *Procedure F*. t_R (*DB-1*, 100–140°) 5.48. B.p. 62°/0.44 Torr. $\alpha_D^{20} = -13.3$ ($c = 1.86$, $CHCl_3$). IR: 2965, 1670, 1615, 1460, 1380, 1280, 1135. ^{1}H-NMR: 0.94 (*t*, $J = 7$, 3 H); 1.06 (*s*,

3 H); 1.10 (*m*, 1 H); 1.24 (*s*, 3 H); 1.28 (*m*, 1 H); 1.60 (*m*, 1 H); 1.76 (*m*, 2 H); 2.10 (*s*, 3 H); 2.20 (*m*, 2 H); 10.12 (*s*, 1 H). ^{13}C-NMR: *Table 2*. MS: 180 (24, M^{+}), 165 (15), 151 (28), 133 (28), 123 (40), 109 (100), 95 (64), 81 (67), 67 (23), 55 (27), 41 (36).

(–)-(5S)-2,5,6,6-Tetramethylcyclohex-1-ene-1-carboxylic Acid ((–)-**11c**). In a 100-ml flask with magnetic stirring, containing neat (–)-**11a** (27.4 g, 165 mmol), O_2 was bubbled through during 56 h. Et_2O (100 ml) was added, and the soln. was extracted with 15% aq. NaOH at 0°. The aq. phase was washed with Et_2O (50 ml), acidified at 0° with 15% aq. HCl, and extracted with Et_2O (3 × 100 ml). The org. phase was dried (Na_2SO_4), evaporated, and distilled to give (–)-**11c** (65%). B.p. 120°/0.7 Torr. $[\alpha]_D^{20} = -65.3$ (*c* = 3.4, $CHCl_3$). IR: 3300, 2970, 1690, 1380, 1290, 1200, 900. ^{1}H-NMR: 0.92 (*d*, *J* = 7, 3 H); 1.04 (*s*, 3 H); 1.12 (*s*, 3 H); 1.47 (*m*, 2 H); 1.62 (*m*, 1 H); 1.76 (*s*, 3 H); 2.03 (*m*, 2 H); 11.2 (br. *s*, OH). ^{13}C-NMR: *Table 2*. MS: 182 (26, M^{+}), 167 (87), 149 (100), 137 (38), 125 (62), 121 (80), 107 (42), 91 (45), 79 (60), 67 (28), 55 (35), 41 (66).

(–)-(5S)-2,5,6,6-Tetramethylcyclohex-1-ene-1-carbonyl Chloride ((–)-**11d**). Oxalyl chloride (0.7 ml, 8 mmol) was added at 0° to a soln. of (–)-**11c** (0.6 g, 3 mmol) in toluene (6 ml) and stirred at r.t. for 12 h. The soln. was concentrated and purified by bulb-to-bulb distillation to furnish (–)-**11d** (83%). B.p. 90–95°/0.6 Torr. $[\alpha]_D^{20} = -51.5$ (*c* = 2.0, $CHCl_3$). IR: 2960, 1780, 1460. ^{1}H-NMR: 0.93 (*d*, *J* = 7, 3 H); 1.04 (*s*, 3 H); 1.18 (*s*, 3 H); 1.48 (*m*, 2 H); 1.61 (*m*, 1 H); 1.80 (*s*, 3 H); 2.05 (*m*, 2 H). ^{13}C-NMR: *Table 2*. MS: 200.5 (0, M^{+}), 165 (100), 149 (53), 137 (23), 121 (68), 105 (35), 95 (49), 79 (34), 41 (29).

(–)-(5S)-2,5,6,6-Tetramethylcyclohex-1-ene-1-methanol ((–)-**12a**). Obtained in 95% yield from (–)-**11a** following *Procedure C*. t_R (*DB-Wax*, 80–110°) 8.46. M.p. 43°. $[\alpha]_D^{20} = -85.8$ (*c* = 1.58, $CHCl_3$). IR: 3350, 2960, 2920, 1440, 970. ^{1}H-NMR: 0.86 (*s*, 3 H); 0.89 (*d*, *J* = 7, 3 H); 1.00 (br. *s*, OH); 1.07 (*s*, 3 H); 1.40 (*m*, 2 H); 1.50 (*m*, 1 H); 1.75 (*s*, 3 H); 1.93 (*m*, 1 H); 2.02 (*m*, 1 H); 4.13 (*q*, *J* = 11, 2 H). ^{13}C-NMR: *Table 3*. MS: 168 (14, M^{+}), 153 (14), 135 (63), 107 (51), 93 (100), 79 (31), 55 (31), 41 (37).

(–)-(5S)-Ethyl-2,6,6-trimethylcyclohex-1-ene-1-methanol ((–)-**12b**). Obtained from (–)-**11b** in 88% yield following *Procedure C*. t_R (*DB-1*, 100–140°) 5.36. M.p. 54–57°. $[\alpha]_D^{20} = -62.6$ (*c* = 1.4, $CHCl_3$). IR: 3650, 2970, 2920, 1470, 1380, 1200, 990. ^{1}H-NMR: 0.86 (*s*, 3 H); 0.92 (*t*, *J* = 7, 3 H); 0.93 (*m*, 2 H); 1.09 (*s*, 3 H); 1.24 (*m*, 1 H); 1.57 (*s*, OH); 1.58 (*m*, 1 H); 1.72 (*m*, 1 H); 1.77 (*s*, 3 H); 1.98 (*m*, 2 H); 4.08 (*d*, *J* = 11, 1 H); 4.18 (*d*, *J* = 11, 1 H). ^{13}C-NMR: *Table 3*. MS: 182 (8, M^{+}), 164 (18), 149 (48), 135 (39), 121 (51), 107 (70), 93 (100), 79 (44), 55 (35), 41 (45).

(–)-β-Irone ((–)-**13a**). Obtained in 77% yield from (–)-**11a** after distillation of the resulting 2:8:90 (–)-*cis*-**10a**/(+)-*trans*-**10a**/(–)-**13a** mixture generated by following *Procedure E*. Purified by prep. GC for analysis. t_R (*DB-1*, 130–180°) 4.21. B.p. 90°/0.03 Torr. $[\alpha]_D^{20} = -65$ (*c* = 1.8, CH_2Cl_2). IR: 2920, 1660, 1600, 1440, 1350, 1250, 980, 780. ^{1}H-NMR: 0.85 (*m*, 1 H); 0.91 (*d*, *J* = 7, 3 H); 0.91 (*s*, 3 H); 1.06 (*s*, 3 H); 1.45 (*m*, 2 H); 1.60 (*m*, 1 H); 1.73 (*s*, 3 H); 2.06 (*m*, 1 H); 2.30 (*s*, 3 H); 6.08 (*d*, *J* = 16, 1 H); 7.25 (*d*, *J* = 16, 1 H). ^{13}C-NMR: *Table 4*. MS: 206 (4, M^{+}), 191 (100), 149 (15), 121 (18), 43 (52).

