Syntheses of the Enantiomers of *Vulcanolide*®

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The synthesis of the enantiomers of *Vulcanolide*® ((±)-**7**) is described, the strongest musk odorant among hundreds of structurally related analogues, by resolution of an intermediate. To this end, we devised a new route which involves the temporary introduction of a modulable functional group in the vicinity of the stereogenic centers (*Scheme 2*). The resolution is based on the chromatographic separation of two diastereoisomeric camphanic acid esters. The strong and characteristic note of racemic *Vulcanolide*® is almost entirely due to the (–)-enantiomer. This synthesis has allowed the preparation of new, structurally related musk odorants.

1. Introduction. – The outstanding place of musk odorants in perfumery derives from their characteristic odor which is referred to as warm, sensual, animal, natural, and to the fact that they are longlasting and tenacious. Interestingly, the musk odor is found in a large variety of structural classes, as exemplified by structures **1**–**6** (*Fig. 1*).

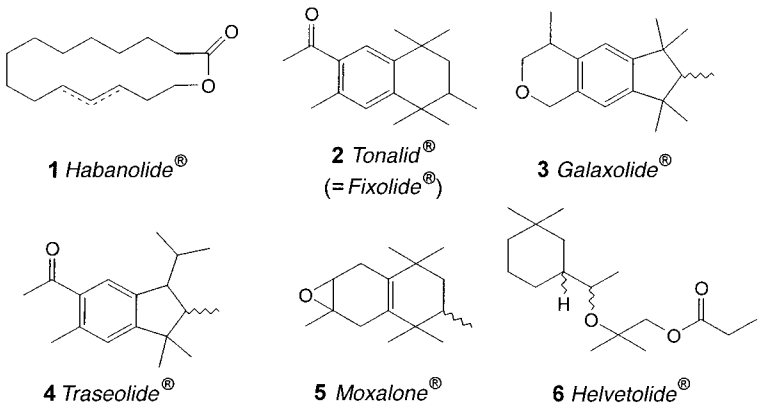

Fig. 1. *Musk odorants*

In recent years, the macrocyclic musk odorants [1] have become increasingly important due to their good biodegradability, but the benzenoid musks *Tonalid*® (*Polak's Frutal Works*; identical to *Fixolide*® (*Givaudan*)) and *Galaxolide*® (*International Flavors and Fragrances*), although showing some bioaccumulation problems, still represent the highest tonnage products (several thousands of tons per year), due to an excellent price/performance ratio [2][3]. *Moxalone*® (*Givaudan*) [4] and *Helvetolide*® (*Firmenich*) [5] represent examples of more recent musk odorants. Interestingly, the structure of *Helvetolide*® is quite unique.

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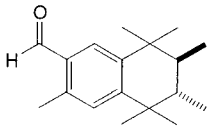
In 1989, we reported that incorporation of supplementary Me groups into the basic skeleton of benzenoid musks leads to excellent new musk odorants, possessing densely packed structures of enhanced lipophilicity but of similar global shape [6]. This allowed the discovery of *Vulcanolide*® ((±)-**7**; *Fig. 2*) which turned out to be 10–20 times stronger than *Tonalid*® (**2**), previously considered as the strongest musk odorant among hundreds of structurally related analogues. Whereas the amount of benzenoid musks in perfume compositions typically exceeds 10%, 0.1% of *Vulcanolide*® ((±)-**7**) displays already a marked effect. Moreover, it is also much more tenacious than *Tonalid*® (**2**).



(±)-**7** *Vulcanolide*®

Fig. 2. *Structure of* Vulcanolide® ((±)-**7**)

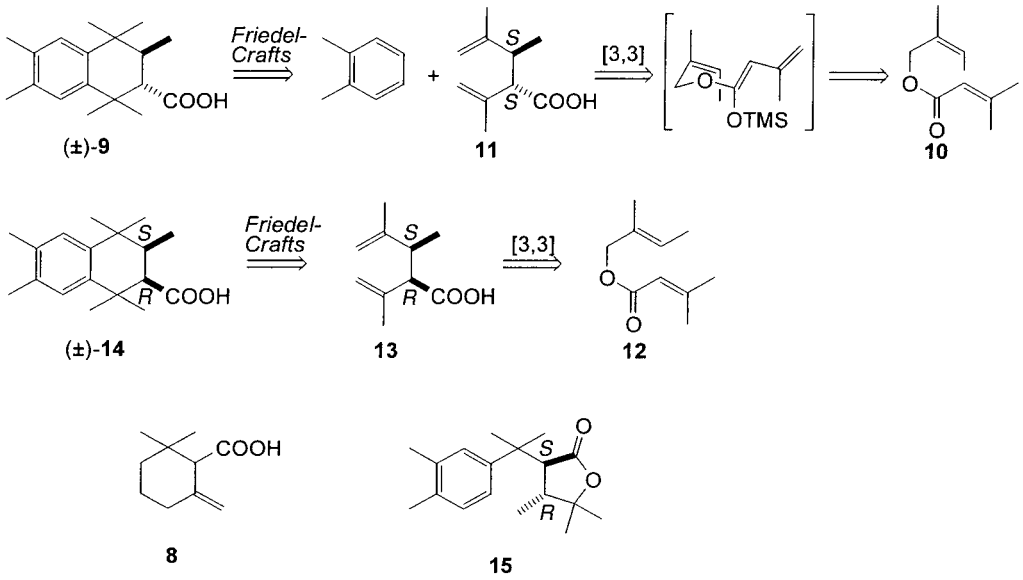
In view of the exceptional odor strength of *Vulcanolide*®, we asked ourselves whether only one enantiomer was responsible for the odor. This would allow the use of even smaller amounts of *Vulcanolide*®, without change in perception and less of a problem for the environment.

The importance of the lipophilic part of the benzenoid musk odorants for the perception of musk odor, as reflected by its structural requirements, has been already discussed [3][6]. Indeed, only the (*S*)-enantiomer of *Tonalid*® is organoleptically active [7]. Similarly, only the *trans*-substituted diastereoisomers of both *Traseolide*® [8] and *Vulcanolide*® (see below) exhibit strong musk character. Very recently, a marked difference in odor intensity was noticed for the enantiomers of both diastereoisomers of *Galaxolide*® [9].

2. Results and Discussion. – For the preparation of the two enantiomers of *Vulcanolide*®, we envisaged the application of classical resolution techniques, but our task was complicated by the fact that derivatization of the aldehyde function with chiral diols or diamines leads to inseparable diastereoisomer mixtures, as the newly created chiral centers are too far away from the pre-existing ones. Therefore, we devised a new synthesis, allowing the temporary introduction of a modulable functional group in the vicinity of the stereogenic centers. In analogy to the successful resolution of γ-cyclogeranic acid (**8**) with (*R*)- or (*S*)-(1-phenylethyl)amine [10], carboxylic acid (±)-**9** was considered a good candidate for resolution. We expected that (±)-**9** would be readily available from ester **10** *via* an *Ireland-Claisen* rearrangement [11], followed by a double *Friedel-Crafts* alkylation-cyclization of *o*-xylene with acid **11** (*Scheme 1*). In the event, **11** (containing 5% of its diastereoisomer) could be readily prepared, but did not undergo the *Friedel-Crafts* alkylation sequence. In contrast, the sequence with the isomeric series **12**–**14**, *via* the intermediacy of lactone **15**, worked well.