(–)-(5'S,E)-4-(5'-Ethyl-2',6',6'-trimethylcyclohex-1'-enyl)but-3-en-2-one ((–)-**13b**). Obtained in 56% yield from a 16:84 (+)-*trans*-**8b**/(–)-*cis*-**8b** mixture following *Procedure E*, after distillation of the resulting 4:13:83 (–)-*cis*-**10b**/(+)-*trans*-**10b**/(–)-**13b** mixture. t_R (*DB-Wax*, 100–140°) 5.05. B.p. 100°/0.03 Torr. $[\alpha]_D^{20} = -49.3$ (*c* = 1.3, $CHCl_3$). IR: 2960, 1670, 1600. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.94 (*t*, *J* = 7, 3 H); 1.00 (*m*, 1 H); 1.07 (*s*, 3 H); 1.11 (*m*, 1 H); 1.30 (*m*, 1 H); 1.59 (*m*, 1 H); 1.74 (*s*, 3 H); 1.78 (*m*, 1 H); 2.05 (*m*, 2 H); 2.31 (*s*, 3 H); 6.07 (*d*, *J* = 16, 1 H); 7.24 (*d*, *J* = 16, 1 H). ^{13}C-NMR: *Table 4*. MS: 220 (5, M^{+}), 205 (100), 149 (15), 135 (10), 121 (15), 43 (57).

(–)-(5S)-6-Carbonyl-1,4,5,5-tetramethylcyclohex-1-ene ((–)-**14**). In a *Parr* autoclave under N_2 a soln. of (–)-**11d** (0.55 g, 3 mmol) and Et_3N (0.46 ml, 3.3 mmol) in toluene (45 ml) was heated at 140° for 3 h. The cold soln. was diluted with Et_2O (50 ml), washed with 15% aq. HCl, sat. aq. $NaHCO_3$, H_2O, dried (Na_2SO_4), concentrated, purified by bulb-to-bulb distillation to give (–)-**14** (45%). B.p. 85°/7 Torr, 60°/2 Torr. $[\alpha]_D^{20} = -19.4$ (*c* = 1.02, $CHCl_3$). IR: 2900, 2860, 2830, 2040, 1420, 1340, 1210. ^{1}H-NMR: 0.87 (*d*, *J* = 7, 3 H); 1.01 (*s*, 3 H); 1.13 (*s*, 3 H); 1.53 (*sext.*, *J* = 5, 1 H); 1.73 (*d*, *J* = 2, 3 H); 1.80 (*m*, 1 H); 2.18 (*m*, 1 H); 5.05 (br. *s*, 1 H). ^{13}C-NMR: 15.6 (*Me*–C(4)); 21.1 (*Me*–C(1)); 23.2 (Me_{cis}–C(5)); 27.9 (Me_{trans}–C(5)); 31.6 (C(3)); 33.3 (C(5)); 36.7 (C(4)); 50.0 (C(6)); 116.5 (C(2)); 122.3 (C(1)); 207.0 (C=O). MS: 164 (87, M^{+}), 149 (59), 121 (100), 105 (48), 93 (50), 79 (49), 41 (37).

(–)-(1S,5S)-2,4,4,5-Tetramethylcyclohex-2-en-1-ol ((–)-*trans*-**15a**). A stream of air was bubbled through a two-phase mixture consisting of (+)-*trans*-**8a** (5.0 g, 30 mmol), $CuSO_4 \cdot 5\,H_2O$ (7.5 g, 30 mmol), dissolved in H_2O (50 ml) and pyridine (2.4 ml, 30 mmol) in Et_2O (150 ml). After 72 h, no more starting material was detected by GC. The mixture was dissolved with Et_2O (100 ml) and washed with H_2O (3 × 100 ml), dried, evaporated to give a 28:4:68 (–)-*trans*-**15a**/(–)-*cis*-**15a**/(–)-**16** mixture (4.2 g, *ca.* 92%) which was purified on SiO_2 (100 g) with 9:1 toluene/AcOEt. (–)-*trans*-**15a** (15% yield) and (–)-**16** (55% yield). Data for (–)-*cis*-**15a** and (–)-**16** have been reported in [15b]. M.p. 79–80°. $[\alpha]_D^{20} = -145.2$ (*c* = 0.6, $CHCl_3$). IR: 3200, 2950, 1450, 1360, 1280, 1210, 1130, 1050,

1030, 1000. ^{1}H-NMR: 0.75 (*s*, 3 H); 0.90 (*d*, *J* = 7, 3 H); 0.98 (*s*, 3 H); 1.50 (br. *s*, OH); 1.60 (*m*, 3 H); 1.76 (*d*, *J* = 2, 3 H); 3.87 (br. *s*, 1 H); 5.25 (*s*, 1 H). ^{13}C-NMR: 15.8 (*Me*–C(5)); 20.9 (Me_{cis}–C(4)); 20.8 (*Me*–C(2)); 28.8 (Me_{trans}–C(4)); 32.5 (C(5)); 35.1 (C(4)); 37.1 (C(6)); 68.6 (C(1)); 131.7 (C(2)); 137.9 (C(3)). MS: 154 (19, $M^{+\cdot}$), 139 (27), 121 (82), 105 (28), 84 (100), 69 (50), 55 (30), 43 (42).

(+)-(3S,5S,8S)-4,4,5,8-Tetramethyl-1-oxaspiro[2.5]octane ((+)-**18**). Obtained in 93% yield from (+)-**17** following *Procedure A* as a 3:32:65 (3*R*,5*S*,8*R*)-**18**/(3*R*,5*S*,8*S*)-**18**/(3*S*,5*S*,8*S*)-**18**. Purified by prep. GC for analysis. t_R (*DB-1*, 80–110°) (3*R*,5*S*,8*R*)-**18**: 5.62; (3*R*,5*S*,8*S*)-**18**: 5.73; (3*S*,5*S*,8*S*)-**18**: 5.81. B.p. 73°/7.8 Torr. α_D^{20} = +36.5. IR: 2900, 1440, 1360, 1200, 1030, 940, 815. ^{1}H-NMR: 0.69 (*d*, *J* = 7, 3 H); 0.75 (*s*, 3 H); 0.84 (*d*, *J* = 7, 3 H); 0.93 (*s*, 3 H); 1.40 (*m*, 3 H); 1.55 (*m*, 2 H); 2.12 (*m*, 1 H); 2.61 (*d*, *J* = 4, 1 H); 2.70 (*d*, *J* = 4, 1 H). ^{13}C-NMR: 15.4 (*Me*–C(8)); 16.4 (*Me*–C(5)); 18.9 (Me_{cis}–C(4)); 20.8 (Me_{trans}–C(4)); 30.0 (C(8)); 31.3 (C(6)); 32.8 (C(7)); 37.5 (C(4)); 38.4 (C(5)); 45.7 (C(2)); 65.1 (C(3)). MS: 168 (11, $M^{+\cdot}$), 153 (49), 123 (77), 95 (49), 81 (91), 55 (100), 41 (91).