As epimerization of (±)-**14** required harsh conditions (AcOH, conc. HCl solution, 190°, 3 days [12]) and gave a 9:1 mixture of (±)-**9** and (±)-**14** in *ca.* 70% yield, this

Scheme 1



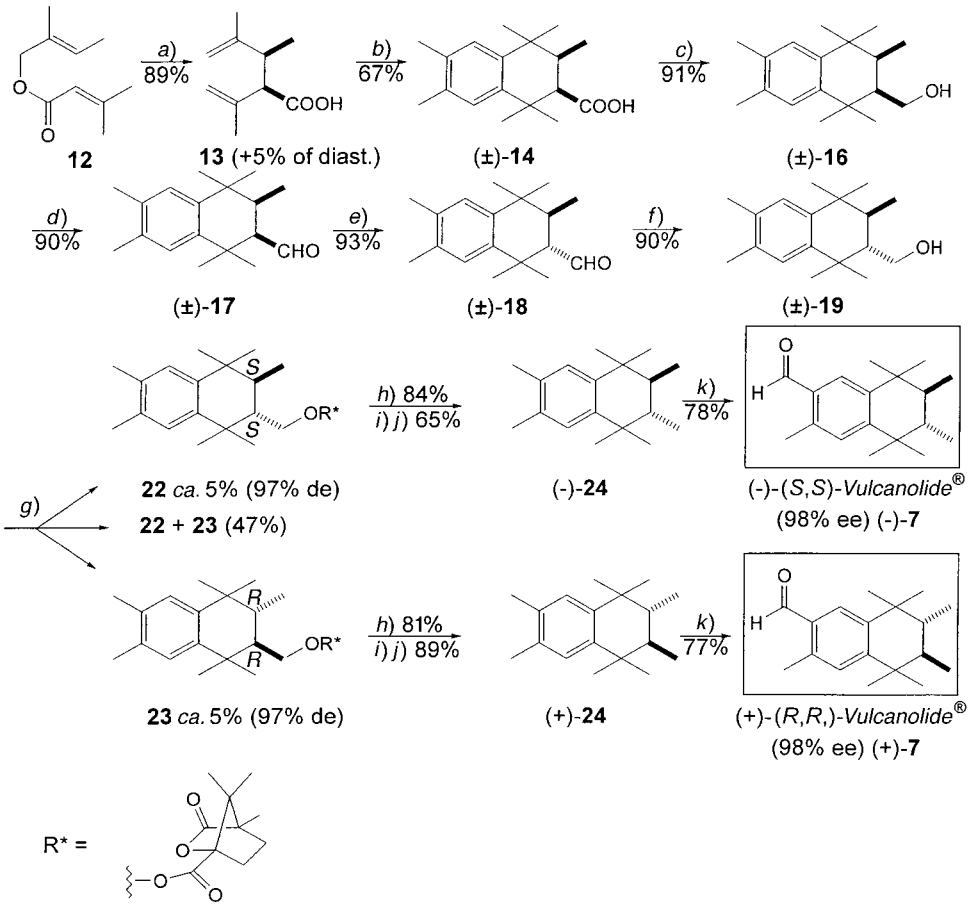
isomerization was postponed to a later stage of the synthesis. The resolution with (±)-(*R*)-(1-phenylethyl)amine was, therefore, attempted on acid (±)-**14**. Unfortunately, we were unable to crystallize an enantiomer-enriched ammonium carboxylate. Neither by variation of the solvent nor by pre-formation of the sodium salt possessing a different melting point phase diagram [13], could we favor crystallization of one enantiomeric species. We were not more successful with other chiral amines such as ephedrine, quinine, cinchonidine, or (−)-(1*R*,2*R*)-cyclohexane-1,2-diamine.

Therefore, we next concentrated our efforts on the derivatization of one of our synthetic intermediates with a chiral auxiliary, hoping that one of these newly formed diastereoisomer pairs would allow chromatographic separation. *Scheme 2* shows the straightforward synthesis of *trans*-disubstituted alcohol (±)-**19** by reduction of (±)-**14** and oxidation of (±)-**16** to the *cis*-aldehyde (±)-**17**, and epimerization to the *trans*-aldehyde (±)-**18** followed by reduction. Whereas MeONa (in MeOH at reflux) was not a strong enough base to effect this isomerization, *t*-BuOK (in *t*-BuOH at reflux) readily afforded a *trans*-rich isomer mixture (85 : 15). Interestingly, the equilibrium could be greatly shifted towards *trans*-aldehyde (±)-**18** by performing the epimerization at 20° ((±)-**18**/(±)-**17** 98 : 2).

After several unsuccessful experiments, all affording inseparable diastereoisomer mixtures (acid chloride of (±)-**14** + (−)-camphor-10,2-sultam [14]; (±)-**17** + diamine **20** [15] or (*R*,*R*)-butane-2,3-diol; (±)-**16** + (−)-camphanoyl chloride (**21**) [16]) (see *Scheme 3*), we finally found that esterification of the *trans*-alcohol (±)-**19** with (−)-camphanoyl chloride (**21**) [16] afforded a separable mixture of camphanic acid esters **22** and **23** (*Scheme 2*).

Chromatographic separation and recrystallization afforded the two chiral, almost diastereoisomerically pure esters **22** and **23** which were separately transformed into

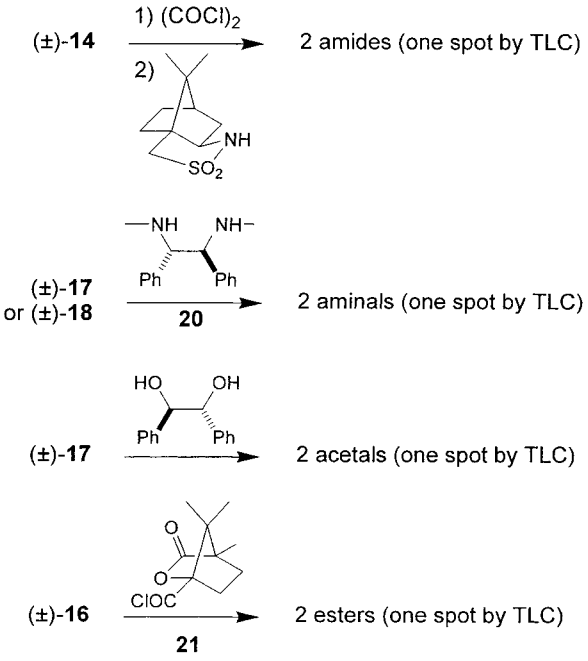
Scheme 2



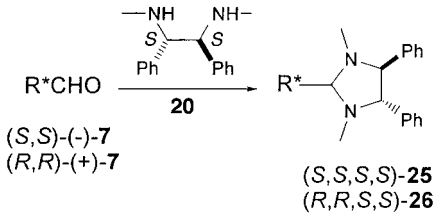
a) See [11b]. *b*) $AlCl_3$ (3.0 equiv.), *o*-xylene, 15 → 25°. *c*) $LiAlH_4$ (5.0 equiv.), Et_2O, reflux. *d*) Pyridinium chlorochromate (PCC; 1.34 equiv.), *Celite*, CH_2Cl_2, 20°. *e*) *t*-BuOK (0.1 equiv.), *t*-BuOH, 20°. *f*) $LiAlH_4$ (1.0 equiv.), Et_2O, −40°. *g*) **21** (1.1 equiv.), pyridine, cat. *N*,*N*-dimethylpyridin-4-amine (DMAP); chromatography. *h*) KOH (1.2 equiv.), EtOH, H_2O, 80°. *i*) TsCl (1.15 equiv.), pyridine, 5°. *j*) $LiBHEt_3$ (2.0 equiv.), THF, 0 → 20°. *k*) See [6].

(−)- and (+)-*Vulcanolide*® ((−)- and (+)-**7**, resp.) of at least 98% ee. This involved the following steps: Saponification to (−)- and (+)-**19**, tosylation and reduction of the crude tosylates with $LiBHEt_3$ [17], and finally oxidation of the resultant hydrocarbons (−)- and (+)-**24** with the cerium(IV) reagent $Ce(NH_4)_2(NO_3)_6$ (CAN) as reported for the synthesis of racemic **7** [6]. The chromatographically purified enantiomers of *Vulcanolide*® were further purified by crystallization from EtOH. As separation on chiral GC columns proved difficult, the enantiomer purity was determined by conversion of (−)-**7** and (+)-**7** into the diastereoisomeric imidazolidines (*S*,*S*,*S*,*S*)-**25** and (*R*,*R*,*S*,*S*)-**26** respectively, with enantiomerically pure (−)-(*S*,*S*)-*N*,*N*-dimethyl-1,2-diphenylethane-1,2-diamine ((−)-(*S*,*S*)-DMPEDA; **20**) (*Scheme 4*) [15]. The diastereoisomer excess

Scheme 3



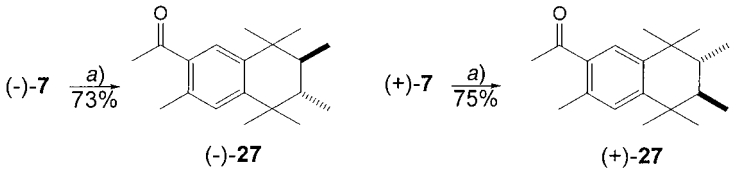
Scheme 4



was shown by NMR to be 98–99% for (*S*,*S*,*S*,*S*)-**25** and 97–98% for (*R*,*R*,*S*,*S*)-**26**. Thus, the enantiomer excesses of (−)-**7** and (+)-**7** are at least 98 and 97%, respectively.

As racemic methyl ketone **27**, a methyl homologue of *Tonalid*® (**2**), is also a very strong musk odorant (stronger than *Tonalid*®, but weaker than *Vulcanolide*®), the two

Scheme 5



a) See [6].

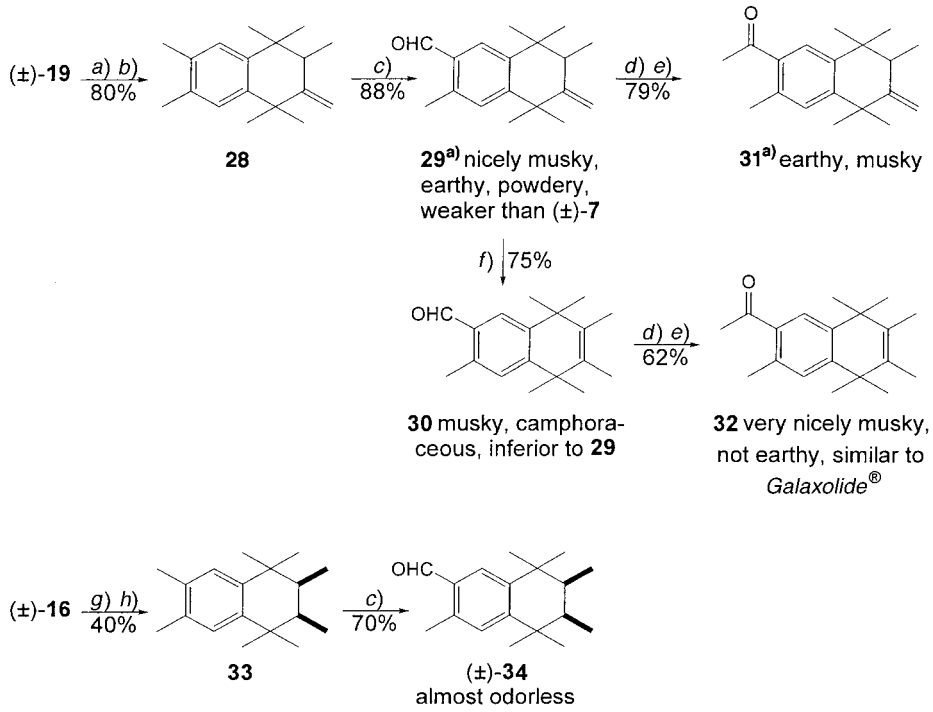
enantiomers of *Vulcanolide*® were converted by MeLi addition and pyridinium chlorochromate (PCC) oxidation into the two enantiomers of **27** (*Scheme 5*).

(−)-*Vulcanolide*® is extremely strong, both on the smelling strip and in perfume compositions. Surprisingly, an earthy note predominates on the smelling strip, but in perfume compositions or by smelling the crystals, the musk character is perceived exclusively. When highly diluted, (−)-*Vulcanolide*® also exhibits the musk odor on the smelling strip. (+)-*Vulcanolide*® is much weaker and less tenacious, although it also possesses an agreeable musk odor. We cannot exclude that the odor of (+)-**7** is due to trace amounts of (−)-**7** (*ca.* 1%). Similarly, (−)-**27** is strongly musky, whereas (+)-**27** is a much weaker musk odorant.

As the extremely strong and characteristic note of racemic *Vulcanolide*® is almost entirely due to the (−)-enantiomer, there was an interest to devise an enantioselective route to (−)-**7**. This [18], as well as the determination of the absolute configuration, has been published separately [19].

The ready accessibility of (±)-**19** also allowed us to prepare new benzenoid musks (*Scheme 6*). Thus, pyrolysis of the methyl carbonate derived from (±)-**19** furnished

Scheme 6



a) BuLi (1.0 equiv.), THF, −15°; ClCOOMe (1.1 equiv.), 0°. *b) 450°, toluene (pyrolysis)*. *c*) $Ce(NH_4)_2(NO_3)_6$ (10.0 equiv.), MeOH, 55° (see [6]). *d*) MeLi (1.1 equiv.), Et_2O, −30°. *e*) PCC (1.4 equiv.), CH_2Cl_2, 20°. *f*) $TsOH \cdot H_2O$ (0.4 equiv.), toluene, 85°. *g*) TsCl (1.44 equiv.), pyridine, 5°, then 20°. *h*) $LiBHEt_3$ (4.0 equiv.), THF and 0 → 65°, then $(CH_2OMe)_2$ and 65 → 100°.