(+)-(1R,6S)-2,2,6-Trimethylcyclohexane-1-carbaldehyde ((+)-*trans*-**19a**). Obtained in 78% overall yield as a 90:10 (+)-*trans*-**19a**/(–)-*cis*-**19a** mixture (α_D^{20} = +1.2) from (–)-citronellal following the procedure described for the racemate [51]. Also obtained in 98% yield from (+)-*trans*-**20a** following *Procedure D*. t_R (*DB-1*, 100–140°) 1.88. B.p. 59°/6 Torr. α_D^{20} = +6.2. IR: 2230, 1720, 1460, 1370. ^{1}H-NMR: 0.83 (*d*, *J* = 7, 3 H); 0.95 (*m*, 1 H); 0.98 (*s*, 3 H); 1.03 (*s*, 3 H); 1.20 (*m*, 1 H); 1.37 (*m*, 1 H); 1.53 (*m*, 2 H); 1.63 (*dd*, *J* = 5, 11, 1 H); 1.78 (*m*, 1 H); 1.98 (*m*, 1 H); 9.63 (*d*, *J* = 5, 1 H). ^{13}C-NMR: *Table 2*. MS: 154 (10, $M^{+\cdot}$), 139 (9), 121 (19), 111 (20), 95 (21), 83 (42), 69 (100), 55 (41), 41 (37).

(–)-(1S,6S)-2,2,6-Trimethylcyclohexane-1-carbaldehyde ((–)-*cis*-**19a**). Obtained in 90% yield from (+)-*cis*-**20a** following *Procedure D*. t_R (*DB-1*, 100–140°) 1.96. B.p. 70°/4 Torr. α_D^{20} = –27.2 (crude material evaporated under high vacuum after oxidation). IR: 2230, 1720, 1460, 1370. ^{1}H-NMR: 0.92 (*m*, 1 H); 0.93 (*d*, *J* = 7, 3 H); 0.94 (*s*, 3 H); 1.04 (*s*, 3 H); 1.42 (*m*, 2 H); 1.65 (*m*, 2 H); 1.75 (*m*, 1 H); 1.95 (*m*, 1 H); 2.0 (*m*, 1 H); 9.96 (*d*, *J* = 5, 1 H). ^{13}C-NMR: *Table 2*. MS: 154 (8, $M^{+\cdot}$), 121 (15), 109 (43), 95 (32), 85 (44), 82 (51), 69 (100), 55 (53), 41 (56).

(+)-(1R,3S,6S)-2,2,3,6-Tetramethylcyclohexane-1-carbaldehyde ((+)-*trans*-**19b**). (+)-**18** (168 g, 1.0 mol, 3:32:65 mixture) was added dropwise to a suspension of $MgBr_2$ (46.0 g, 0.25 mol) in refluxing toluene (1.0 l). After 5 h, the cold soln. was poured on ice, diluted with Et_2O (220 ml), washed with aq. sat. NH_4Cl until neutral, dried (Na_2SO_4), concentrated, and distilled to give a 53:47 (+)-*trans*-**19b**/(–)-*cis*-**19b** mixture in 91% yield. Further treatment following *Procedure F* gave a 90:10 (+)-*trans*-**19b**/(–)-*cis*-**19b** in 81% overall yield. Also obtained in 71% yield from (+)-*trans*-**20b** following *Procedure D*. t_R (*DB-1*, 80–110°) 3.15. B.p. 68°/3.9 Torr. $[\alpha]_D^{20}$ = +7.4 (*c* = 2.5, $CHCl_3$). IR: 2900, 2700, 1720, 1450, 1390, 1360, 1190, 1170, 1135, 1020. ^{1}H-NMR: 0.81 (*d*, *J* = 7, 3 H); 0.84 (*d*, *J* = 7, 3 H); 0.90 (*s*, 3 H); 0.96 (*s*, 3 H); 1.01 (*m*, 1 H); 1.20 (*m*, 1 H); 1.29 (*m*, 1 H); 1.44 (*m*, 1 H); 1.60 (*dd*, *J* = 5, 11, 1 H); 1.76 (*m*, 1 H); 1.99 (*m*, 1 H); 9.68 (*d*, *J* = 5, 1 H). ^{13}C-NMR: *Table 2*. MS: 168 (5, $M^{+\cdot}$), 135 (8), 124 (16), 98 (37), 83 (100), 69 (60), 55 (78), 41 (50).

(–)-(1S,3S,6S)-2,2,3,6-Tetramethylcyclohexane-1-carbaldehyde ((–)-*cis*-**19b**). Obtained in 90% yield from (+)-*cis*-**20b** following *Procedure D*. t_R (*DB-1*, 80–110°) 3.28. B.p. 68°/4.2 Torr. $[\alpha]_D^{20}$ = –1.84 (*c* = 2.9, CCl_4; crude material evaporated under high vacuum after oxidation). IR: 2940, 1710, 1450, 1380, 1360, 1140, 1040, 1020, 970. ^{1}H-NMR: 0.87 (*d*, *J* = 7, 3 H); 0.88 (*d*, *J* = 7, 3 H); 0.89 (*s*, 3 H); 0.94 (*s*, 3 H); 1.48 (*m*, 2 H); 1.64 (*m*, 2 H); 1.81 (*m*, 1 H); 1.93 (*t*, *J* = 5, 1 H); 2.00 (*m*, 1 H); 10.02 (*d*, *J* = 5, 1 H). ^{13}C-NMR: *Table 2*. MS: 168 (2, $M^{+\cdot}$), 135 (7), 123 (8), 109 (9), 97 (13), 84 (100), 69 (29), 55 (49), 41 (33).

(+)-(1R,6S)-2,2,6-Trimethylcyclohexane-1-methanol ((+)-*trans*-**20a**). Synthesized in 90% yield as a 90:10 mixture of (+)-*trans*-**20a**/(+)-*cis*-**20a** following *Procedure C*. Pure (+)-*trans*-**20a** was obtained by prep. GC. t_R (*DB-1*, 100–140°) 2.55. B.p. 60–65°/1 Torr. $[\alpha]_D^{20}$ = +10.8 (*c* = 1.35, CCl_4). IR: 3500, 2960, 2930, 2875, 1490, 1460, 1450, 1390, 1370, 1280, 1030. ^{1}H-NMR: 0.80 (*dt*, *J* = 3, 11, 1 H); 0.88 (*s*, 3 H); 0.93 (*m*, 1 H); 0.99 (*d*, *J* = 7, 3 H); 1.00 (*s*, 3 H); 1.13 (br. *s*, OH); 1.20 (*m*, 1 H); 1.33 (*m*, 1 H); 1.46 (*m*, 2 H); 1.56 (*m*, 1 H); 1.67 (*m*, 1 H); 3.67 (*d*, *J* = 11, 1 H); 3.81 (*d*, *J* = 11, 1 H). ^{13}C-NMR: *Table 3*. MS: 156 (1, $M^{+\cdot}$), 138 (4), 123 (33), 95 (30), 81 (50), 69 (100), 55 (45), 41 (27).