[a]) Mixture of regioisomers.

hydrocarbon **28**. Cerium(IV) oxidation gave **29** (+constitutional isomer). TsOH-Catalyzed isomerization of the C=C bond afforded aldehyde **30**. These two aldehydes were converted into the methyl ketones **31** and **32** by MeLi addition followed by PCC oxidation.

All four compounds **29**–**32** are musk odorants, but only aldehyde **29** and ketone **32** possess a pronounced and fine musk odor.

In view of the extremely powerful musk odor of *Vulcanolide*® ((±)-**7**), we questioned our earlier statement [6] which proposed that the *cis*-diastereoisomer (±)-**34** of *Vulcanolide*®, although much weaker than *Vulcanolide*®, was still a strong musk odorant. Indeed, the pleasant musky character, devoid of any earthy notes, could just as well be due to trace amounts of the *trans*-diastereoisomer (±)-**7**. Therefore, (±)-**16** was converted *via* the isomerically pure hydrocarbon **33** into the *cis*-aldehyde (±)-**34** by applying the same reaction sequence as for the *trans*-isomers. Interestingly, aldehyde (±)-**34** proved to be almost odorless.

Experimental Part

General. TLC: silica gel *F-254* plates (*Merck*); detection with EtOH/anisaldehyde/H_2SO_4 18:1:1. Column chromatography: silica gel *60* (*Merck*; 0.063–0.2 mm, 70–230 mesh, ASTM); FC = flash chromatography. GC: *Varian* instrument, model *3500*; cap. columns: *DB1 30 W* (15 m × 0.319 mm), *DB-WAX 15W* (15 m × 0.32 mm); chiral cap. column: *Megadex 5* (16 m × 0.25 mm; *Megadex Capillary Columns Laboratory*, Via Plinio 29, I-20025 Legnano, Italy) or *CP-Chirasil-DEX CB* (25 m × 0.25 mm; *Chrompack*), carrier gas He at 0.63 bar. Optical rotations: 1-ml cell, *Perkin-Elmer-241* polarimeter. ^{1}H- and ^{13}C-NMR: *Bruker WH-360* (360 MHz). MS: *Finnigan-1020* automated GC/MS instrument; electron energy 70 eV.

*(2*RS,*3*RS*)-3,4-Dimethyl-2-(1-methylethenyl)pent-4-en-1-oic Acid* (**11**). Prepared from **10** according to [11], with lithium diisopropylamide (1.1 equiv.) and chlorotrimethylsilane (1.1 equiv.): 80% yield (containing 3% of diastereoisomer **13**; only detected on a *DB-WAX* GC column): M.p. 94–96°. ^{1}H-NMR: 1.11 (*d*, *J* = 7.3 H); 1.64 (*s*, 3 H); 1.78 (*s*, 3 H); 2.81 (*dq*, *J* = 12, 7, 1 H); 3.11 (*d*, *J* = 12, 1 H); 4.75 (*s*, 2 H); 4.94 (*s*, 2 H); 11.25 (br., 1 H). ^{13}C-NMR: 179.6 (*s*); 146.6 (*s*); 141.3 (*s*); 116.0 (*t*); 112.2 (*t*); 58.1 (*d*); 41.6 (*d*); 19.4 (*q*); 18.6 (*q*); 18.0 (*q*). MS: 168 (trace, $M^{+\cdot}$), 153 (6), 139 (2), 123 (26), 111 (16), 100 (28), 82 (19), 69 (82), 53 (12), 41 (100).

*(2*RS,*3*SR*)-3,4-Dimethyl-2-(1-methylethenyl)pent-4-en-1-oic Acid* (**13**) [11b]. Prepared from **12** according to [11], with lithium diisopropylamide (1.1 equiv.) and chlorotrimethylsilane (1.1 equiv.): 89% yield (containing 5% of diastereoisomer **11**, only detected on a *DB-WAX* GC column). According to [11b], use of lithium cyclohexylisopropylamide (1.2 equiv.) in THF (without hexane) and chlorotrimethylsilane (2.0 equiv.) afforded **13** in 98% yield and 100% diastereoselectivity.

*(2*RS,*3*SR*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-carboxylic Acid* ((±)-**14**). A soln. of **13** (10.0 g, 59.5 mmol) in *o*-xylene (100 ml) was added during 20 min to a suspension of $AlCl_3$ (23.8 g, 178.6 mmol) in *o*-xylene (150 ml) at 15°. After the end of the addition, GC analysis showed that **13** had been completely converted to lactone **15**. Stirring was continued at 20–25° until disappearance of **15** (40 min). The mixture was then poured on conc. HCl soln./ice (−10°) and extracted (Et_2O, 3 ×). The org. phases were washed to neutrality (H_2O, 2 ×) and treated with 5% aq. NaOH soln. After 3 alkaline extractions (5% aq. NaOH soln.), the aq. phases were acidified (conc. HCl soln.) and extracted (Et_2O, 3 ×). The org. phases were washed (H_2O (3 ×), then sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated (16.0 g). Crystallization from petroleum ether (80–100°) containing some acetone afforded pure (±)-**14** (11.0 g, 67%) and 3.67 g of residue from the mother liquors containing 30% of (±)-**14** (6%). M.p. 182–185°. ^{1}H-NMR: 1.12 (*d*, *J* = 7, 3 H); 1.27 (*s*, 3 H); 1.30 (*s*, 3 H); 1.38 (*s*, 3 H); 1.48 (*s*, 3 H); 2.23 (2*s*, 6 H); 2.27 (*m*, 1 H); 2.82 (*d*, *J* = 4, 1 H); 7.07 (2*s*, 2 H); COOH not visible. ^{13}C-NMR: 180.1 (*s*); 141.0 (*s*); 140.8 (*s*); 134.0 (*s*); 133.9 (*s*); 127.9 (*d*); 127.0 (*d*); 54.0 (*d*); 38.8 (*d*); 37.0 (*s*); 35.8 (*s*); 34.7 (*q*); 33.8 (*q*); 27.9 (*q*); 26.6 (*q*); 19.5 (2*q*); 14.7 (*q*). MS: 274 (26, $M^{+\cdot}$), 259 (52), 213 (100), 198 (18), 173 (17), 157 (13), 141 (13), 128 (13), 115 (10), 91 (9), 41 (17).

*(2*RS,*3*RS*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-carboxylic Acid* ((±)-**9**. Isolated from an unexpected oxidation during an epimerization experiment to convert (±)-**17** into (±)-**18** (*t*-BuOK, *t*-BuOH, 85°). Also obtained in *ca*. 70% yield by epimerization of (±)-**14** (AcOH, conc. HCl soln., 190°, 3 days)

according to [12]. M.p. 191–200°. ^{1}H-NMR: 1.08 (*d*, *J* = 7, 3 H); 1.13 (*s*, 3 H); 1.34 (*s*, 3 H); 1.35 (*s*, 3 H); 1.44 (*s*, 3 H); 2.14 (*dq*, *J* = 12, 7, 1 H); 2.24 (2*s*, 6 H); 2.63 (*d*, *J* = 12, 1 H); 7.09 (*s*, 1 H); 7.11 (*s*, 1 H); COOH not visible. ^{13}C-NMR: 181.1 (*s*); 141.7 (*s*); 140.1 (*s*); 134.3 (*s*); 134.1 (*s*); 128.3 (*d*); 126.7 (*d*); 54.7 (*d*); 37.4 (*s*); 36.4 (*s*); 35.8 (*d*); 34.7 (*q*); 29.6 (*q*); 29.0 (*q*); 28.2 (*q*); 25.9 (*q*); 19.5 (*q*); 13.8 (*q*). MS: 274 (29, $M^{+\bullet}$), 259 (49), 213 (100), 198 (20), 184 (12), 171 (12), 157 (11), 141 (11), 128 (10), 115 (8), 91 (8), 45 (11).

*(2*RS,*3*SR*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-methanol* ((±)-**16**). A soln. of (±)-**14** (33.6 g, 122.7 mmol) in Et_2O (400 ml) was added to a suspension of $LiAlH_4$ (6.30 g, 165.7 mmol) in Et_2O (200 ml) at such a rate that a gentle reflux of the mixture was maintained. After complete addition (70 min), the mixture was heated under reflux for 1 h (99% conversion by GC) and treated successively (and cautiously) with H_2O (6.3 ml), 5% aq. NaOH soln. (6.3 ml), and H_2O (12.6 ml). The soln. obtained after filtration of the white precipitate was dried (Na_2SO_4) and evaporated: (±)-**16** (29.9 g, 91%) which was used without further purification (98% pure by GC). White solid. M.p. 95–97°. ^{1}H-NMR: 0.88 (*d*, *J* = 7, 3 H); 1.22 (*s*, 3 H); 1.26 (*s*, 3 H); 1.34 (2*s*, 6 H); 1.96 (*m*, 1 H); 2.20 (*m*, 1 H); 2.23 (2*s*, 6 H); 3.83 (*dd*, *J* = 11, 9, 1 H); 3.92 (*dd*, *J* = 11, 4.5, 1 H); 7.05 (*s*, 1 H); 7.07 (*s*, 1 H); OH not visible. ^{13}C-NMR: 142.1 (*s*); 140.9 (*s*); 133.9 (*s*); 133.8 (*s*); 128.0 (*d*); 127.2 (*d*); 61.9 (*t*); 46.7 (*d*); 38.9 (*d*); 37.3 (*s*); 35.5 (*s*); 34.2 (*q*); 33.9 (*q*); 28.1 (*q*); 27.2 (*q*); 19.6 (*q*); 19.5 (*q*); 11.9 (*q*). MS: 260 (28, $M^{+\bullet}$), 245 (44), 227 (36), 215 (15), 199 (25), 185 (100), 171 (44), 159 (24), 145 (22), 57 (21).

*(2*RS,*3*SR*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-carbaldehyde* ((±)-**17**). A soln. of (±)-**16** (29.3 g, 112 mmol) in CH_2Cl_2 (200 ml) was added in 1 h at 20° to a slurry of PCC (32.2 g, 150 mmol) and *Celite* (32.2 g) in CH_2Cl_2 (300 ml). The mixture was stirred for 1 h and filtered twice through silica gel. After evaporation, the residue was dissolved in Et_2O and the soln. washed successively with 5% aq. HCl soln., H_2O, sat. aq. $NaHCO_3$ soln., and sat. aq. NaCl soln., dried (Na_2SO_4), and evaporated: (±)-**17** (26.4 g, 90%) which was used without further purification (95% pure by GC). White solid. M.p. 93.5–96°. ^{1}H-NMR: 1.05 (*d*, *J* = 7, 3 H); 1.17 (*s*, 3 H); 1.27 (*s*, 3 H); 1.30 (*s*, 3 H); 1.40 (*s*, 3 H); 2.25 (2*s*, 6 H); 2.34 (*m*, 2 H); 7.10 (*s*, 1 H); 7.14 (*s*, 1 H); 9.69 (*d*, *J* = 5, 1 H). ^{13}C-NMR: 206.0 (*d*); 141.6 (*s*); 139.7 (*s*); 134.6 (*s*); 134.5 (*s*); 128.4 (*d*); 126.9 (*d*); 63.0 (*d*); 38.7 (*d*); 36.9 (*s*); 35.0 (*s*); 34.0 (*q*); 32.6 (*q*); 28.1 (*q*); 27.9 (*q*); 19.6 (*q*); 19.5 (*q*); 14.7 (*q*). MS: 258 (30, $M^{+\bullet}$), 243 (22), 215 (63), 173 (100), 159 (81), 147 (57), 119 (19), 57 (47), 44 (30).

*(2*RS,*3*RS*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-carbaldehyde* ((±)-**18**). A soln. of (±)-**17** (26.4 g, 102 mmol) in *t*-BuOH (100 ml) was treated with KO(*t*-Bu) (1.15 g, 10 mmol) and stirred at 20° for 24 h. After addition of Et_2O (200 ml) and H_2O, the product was extracted, washed (H_2O (3×), then sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated: (±)-**18** (containing 3% of (±)-**17**) (24.5 g, 93%) which was used without further purification (95% pure by GC). White solid. ^{1}H-NMR: 0.97 (*d*, *J* = 6.5, 3 H); 1.08 (*s*, 3 H); 1.33 (*s*, 3 H); 1.38 (*s*, 3 H); 1.40 (*s*, 3 H); 2.23 (2*s*, 6 H); 2.27 (*m*, 2 H); 7.06 (*s*, 1 H); 7.12 (*s*, 1 H); 9.75 (*d*, *J* = 5, 1 H). ^{13}C-NMR: 206.5 (*d*); 141.8 (*s*); 140.9 (*s*); 134.4 (*s*); 134.2 (*s*); 128.0 (*d*); 126.5 (*d*); 59.2 (*d*); 37.0 (*s*); 36.6 (*s*); 34.2 (*d*); 29.8 (*q*); 28.5 (*q*); 27.5 (*q*); 25.8 (*q*); 19.5 (*q*); 19.4 (*q*); 14.0 (*q*). MS: 258 (94, $M^{+\bullet}$), 243 (61), 215 (72), 199 (46), 185 (98), 173 (100), 159 (59), 29 (35).