(+)-(1S,6S)-2,2,6-Trimethylcyclohexane-1-methanol ((+)-*cis*-**20a**). Isolated by prep. GC from the reaction mixture described above. t_R (*DB-1*, 100–140°) 2.75. B.p. 60–65°/1 Torr. $[\alpha]_D^{20}$ = +6.6 (*c* = 0.8, CCl_4). IR: 3500, 2960, 2930, 2875, 1465, 1390, 1370, 1245, 1225, 1160, 1070. ^{1}H-NMR: 0.98 (*d*, *J* = 7, 3 H); 1.00 (*s*, 3 H); 0.9–1.3 (*m*, 4 H); 1.4–1.5 (*m*, 3 H); 1.66 (br. *s*, OH); 1.99 (*m*, 1 H); 3.69 (*d*, *J* = 5, 1 H); 3.75 (*d*, *J* = 5, 1 H). ^{13}C-NMR: *Table 3*. MS: 156 (0, $M^{+\cdot}$), 138 (4), 123 (28), 95 (34), 81 (42), 69 (100), 55 (40), 41 (25).

(+)-(1R,3S,6S)-2,2,3,6-Tetramethylcyclohexane-1-methanol ((+)-*trans*-**20b**). When a 9:1 (+)-*trans*-**19b**/(–)-*cis*-**19b** mixture was subjected to *Procedure C*, a mixture of (+)-*trans*-**20b**/(+)-*cis*-**20b** was obtained in 90% yield, from which pure (+)-*trans*-**20b** was obtained by prep. GC. t_R (*DB-1*, 130–180°) 1.88. B.p. 67°/0.8 Torr. $[\alpha]_D^{20}$ = +1.7 (*c* = 4.5, $CHCl_3$). IR: 3260, 2940, 1450, 1380, 1360, 1200, 1005. ^{1}H-NMR: 0.70 (*s*, 3 H); 0.75 (*m*, 1 H);

0.82 (*d*, *J* = 7, 3 H); 0.90 (*m*, 1 H); 0.98 (*d*, *J* = 7, 3 H); 0.99 (*s*, 3 H); 1.05 (*m*, 1 H); 1.20 (*m*, 2 H); 1.40 (*m*, 1 H); 1.74 (*m*, 1 H); 1.65 (*m*, 1 H); 3.68 (*d*, *J* = 11, 1 H); 3.83 (*d*, *J* = 11, 1 H). ^{13}C-NMR: *Table 3*. MS: 170 (3, M^{+}), 152 (5), 137 (39), 109 (50), 96 (55), 83 (100), 69 (85), 55 (90), 41 (48).

(+)-(1S,3S,6S)-2,2,3,6-Tetramethylcyclohexane-1-methanol ((+)-*cis*-**20b**). Isolated from the reaction mixture described above *via* prep. GC. t_R (*DB-1*, 130–180°) 1.93. B.p. 70°/1 Torr. $[\alpha]_D^{20}$ = +10.5 (*c* = 3.3, $CHCl_3$). IR: 3250, 2940, 1450, 1380, 1360, 1200, 1005. ^{1}H-NMR: 0.79 (*d*, *J* = 7, 3 H); 0.89 (*s*, 3 H); 0.98 (*d*, 3 H); 1.05 (*s*, 3 H); 0.85–1.05 (*m*, 2 H); 1.20 (*m*, 2 H); 1.30 (*m*, 1 H); 1.40 (*m*, 2 H); 1.50 (br. *s*, OH); 3.72 (*m*, 2 H). ^{13}C-NMR: *Table 3*. MS: 170 (2, M^{+}), 152 (4), 137 (40), 109 (50), 96 (52), 83 (100), 69 (87), 55 (89), 41 (53).

(+)-(1'S,6'S,E)-4-(2',2',6'-Trimethylcyclohexyl)but-3-en-2-one ((+)-**21a**). Obtained in 59% yield from a 92:8 (+)-*trans*-**19a**/(−)-*cis*-**19a** mixture following *Procedure E*. B.p. 61°/0.4 Torr. α_D^{20} = +30.0. IR: 2925, 1680, 1620, 1460, 1360, 1250, 1180, 990. ^{1}H-NMR: 0.75 (*d*, *J* = 7, 3 H); 0.83 (*s*, 3 H); 0.90 (*s*, 3 H); 0.91 (*m*, 1 H); 1.20 (*m*, 1 H); 1.45 (*m*, 1 H); 1.52 (*m*, 4 H); 1.75 (*m*, 1 H); 2.27 (*s*, 3 H); 6.03 (*d*, *J* = 15, 1 H); 6.57 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 194 (4, M^{+}), 176 (5), 161 (6), 151 (28), 136 (25), 109 (95), 95 (86), 81 (56), 69 (40), 55 (40), 43 (100).

(+)-(1'S,3'S,6'S,E)-4-(2',2',3',6'-Tetramethylcyclohexyl)but-3-en-2-one ((+)-**21b**). Obtained in 62% yield from a 90:10 (+)-*trans*-**19b**/(−)-*cis*-**19b** mixture following *Procedure E*. B.p. 62°/0.01 Torr. $[\alpha]_D^{20}$ = +29.8 (*c* = 1.1, $CHCl_3$). IR: 2960, 2920, 1670, 1620, 1450, 1360, 1250, 990. ^{1}H-NMR: 0.74 (*d*, *J* = 7, 3 H); 0.76 (*s*, 3 H); 0.83 (*s*, 3 H); 0.85 (*d*, *J* = 7, 3 H); 0.8–1.10 (*m*, 2 H); 1.15–1.35 (*m*, 2 H); 1.40–1.60 (*m*, 2 H); 1.74 (*m*, 1 H); 2.27 (*s*, 3 H); 6.03 (*d*, *J* = 15, 1 H); 6.62 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 208 (8, M^{+}), 193 (7), 165 (17), 150 (33), 137 (23), 124 (36), 111 (97), 109 (100), 95 (80), 81 (79), 69 (26), 55 (57), 43 (96).