*(2*RS,*3*RS*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-methanol* (±)-**19**). A soln. of (±)-**18** (24.53 g, 95.1 mmol) in hot Et_2O (250 ml) (solubility!) was added to a cooled (−40°) suspension of $LiAlH_4$ (3.62 g, 95.1 mmol) in Et_2O (50 ml). The mixture was stirred for 2 h and was treated successively (and cautiously) with H_2O (3.6 ml), 5% aq. NaOH soln. (3.6 ml), and H_2O (7.2 ml). The soln. obtained after filtration of the white precipitate was dried (Na_2SO_4) and evaporated: (±)-**19** (22.3 g, 90%) which was used without further purification (95% pure by GC). White solid. M.p. 124–126°. ^{1}H-NMR: 1.11 (*s*, 3 H); 1.16 (*d*, *J* = 7, 3 H); 1.20 (*s*, 3 H); 1.34 (*s*, 3 H); 1.40 (*s*, 3 H); 1.50 (*ddd*, *J* = 12, 5, 2.3, 1 H); 1.85 (*dq*, *J* = 12, 7, 1 H); 2.23 (2*s*, 6 H); 3.86 (*dd*, *J* = 12, 5, 1 H); 3.97 (*dd*, *J* = 5, 2.3, 1 H); 7.07 (*s*, 1 H); 7.11 (*s*, 1 H); OH not visible. ^{13}C-NMR: 142.6 (*s*); 142.5 (*s*); 133.8 (*s*); 133.7 (*s*); 128.0 (*d*); 127.9 (*d*); 62.6 (*t*); 47.5 (*d*); 37.5 (2*s*); 37.2 (*d*); 30.0 (*q*); 29.1 (*q*); 27.1 (*q*); 25.6 (*q*); 19.5 (2*q*); 13.5 (*q*). MS: 260 (36, $M^{+\bullet}$), 245 (35), 227 (45), 212 (23), 199 (32), 185 (100), 171 (42), 31 (61).

*[(2*S,*3*S*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalen-2-yl]methyl (1*S,*4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate* (**22**) *and [(2*R,*3*R*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalen-2-yl]methyl (1*S,*4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate* (**23**). (−)-Camphanoyl chloride (**21**; 20.45 g, 94.4 mmol) was introduced portionwise to a stirred, cooled (0°) soln. of (±)-**19** (22.3 g, 85.8 mmol), *N*,*N*-dimethylpyridin-4-amine (DMAP) (100 mg), and pyridine (80 ml). After complete addition, stirring was continued at 20° for 1 h. The mixture was then poured into 5% HCl soln. (200 ml) and extracted (4×) with Et_2O. The org. layers were washed with dil. aq. $CuSO_4$ soln. (3×), then with sat. aq. $NaHCO_3$ soln., H_2O, and sat. aq. NaCl soln., dried (Na_2SO_4), and evaporated to give a white solid (27.0 g, 71.5%) of a 1:1 diastereoisomer mixture **22**/**23**. The two esters were separated by FC (SiO_2 (240–400 mesh; 240 g for 4 g of esters), cyclohexane/Et_2O 98:2). The first-eluted diastereoisomer **22** (6.70 g, 18%) showed a

diastereoisomer excess of 92% by GC (*HP-1* methylsilicon column, 250°), the second-eluted diastereoisomer **23** (4.70 g, 12%) a diastereoisomer excess of 85%. In addition, 13.50 g (36%) of mixed fractions were collected. After further chromatographic purification of the enriched fractions, followed by recrystallization (petroleum ether (80–100°), **22** (*ca.* 5%) and **23** (*ca.* 5%) were obtained with 97% de (by GC, *HP-1* methylsilicon column (*P* 16.7, *T* 250° isotherm.)).

Data of **22**: M.p. 136.9–138.6°. $[\alpha]_D^{20} = -14.7$ ($c = 1.20$, $CHCl_3$). ^{1}H-NMR: 0.98 (*s*, 3 H); 1.05 (*d*, *J* = 7, 3 H); 1.08 (*s*, 3 H); 1.10 (*s*, 3 H); 1.11 (*s*, 3 H); 1.19 (*s*, 3 H); 1.33 (*s*, 3 H); 1.42 (*s*, 3 H); 1.72 (*m*, 2 H); 1.90 (*m*, 2 H); 2.04 (*m*, 1 H); 2.23 (2*s*, 6 H); 2.41 (*m*, 1 H); 4.38 (*dd*, *J* = 12, 4, 1 H); 4.58 (*dd*, *J* = 12, 3, 1 H); 7.07 (*s*, 1 H); 7.11 (*s*, 1 H). ^{13}C-NMR: 178.2 (*s*); 167.7 (*s*); 142.3 (*s*); 141.9 (*s*); 134.0 (2*s*); 128.0 (*d*); 127.8 (*d*); 91.1 (*s*); 65.8 (*t*); 54.8 (*s*); 54.1 (*s*); 44.7 (*d*); 37.6 (*s*); 37.2 (*s*); 37.2 (*d*); 30.7 (*t*); 30.0 (*q*); 29.1 (*q*); 28.9 (*t*); 27.0 (*q*); 25.5 (*q*); 19.5 (2*q*); 16.8 (2*q*); 13.4 (*q*); 9.7 (*q*). MS (direct injection): 440 (3, $M^{+\bullet}$), 227 (100), 185 (38), 149 (33).

Data of **23**: M.p. 139.1–141.3°. $[\alpha]_D^{20} = +7.6$ ($c = 1.05$, $CHCl_3$). ^{1}H-NMR: almost identical with that of **22**, but 1.40 (instead of 1.42) and 4.55 (instead of 4.58). ^{13}C-NMR: 178.1 (*s*); 167.7 (*s*); 142.3 (*s*); 141.8 (*s*); 134.0 (2*s*); 128.0 (*d*); 127.9 (*d*); 91.1 (*s*); 65.8 (*t*); 54.8 (*s*); 54.1 (*s*); 44.6 (*d*); 37.5 (*s*); 37.2 (*s*); 37.1 (*d*); 30.7 (*t*); 30.0 (*q*); 29.1 (*q*); 29.0 (*t*); 27.2 (*q*); 25.5 (*q*); 19.5 (2*q*); 16.9 (2*q*); 13.5 (*q*); 9.7 (*q*). MS: 440 (12, $M^{+\bullet}$), 227 (100), 185 (34).

*(−)-(2*S*,3*S*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-methanol* ((−)-**19**). A soln. of ester **22** (3.00 g, 6.82 mmol) in hot EtOH (50 ml) (solubility!) was treated with a soln. of KOH (458 mg, 8.18 mmol) in H_2O (20 ml) and heated at 80° for 15 h. The soln. was poured into H_2O and the product extracted twice with Et_2O. The basic aq. layer was acidified to recover the camphanic acid. The org. layer was washed (H_2O and sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated to give a white solid. FC (SiO_2, cyclohexane/Et_2O 85:15) afforded (−)-(**19**) (1.49 g, 84%), 98% ee by ^{1}H-NMR (shift reagent: [Eu(hfbc)$_3$], hfbc = (+)-3-(heptafluorobutanoyl)camphorato). $[\alpha]_D^{20} = -31.3$ ($c = 1.26$, $CHCl_3$).

*(+)-(2*R*,3*R*)-1,2,3,4-Tetrahydro-1,1,3,4,4,6,7-heptamethylnaphthalene-2-methanol* ((+)-(**19**)). As described for (−)-**19**, with **23** (3.00 g, 6.82 mmol), EtOH (50 ml), KOH (458 mg, 8.18 mmol), and H_2O (20 ml): (+)-**19** (1.44 g, 81%), 91% ee by ^{1}H-NMR (shift reagent: [Eu(hfbc)$_3$]). Recrystallization from MeOH/petroleum ether (80–100°) furnished enantiomerically almost pure (+)-**19** (0.89 g), >98% ee. M.p. 111.6–113.3°. $[\alpha]_D^{20} = 31.6$ ($c = 1.12$, $CHCl_3$).

*(−)-(2*S*,3*S*)-1,2,3,4-Tetrahydro-1,1,2,3,4,4,6,7-octamethylnaphthalene* ((−)-**24**). A mixture of (−)-**19** (1.41 g, 5.40 mmol), TsCl (1.19 g, 6.24 mmol), and pyridine (6 ml) was kept in the refrigerator for 23 h and at 20° for 1 h. The mixture was then poured into a cold 10% aq. HCl soln. and the tosylate extracted with Et_2O. The org. layer was then rapidly washed (cold H_2O, sat. aq. $NaHCO_3$ soln., H_2O, and sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated. The crude tosylate (2.53 g) was dissolved in THF (40 ml), cooled to 0°, and treated dropwise with a 1M $LiBHEt_3$ in THF (10.85 ml, 10.85 mmol). The soln. was allowed to reach 20° and stirred for 4 h. Excess hydride was decomposed by careful addition of H_2O (2 ml), 3N aq. NaOH (5 ml), and aq. 30% H_2O_2 soln. (5 ml). Extraction with pentane, washing (H_2O, sat. aq. NaCl soln.), drying (Na_2SO_4), and evaporation gave a white solid (1.37 g). FC (SiO_2, cyclohexane) afforded (−)-**24** (750 mg, 65%). M.p. 140.8–142.9°. $[\alpha]_D^{20} = -46.7$ ($c = 1.00$, $CHCl_3$). Anal. data: identical with those reported for (±)-**24** [6].

*(+)-(2*R*,3*R*)-1,2,3,4-Tetrahydro-1,1,2,3,4,4,6,7-octamethylnaphthalene* ((+)-**24**). As described for (−)-**24**, with (+)-**19** (0.89 g, 3.42 mmol), TsCl (783 mg, 4.11 mmol), and pyridine (4 ml), and then with 1M $LiBHEt_3$ in THF (6.90 ml, 6.90 mmol). The white solid (802 mg) was submitted to FC (SiO_2, cyclohexane): (+)-**24** (731 mg, 89%). M.p. 140.2–141.1°. $[\alpha]_D^{20} = +46.3$ ($c = 1.34$, $CHCl_3$). Anal. data: identical with those reported for (±)-**24** [6].

*(−)-(6*S*,7*S*)-5,6,7,8-Tetrahydro-3,5,5,6,7,8,8-heptamethylnaphthalene-2-carbaldehyde* (=*(−)-(*S,S*)*-Vulcanolide®; (−)-**7**). Following the procedure for the racemic sequence [6], (−)-**24** (702 mg, 2.88 mmol) afforded (−)-**7** (580 mg, 78%). The ee (98%) was determined by measurement of the MeN ^{1}H-NMR signals (1.90 and 2.08) of aminal (*S,S,S,S*)-**25** (prepared from (−)-**7** and (−)-(*S,S*)-DMPEDA (**20**) in the presence of 4-Å molecular sieves in Et_2O at 20° [15]) and of its diastereoisomer (*R,R,S,S*)-**26** (1.87 and 2.10). An extra-pure sample of (−)-**7** (205 mg) was obtained by recrystallization from EtOH. M.p. 136.4–138.2°. $[\alpha]_D^{20} = -50.2$ ($c = 0.72$, $CHCl_3$). Anal. data: identical with those reported for (±)-**7** [6].

*(+)-(6*R*,7*R*)-5,6,7,8-Tetrahydro-3,5,5,6,7,8,8-heptamethylnaphthalene-2-carbaldehyde* (*(+)-(*R,R*)*-Vulcanolide®; (+)-**7**). Following the procedure for the racemic sequence [6], (+)-**24** (703 mg, 2.88 mmol) afforded (+)-**7** (569 mg, 77%). The ee (98%) was determined by measurement of the MeN ^{1}H-NMR signals (1.87 and 2.10) of aminal (*R,R,S,S*)-**26** (prepared from (−)-**7** and (−)-(*S,S*)-DMPEDA (**20**) in the presence of 4-Å molecular sieves in Et_2O at 20° [15]) and of its diastereoisomer (*S,S,S,S*)-**25** (1.90 and 2.08). An extra-pure sample of (+)-**7** (110 mg) was obtained by recrystallization from EtOH. $[\alpha]_D^{20} = +49.3$ ($c = 0.81$, $CHCl_3$). Anal. data: identical with those reported for (±)-**7** [6].

(−)-(6S,7S)-1-(5,6,7,8-Tetrahydro-3,5,5,6,7,8,8-heptamethylnaphthalen-2-yl)ethan-1-one ((−)-**27**). Following the procedure for the racemic sequence [6], (−)-**7** (100 mg, 0.387 mmol) afforded (−)-**27** (77 mg, 73%). $[\alpha]_D^{20} = -32.8$ ($c = 0.70$, $CHCl_3$). Spectra: identical with those reported for (±)-**27** [6].

(+)-(6R,7R)-1-(5,6,7,8-Tetrahydro-3,5,5,6,7,8,8-heptamethylnaphthalen-2-yl)ethan-1-one ((+)-**27**). Following the procedure for the racemic sequence [6], (+)-**7** (101 mg, 0.391 mmol) afforded (+)-**27** (80 mg, 75.5%). $[\alpha]_D^{20} = +32.9$ ($c = 0.70$, $CHCl_3$). Spectra: identical with those reported for (±)-**27** [6].