(+)-(1'S,6'S,E)-1-(2',2',6'-Trimethylcyclohexyl)pent-1-en-3-one ((+)-**21c**). Obtained in 58% yield from a 92:8 (+)-*trans*-**19a**/(−)-*cis*-**19a** mixture following *Procedure E*. B.p. 62°/0.16 Torr. $[\alpha]_D^{20}$ = +31.5 (*c* = 1.7, $CHCl_3$). IR: 2925, 1675, 1625, 1460, 1370, 1200, 1125, 990. ^{1}H-NMR: 0.75 (*d*, *J* = 7, 3 H); 0.83 (*s*, 3 H); 0.93 (*s*, 3 H); 0.95 (*m*, 1 H); 1.11 (*t*, *J* = 7, 3 H); 1.20 (*m*, 1 H); 1.44 (*m*, 2 H); 1.52 (*m*, 3 H); 1.75 (*m*, 1 H); 2.58 (*q*, *J* = 7, 2 H); 6.05 (*d*, *J* = 15, 1 H); 6.60 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 208 (5, M^{+}), 179 (12), 165 (18), 136 (37), 123 (52), 109 (52), 95 (100), 81 (49), 69 (52), 57 (78), 41 (56).

(+)-(1'S,3'S,6'S)-1-(2',2',3',6'-Tetramethylcyclohexyl)pent-1-en-3-one ((+)-**21d**). Obtained in 70% yield from a 90:10 (+)-*trans*-**19b**/(−)-*cis*-**19b** mixture following *Procedure E*. B.p. 84°/0.3 Torr. $[\alpha]_D^{20}$ = +29.5 (*c* = 1.7, $CHCl_3$). IR: 2960, 2920, 1670, 1625, 1450, 1360, 1200, 1120, 990. ^{1}H-NMR: 0.73 (*d*, *J* = 7, 3 H); 0.75 (*s*, 3 H); 0.82 (*s*, 3 H); 0.84 (*d*, *J* = 7, 3 H); 1.00 (*m*, 1 H); 1.11 (*t*, *J* = 7, 3 H); 1.27 (*m*, 2 H); 1.46 (*m*, 2 H); 1.54 (*m*, 1 H); 1.74 (*m*, 1 H); 2.58 (*q*, *J* = 7, 2 H); 6.04 (*d*, *J* = 15, 1 H); 6.64 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 222 (7, M^{+}), 207 (4), 193 (12), 179 (12), 165 (13), 150 (32), 138 (27), 123 (99), 109 (57), 95 (80), 81 (99), 55 (100), 41 (49).

(+)-(1'S,6'S,E)-1-(2',2',6'-Trimethylcyclohexyl)hex-1-en-3-one ((+)-**21e**). Obtained in 51% yield from a 92:8 (+)-*trans*-**19a**/(−)-*cis*-**19a** mixture following *Procedure E*. B.p. 70°/0.14 Torr. $[\alpha]_D^{20}$ = +31.5 (*c* = 1.7, $CHCl_3$). IR: 2960, 1670, 1625, 1460, 1370, 1190, 990. ^{1}H-NMR: 0.76 (*d*, *J* = 7, 3 H); 0.83 (*s*, 3 H); 0.90 (*s*, 3 H); 0.96 (*t*, *J* = 7, 3 H); 0.8–1.0 (*m*, 1 H); 1.20 (*m*, 1 H); 1.44 (*m*, 2 H); 1.52 (*m*, 3 H); 1.65 (*sext.*, *J* = 7, 2 H); 1.74 (*m*, 1 H); 2.54 (*t*, *J* = 7, 2 H); 6.05 (*d*, *J* = 15, 1 H); 6.58 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 222 (4, M^{+}), 207 (5), 179 (30), 136 (46), 109 (48), 95 (100), 81 (50), 71 (63), 55 (49), 43 (37).

(+)-(1'S,3'S,6'S,E)-1-(2',2',3',6'-Tetramethylcyclohexyl)hex-1-en-3-one ((+)-**21f**). Obtained in 50% yield from a 90:10 (+)-*trans*-**19b**/(−)-*cis*-**19b** mixture following *Procedure E*. B.p. 85°/0.1 Torr. α_D^{20} = +23.6. IR: 2960, 1670, 1625, 1460, 1370, 1190, 990. ^{1}H-NMR: 0.73 (*d*, *J* = 7, 3 H); 0.76 (*s*, 3 H); 0.82 (*s*, 3 H); 0.86 (*d*, *J* = 7, 3 H); 0.95 (*t*, *J* = 7, 3 H); 0.74–1.07 (*m*, 1 H); 1.20 (*m*, 1 H); 1.29 (*m*, 1 H); 1.44 (*m*, 1 H); 1.50 (*m*, 1 H); 1.55 (*m*, 1 H); 1.65 (*sext.*, *J* = 7, 2 H); 1.74 (*m*, 1 H); 2.53 (*t*, *J* = 7, 2 H); 6.04 (*d*, *J* = 15, 1 H); 6.63 (*dd*, *J* = 11, 15, 1 H). ^{13}C-NMR: *Table 4*. MS: 236 (3, M^{+}), 193 (17), 165 (14), 150 (36), 139 (62), 123 (47), 109 (54), 95 (100), 81 (89), 71 (90), 55 (73), 43 (53).

(+)-(1'R,6'S)-4-(2',2',6'-Trimethylcyclohexyl)butan-2-one ((+)-**22a**). Obtained in 94% yield from (+)-**21a** following *Procedure G*. B.p. 70°/0.45 Torr. α_D^{20} = +10.9. IR: 2920, 1720, 1470, 1370, 1160, 980. ^{1}H-NMR: 0.56 (*m*, 1 H); 0.81 (*s*, 3 H); 0.89 (*d*, *J* = 7, 3 H); 0.89 (*s*, 3 H); 0.8–1.0 (*m*, 1 H); 1.15 (*m*, 1 H); 1.34 (*m*, 3 H); 1.44 (*m*, 2 H); 1.61 (*m*, 1 H); 1.71 (*m*, 1 H); 2.14 (*s*, 3 H); 2.35–2.58 (*m*, 2 H). ^{13}C-NMR: *Table 4*. MS: 196 (4, M^{+}), 181 (4), 163 (15), 138 (18), 123 (43), 109 (33), 95 (69), 82 (74), 69 (100), 55 (52), 43 (82).

(+)-(1'R,3'S,6'S)-4-(2',2',3',6'-Tetramethylcyclohexyl)butan-2-one ((+)-**22b**). Obtained in 87% yield from (+)-**21b** following *Procedure G*. B.p. 80°/0.6 Torr. α_D^{20} = +6.9. IR: 2960, 2940, 1720, 1460, 1360, 1220, 1160, 1040. ^{1}H-NMR: 0.50 (*m*, 1 H); 0.65 (*s*, 3 H); 0.82 (*d*, *J* = 7, 3 H); 0.80–0.90 (*m*, 1 H); 0.88 (*d*, *J* = 7, 3 H); 0.88 (*s*, 3 H); 1.00 (*m*, 1 H); 1.18 (*m*, 1 H); 1.22 (*m*, 1 H); 1.35 (*m*, 2 H); 1.60 (*m*, 1 H); 1.72 (*m*, 1 H); 2.13 (*s*, 3 H); 2.35–2.58 (*m*, 2 H). ^{13}C-NMR: *Table 4*. MS: 210 (4, M^{+}), 177 (8), 152 (9), 137 (20), 123 (13), 109 (38), 83 (46), 69 (49), 55 (59), 43 (100).

(+)-(1'R,6'S)-1-(2',2',6'-Trimethylcyclohexyl)pentan-3-one ((+)-**22c**). Obtained in 72% yield from (+)-**21c** following *Procedure G*. B.p. 70°/0.2 Torr. $[\alpha]_D^{20} = +9.6$ ($c = 2.1$, $CHCl_3$). IR: 2920, 1715, 1460, 1370, 1110. ^{1}H-NMR: 0.55 (*m*, 1 H); 0.80 (*s*, 3 H); 0.85–0.95 (*m*, 1 H); 0.88 (*d*, $J = 7$, 3 H); 0.88 (*s*, 3 H); 1.05 (*t*, $J = 7$, 3 H); 1.15 (*m*, 1 H); 1.34 (*m*, 3 H); 1.43 (*m*, 2 H); 1.62 (*m*, 1 H); 1.70 (*m*, 1 H); 2.33–2.55 (*m*, 2 H); 2.41 (*q*, $J = 7$, 2 H). ^{13}C-NMR: *Table 4*. MS: 210 (5, M^+), 181 (14), 177 (12), 163 (19), 138 (38), 123 (58), 109 (18), 95 (55), 83 (54), 69 (73), 57 (100).

(+)-(1'R,3'S,6'S)-1-(2',2',3',6'-Tetramethylcyclohexyl)pentan-3-one ((+)-**22d**). Obtained in 98% yield from (+)-**21d** following *Procedure G*. B.p. 75°/0.2 Torr. $[\alpha]_D^{20} = +5.0$ ($c = 1.2$, $CHCl_3$). IR: 2960, 2920, 1720, 1460, 1370, 1110. ^{1}H-NMR: 0.49 (*m*, 1 H); 0.65 (*s*, 3 H); 0.81 (*d*, $J = 7$, 3 H); 0.88 (*s*, 3 H); 0.88 (*d*, $J = 7$, 3 H); 0.75–0.93 (*m*, 1 H); 0.97 (*m*, 1 H); 1.05 (*t*, $J = 7$, 3 H); 1.14 (*m*, 1 H); 1.23 (*m*, 1 H); 1.34 (*m*, 2 H); 1.60 (*m*, 1 H); 1.74 (*m*, 1 H); 2.42 (*q*, $J = 7$, 2 H); 2.32–2.54 (*m*, 2 H). ^{13}C-NMR: *Table 4*. MS: 224 (3, M^+), 195 (6), 152 (15), 137 (24), 123 (18), 109 (36), 97 (41), 83 (65), 69 (50), 57 (100).

(+)-(1'R,6'S)-1-(2',2',6'-Trimethylcyclohexyl)hexan-3-one ((+)-**22e**). Obtained in 70% yield from (+)-**21e** following *Procedure G*. B.p. 74°/0.29 Torr. $\alpha_D^{20} = +8.5$. IR: 2925, 1715, 1460, 1370, 1125. ^{1}H-NMR: 0.54 (*m*, 1 H); 0.80 (*s*, 3 H); 0.86–0.96 (*m*, 1 H); 0.87 (*d*, $J = 7$, 3 H); 0.87 (*s*, 3 H); 0.91 (*t*, $J = 7$, 3 H); 1.14 (*m*, 1 H); 1.33 (*m*, 3 H); 1.43 (*m*, 2 H); 1.60 (*sext.*, $J = 7$, 2 H); 1.63 (*m*, 1 H); 1.68 (*m*, 1 H); 2.37 (*t*, $J = 7$, 2 H); 2.30–2.54 (*m*, 2 H). ^{13}C-NMR: *Table 4*. MS: 224 (4, M^+), 191 (9), 181 (17), 163 (22), 138 (47), 123 (64), 109 (19), 99 (41), 95 (58), 81 (53), 69 (100), 55 (57), 43 (90).

(+)-(1'R,3'S,6'S)-1-(2',2',3',6'-Tetramethylcyclohexyl)hexan-3-one ((+)-**22f**). Obtained in 96% yield from (+)-**21f** following *Procedure G*. B.p. 80°/0.05 Torr. $\alpha_D^{20} = +8.8$. IR: 2920, 1705, 1460, 1360, 790. ^{1}H-NMR: 0.49 (*m*, 1 H); 0.65 (*s*, 3 H); 0.75–1.07 (*m*, 2 H); 0.81 (*d*, $J = 7$, 3 H); 0.87 (*d*, $J = 7$, 3 H); 0.87 (*s*, 3 H); 0.91 (*t*, $J = 7$, 3 H); 1.18 (*m*, 1 H); 1.26 (*m*, 1 H); 1.33 (*m*, 2 H); 1.60 (*sext.*, $J = 7$, 2 H); 1.77 (*m*, 2 H); 2.37 (*t*, $J = 7$, 2 H); 2.31–2.54 (*m*, 2 H). ^{13}C-NMR: *Table 4*. MS: 238 (12, M^+), 195 (13), 177 (11), 152 (20), 137 (23), 109 (22), 97 (30), 83 (43), 71 (82), 55 (66), 43 (100), 41 (81).

REFERENCES

[1] a) F. Tiemann, P. Kruger, *Chem. Ber.* **1893,** *26,* 2675; b) *ibid.* **1898,** *31,* 809, 870, 874, 1737.

[2] L. Ruzicka, C. F. Seidel, H. Schinz, *Helv. Chim. Acta* **1933,** *16,* 1143.

[3] a) L. Ruzicka, C. F. Seidel, H. Schinz, M. Pfeiffer, *Helv. Chim. Acta* **1947,** *30,* 1807; b) H. Schinz, L. Ruzicka, C. F. Seidel, Ch. Tavel, *ibid.* **1947,** *30,* 1810; c) *ibid.* **1948,** *31,* 257.

[4] a) Y. R. Naves, *Helv. Chim. Acta* **1948,** *31,* 151; b) *ibid.* **1948,** *31,* 1871.

[5] a) Y. R. Naves, *Bull. Soc. Chim. Fr.* **1950,** *17,* D99; b) H. Schinz, 'Die Veilchenriechstoffe', *Fortschr. Chem. Org. Naturst.* **1951,** *8,* 146.

[6] a) E. Gildemeister, F. Hoffmann, *Riechst. Aromen* **1963,** *IIIc,* 368; b) 'Die aetherischen Öle', Akademie Verlag Berlin, 1956, Vol. IV, p. 460.

[7] a) V. Rautenstrauch, G. Ohloff, *Helv. Chim. Acta* **1971,** *54,* 1776; b) *ibid.* **1972,** *55,* 2686.

[8] a) R. ter Heide, N. Provatoroff, P. C. Traas, P. J. de Valois, N. Van der Plasse, H. J. Wobben, R. Timmer, *J. Agric. Food Chem.* **1975,** *23,* 950; b) Y. R. Naves, *Riv. Ital. EPPOS* **1977,** *59,* 507.

[9] a) F. J. Marner, L. Jaenicke, *Helv. Chim. Acta* **1989,** *72,* 287; b) W. Krick, F. J. Marner, L. Jaenicke, *ibid.* **1984,** *67,* 318; c) Y. R. Naves, P. Ardizio, *C. R. Hebd. Séances Acad. Sci.* **1954,** *238,* 2444; d) L. and J. Crabalona, *Parfums Cosm. Savons* **1954,** *100,* 15.

[10] a) F. J. Marner, T. Range, W. A. König, *Helv. Chim. Acta* **1990,** *73,* 2165; b) A. Galfré, P. Martin, M. Petrzilka, *J. Essent. Oil Res.* **1993,** *5,* 265.

[11] a) F. J. Marner, D. Gladtke, L. Jaenicke, *Helv. Chim. Acta* **1988,** *71,* 1331; b) L. Jaenicke, F. J. Marner, *Progr. Chem. Org. Nat. Prod.* **1986,** *50,* 1.

[12] a) J. Crabalona, *Fr. Ses. Parfums* **1959,** *13,* 22; b) C. F. Seidel, L. Ruzicka, *Helv. Chim. Acta* **1952,** *35,* 1826; c) Hs. H. Günthard, C. F. Seidel, L. Ruzicka, *ibid.* **1952,** *35,* 1820; d) P. Bächli, C. F. Seidel, H. Schinz, L. Ruzicka, *ibid.* **1949,** *32,* 1744; e) L. Ruzicka, C. F. Seidel, H. Schinz, M. Pfeiffer, *ibid.* **1942,** *25,* 188; f) L. Ruzicka, C. F. Seidel, G. Firmenich, *ibid.* **1941,** *24,* 1434.

[13] a) Y. Ohtsuka, F. Itoh, T. Oishi, *Chem. Pharm. Bull. Tokyo* **1991,** *39,* 2540; b) D. Helmlinger, G. Fràter, *Helv. Chim. Acta* **1989,** *72,* 1515; c) V. Rautenstrauch, B. Willhalm, W. Thommen, G. Ohloff, *ibid.* **1984,** *67,* 325; d) M. Miyashita, N. Makino, M. Singh, A. Yoshikoshi, *J. Chem. Soc., Perkin Trans. 1* **1982,** 1303; e) H. E. Eschinazi, *J. Am. Chem. Soc.* **1959,** *81,* 2905.

[14] K. H. Schulte-Elte, H. Pamingle, A. P. Uijttewaal, R. L. Snowden, *Helv. Chim. Acta* **1992,** *75,* 759.
[15] a) C. Chapuis, B. Winter, K. H. Schulte-Elte, *Tetrahedron Lett.* **1992,** *33,* 6135; b) C. Chapuis, R. Brauchli, W. Thommen, *Helv. Chim. Acta* **1993,** *76,* 535; c) J. P. Gesson, J. C. Jacquesy, B. Renoux, *Tetrahedron* **1989,** *45,* 5853.
[16] C. Chapuis, R. Brauchli, *Helv. Chim. Acta* **1992,** *75,* 1527.
[17] a) C. Chapuis, K. H. Schulte-Elte, H. Pamingle, C. Margot (to *Firmenich SA*) EP-A1-449.034 (2.10.91) (*CA:* **1992,** *116,* 235920c); b) D. Kastner, B. Maurer, *Parfuem. Kosmet.* **1990,** *71,* 411, 532.
[18] a) H. Favre, H. Schinz, *Helv. Chim. Acta* **1958,** *41,* 1368; b) J. Garnero, D. Joulain (to *Robertet Cie*) FP-2404616 (30.9.1977) (*CA:* **1980,** *92,* 22656v); c) T. Kawanobe, M. Iwamoto, K. Kogami, M. Matsui, in 'Flavors and Fragances: A World Perspective'; 10th Int. Congress of Essentials Oils, Eds. B. M. Lawrence, B. D. Mookherjee, and B. J. Willis, 1986, p. 801; d) K. Mori, T. Kitahara, T. Kawanobe, M. Iwamoto, Y. Katsuta (to *Hasegawa Co. Ltd.*) JP-61.243.035 (29.10.1986) (*CA:* **1987,** *106,* 120104r).
[19] O. Takazawa, K. Kogami, K. Hayashi, *Bull. Chem. Soc. Jpn.* **1985,** *58,* 389.
[20] a) C. Nussbaumer, G. Fràter, *Helv. Chim. Acta* **1988,** *71,* 619; b) T. Kawanobe, M. Iwamoto, M. Katsuta, H. Tamura, K. Kojo (to *Hasegawa Co. Ltd*) JP-61.243.041 (29.10.1986) (*CA:* **1987,** *106,* 120105s).
[21] a) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965,** *87,* 1353; b) P. Mosset, R. Gree, *Synth. Commun.* **1985,** *15,* 749; c) H. Bouda, M. E. Borredon, M. Delmas, A. Gasset, *ibid.* **1987,** *17,* 503; d) B. Byrne, L. Lafleur, *Tetrahedron Lett.* **1986,** *27,* 1233.
[22] a) H. Schostarez, L. A. Paquette, *J. Am. Chem. Soc.* **1981,** *103,* 722; b) A. Leone-Bay, L. A. Paquette, *J. Org. Chem.* **1982,** *47,* 4173.
[23] B. Maurer, A. Hauser, *Helv. Chim. Acta* **1983,** *66,* 2223.
[24] J. Garnero, D. Joulain, *Bull. Soc. Chim. Fr.* **1979,** *II,* 15.
[25] K. Omura, D. Swern, *Tetrahedron* **1978,** *34,* 1651.
[26] T. Kawanobe, M. Iwamoto, K. Kogami, M. Matsui, *Agric. Biol. Chem.* **1987,** *51,* 791.
[27] a) B. Maurer, A. Hauser, J. C. Froidevaux, *Helv. Chim. Acta* **1989,** *72,* 1400; b) B. Maurer, A. Hauser, *Riv. Ital. EPPOS* **1991,** *73,* 116.
[28] R. Zerbes, S. Linke, K. H. Mohrmann, W. Reiser (to *Bayer AG*) EP-A2-0124011 (7.11.84) (*CA:* **1985,** *102,* 78707e).
[29] L. Ruzicka, H. Schinz, *Helv. Chim. Acta* **1940,** *23,* 959.
[30] A. M. Moiseenkov, V. V. Veselovskii, V. A. Dragan, G. A. Stashina, V. M. Zhulin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989,** *11,* 2607.
[31] J. Garnero, D. Joulain, *Riv. Ital EPPOS* **1981,** *63,* 141.
[32] K. H. Schulte-Elte, B. Müller, C. Chapuis, in preparation.
[33] N. Müller, W. Hoffmann. *Synthesis* **1975,** 781.
[34] a) R. Adams, L. H. Ulich, *J. Am. Chem. Soc.* **1920,** *42,* 599; b) C. R. Engel, G. Just, *Can. J. Chem.* **1955,** *33,* 1515.
[35] a) F. Naef, R. Decorzant, *Tetrahedron* **1986,** *42,* 3245; b) J. D. Wuest, A. M. Madonik, D. C. Gordon, *J. Org. Chem.* **1977,** *42,* 2111.
[36] C. Fehr, *Chimia* **1991,** *45,* 253.
[37] A. Gopalan, P. Magnus, *J. Am. Chem. Soc.* **1980,** *102,* 1756.
[38] F. Mohamadi, N. Richards, W. Guida, R. Liskamp, M. Lipton, C. Canfield, G. Chang, T. Hendrickson, W. Still, *J. Comput. Chem.* **1990,** *11,* 440.
[39] a) C. J. W. Brooks, G. Lindsay, K. H. Overton, *J. Chem. Soc. (C)* **1970,** 203; b) J. R. Hlubucek, A. J. Aasen, S. O. Almqvist, C. R. Enzell, *Acta Chem. Scand., Ser. B28* **1974,** *1,* 18.
[40] a) A. M. Sakharov, I. P. Skibida, *J. Mol. Catal.* **1988,** *48,* 157; b) C. Jallabert, C. Lapinte, H. Riviere, *ibid.* **1982,** *14,* 75; c) C. Jallabert, H. Riviere, *Tetrahedron* **1980,** *36,* 1191; d) P. Capdevielle, P. Audebert, M. Maumy, *Tetrahedron Lett.* **1984,** *25,* 4397; e) V. P. Tretyakov, G. P. Zimtseva, E. S. Rudakov, A. V. Bogdanov, *React. Kinet. Catal. Lett.* **1982,** *19,* 263; f) S. Bhaduri, N. Y. Sapre, *J. Chem. Soc., Dalton Trans.* **1981,** 2585; g) M. Munakata, S. Nishibayashi, H. Sakamoto, *J. Chem. Soc., Chem. Commun.* **1980,** 219.
[41] a) G. V. Subbaraju, Z. Urbanczyk-Lipkowska, S. N. Newaz, M. S. Manhas, A. K. Bose, *Tetrahedron* **1992,** *48,* 10087; b) G. V. Subbaraju, V. Subbaraju, M. S. Manhas, A. K. Bose, *Synthesis* **1992,** *9,* 816.
[42] P. Bächli, H. Schinz, *Helv. Chim. Acta* **1951,** *34,* 1168.
[43] C. Chapuis, C. Margot, K. H. Schulte-Elte, H. Pamingle (to *Firmenich S. A.*). EP-A1-374-509 (27.6.90) (*CA:* **1991,** *114,* 43240t).
[44] D. Serramedan, F. Marc, M. Pereyre, C. Filliatre, P. Chabardès, B. Delmond, *Tetrahedron Lett.* **1992,** *33,* 4457.

[45] K. H. Schulte-Elte, C. Margot, D. P. Simmons, C. Chapuis, D. Reichlin (to *Firmenich SA*) EP-A1-457.022 (21.11.91) priority (16.5.90) CH-1671/90 (*CA:* **1992,** *117,* 8242k).
[46] A. Storni, Ph. D. Thesis, No. 3203, ETH-Zürich, 1962, p. 64.
[47] K. H. Schulte-Elte, W. Giersch, B. Winter, H. Pamingle, G. Ohloff, *Helv. Chim. Acta* **1985,** *68,* 1961.
[48] V. K. Singh, *Synthesis* **1992,** *7,* 605.
[49] a) T. Ohmoto, A. Shimada, T. Yamamoto (to *Takasago Perf. Co. Ltd.*) EP-Al-456.932 (21.11.91) priority (17.5.90) JP-125520/90 (*CA:* **1992,** *116,* 128234k); b) A. Shimada, T. Ohmoto, T. Yamamoto (to *Takasago Perf. Co. Ltd.*) JP-0421.649 (24.1.92) priority (17.5.90) JP-125521/90 (*CA:* **1992,** *117,* 25973s); c) A. Shimada, T. Ohmoto, T. Yamamoto, 34th Symposium of Terpenes, Essential oils and Aromatic Chemistry, 23–25 Oct., 1990, Takamatsu, p. 101.
[50] a) D. P. Simmons, C. Chapuis (to *Firmenich SA*) EP-Bl-324.111 (19.7.89) (*CA:* **1990,** *112,* 118318u); b) C. Margot, Xth Congress of ECRO, 23–28 Aug., 1992, Munich; c) D. P. Simmons, D. Reichlin, D. Skuy, C. Margot, *Helv. Chim. Acta,* in preparation.
[51] D. P. Simmons, D. Reichlin, D. Skuy, *Helv. Chim. Acta* **1988,** *71,* 1000.
[52] a) R. Buchecker, R. Egli, H. Regel-Wild, C. Tscharner, C. H. Eugster, G. Uhde, G. Ohloff, *Helv. Chim. Acta* **1973,** *56,* 2548; b) G. Ohloff, C. Vial, *ibid.* **1977,** *60,* 2767; c) T. Oritani, K. Yamashita, *Agric. Biol. Chem.* **1987,** *51,* 1271.
[53] R. P. Adams, T. A. Zanoni, L. Hogge, *J. Nat. Prod.* **1985,** *48,* 673.
[54] T. Yamamoto, H. Matsuda T. Ohmoto, A. Shimada, T. Sato, 12th Int. Congr. of Flavors Fragances and Essential Oils 4–8 Oct., 1992, Vienna, Eds. H. Woidich and G. Buchbauer, p. 442.
[55] a) V. Prelog, H. Frick, *Helv. Chim. Acta* **1948,** *31,* 417; b) D. R. de Haan, D. K. Kettenes (to *P. F. W. Beheer*) DP-2353578 (9.5.74) (*CA:* **1974,** *81,* 25196d); c) M. de Botton *Bull. Soc. Chim. Fr.* **1966,** 2212, 2466; d) L. Colombi, A. Bosshard, H. Schinz, C. F. Seidel, *Helv. Chim. Acta* **1951,** *34,* 265.
[56] N. W. Davies, *Perfum. Flavor* **1984,** *8,* 3.
[57] F. Chialva, P. A. P. Liddle, F. Ulian, P. de Smedt, *Riv. Ital. EPPOS* **1980,** *6,* 297.