(±)-1,2,3,4-Tetrahydro-1,1,2,4,4,6,7-heptamethyl-3-methylenenaphthalene (**28**). A soln. of (±)-**19** (12.7 g, 48.8 mmol) in THF (250 ml) was cooled to −15° and treated with 1.7M BuLi (28.7 ml, 48.8 mmol). After complete addition (10 min), the soln. was stirred for 15 min and treated with $ClCO_2Me$ (5.08 g, 4.13 ml, 53.7 mmol). Stirring was continued at 0° for 10 min. After addition of Et_2O and H_2O, the product was extracted, washed (H_2O (3×), then sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated to afford the corresponding carbonate (15.0 g), which was dissolved in toluene (220 ml) and pyrolyzed at 450° (1 ml/min, quartz tube (4.7 m), N_2). The condensed soln. was evaporated, the residue bulb-to-bulb distilled (oven temp. 140°/0.3 Torr), and the distillate (9.97 g) purified by chromatography (SiO_2, petroleum ether (50–70°): **28** (9.40 g, 80%). ^{1}H-NMR: 1.06 (*d*, *J* = 7.3, 3 H); 1.09 (*s*, 3 H); 1.25 (*s*, 3 H); 1.43 (*s*, 3 H); 1.48 (*s*, 3 H); 2.23 (*s*, 3 H); 2.24 (*s*, 3 H); 2.48 (*q*, *J* = 7, 1 H); 4.86 (*s*, 1 H); 5.05 (*s*, 1 H); 7.07 (*s*, 1 H); 7.11 (*s*, 1 H). ^{13}C-NMR: 158.7 (*s*); 142.7 (*s*); 141.6 (*s*); 134.0 (*s*); 133.8 (*s*); 128.2 (*d*); 126.5 (*d*); 106.5 (*t*); 45.6 (*d*); 39.8 (*s*); 38.3 (*s*); 34.1 (prob. 2*q*); 32.0 (*q*); 30.3 (*q*); 25.6 (*q*); 19.5 (*q*); 15.0 (*q*). MS: 242 (16, $M^{+\bullet}$), 228 (20), 227 (100), 197 (9), 185 (15), 171 (10), 170 (10).

(±)-5,6,7,8-Tetrahydro-3,5,5,6,8,8-hexamethyl-7-methylenenaphthalene-2-carbaldehyde/(±)-5,6,7,8-Tetrahydro-3,5,5,7,8,8-hexamethyl-6-methylene naphthalene-2-carboxaldehyde (**29**). Following the procedure for (±)-**7** [6], **28** (3.50 g, 14.46 mmol) afforded **29** (3.24 g, 88%) as a 3:2 mixture of constitutional isomers. ^{1}H-NMR: 1.06 (*d*, *J* = 7, 3 H); 1.17 (*s*, 3 H); 1.29 (1.27) (*s*, 3 H); 1.47 (*s*, 3 H); 1.50 (1.52) (*s*, 3 H); 2.48 (*q*, *J* = 7, 1 H); 2.64 (2.63) (*s*, 3 H); 4.93 (*s*, 1 H); 5.06 (*s*, 1 H); 7.23 (7.18) (*s*, 1 H); 7.76 (7.80) (*s*, 1 H); 10.21 (10.23) (*s*, 1 H). ^{13}C-NMR: 192.7 (*d*); 157.4 (*s*); 151.0 (151.6) (*s*); 143.6 (142.8) (*s*); 137.7 (137.5) (*s*); 132.2 (132.6) (*s*); 130.6 (131.3) (*d*); 129.8 (128.9) (*d*); 107.6 (*t*); 45.7 (*d*); 40.5 (39.9) (*s*); 38.4 (39.0) (*s*); 33.8 (34.0) (*q*); 32.0 (32.4) (*q*); 30.3 (*q*); 25.6 (25.5) (*q*); 19.3 (19.2) (*q*); 15.1 (15.3) (*q*). MS: 256 (20, $M^{+\bullet}$), 241 (100), 199 (17), 185 (38), 171 (55), 156 (36), 142 (26), 128 (25), 115 (21).

5,8-Dihydro-3,5,5,6,7,8,8-heptamethylnaphthalene-2-carbaldehyde (**30**). A soln. of **29** (1.50 g, 5.86 mmol) in toluene (50 ml) was treated with $TsOH \cdot H_2O$ (500 mg) and heated at 85° for 3 h. The mixture was cooled and poured into ice/sat. aq. $NaHCO_3$ soln. and extracted with pentane (3×). The org. phase was washed (5% aq. NaOH soln., H_2O (3×), then sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated, and the residue bulb-to-bulb distilled (oven temp. 120°/0.04 Torr): **30** (1.21 g (93% pure), 75%). ^{1}H-NMR: 1.38 (*s*, 6 H); 1.39 (*s*, 6 H); 1.76 (*s*, 6 H); 2.63 (*s*, 3 H); 7.24 (*s*, 1 H); 7.82 (*s*, 1 H); 10.21 (*s*, 1 H). ^{13}C-NMR: 192.7 (*d*); 149.2 (*s*); 141.3 (*s*); 136.9 (*s*); 132.2 (*s*); 131.6 (*d*); 130.0 (*s* + *d*); 129.5 (*s*); 38.4 (*s*); 37.9 (*s*); 30.5 (2*q*); 30.1 (2*q*); 19.4 (*q*); 15.3 (*q*); 15.2 (*q*). MS: 256 (7, $M^{+\bullet}$), 241 (57), 226 (47), 213 (33), 198 (100), 165 (23), 153 (17), 113 (68).

(±)-1-(5,6,7,8-Tetrahydro-3,5,5,6,8,8-hexamethyl-7-methylenenaphthalen-2-yl)ethan-1-one/(±)-1-(5,6,7,8-Tetrahydro-3,5,5,7,8,8-hexamethyl-6-methylenenaphthalen-2-yl)ethan-1-one (**31**). Following the procedure for (±)-**27** [6], **29** (224 mg, 0.86 mmol) afforded **31** (187 mg, 79%) as a 3:2 mixture of constitutional isomeres. ^{1}H-NMR: 1.06 (*d*, *J* = 7, 3 H); 1.15 (1.13) (*s*, 3 H); 1.28 (1.26) (*s*, 3 H); 1.45 (1.46) (*s*, 3 H); 1.50 (1.52) (*s*, 3 H); 2.50 (*m*, 1 H); 2.52 (2.51) (*s*); 2.59 (2.60) (*s*, 3 H); 4.91 (*s*, 1 H); 5.08 (*s*, 1 H); 7.20 (7.16) (*s*, 1 H); 7.68 (7.72) (*s*, 1 H). ^{13}C-NMR: 201.4 (*s*); 157.7 (*s*); 148.4 (149.2) (*s*); 142.7 (141.8) (*s*); 135.9 (135.7) (*s*); 135.4 (135.6) (*s*); 130.8 (129.1) (*d*); 127.0 (128.7) (*d*); 107.4 (*t*); 45.8 (45.7) (*d*); 40.2 (39.8) (*s*); 38.3 (38.8) (*s*); 33.8 (34.1) (*q*); 32.0 (32.3) (*q*); 30.4 (30.2) (*q*); 29.4 (*q*); 25.6 (25.4) (*q*); 21.5 (*q*); 15.1 (15.2 (*q*). MS: 270 (7, $M^{+\bullet}$), 255 (61), 213 (8), 199 (7), 185 (10), 171 (17), 155 (8), 141 (8), 128 (8), 43 (100).

1-(5,8-Dihydro-3,5,5,6,7,8,8-heptamethylnaphthalen-2-yl)ethan-1-one (**32**). Following the procedure for (±)-**27** [6], **30** (306 mg, 1.19 mmol) afforded **31** (200 mg, 62%). ^{1}H-NMR: 1.36 (*s*, 6 H); 1.38 (*s*, 6 H); 1.76 (*s*, 6 H); 2.54 (*s*, 3 H); 2.59 (*s*, 3 H); 7.22 (*s*, 1 H); 7.75 (*s*, 1 H). ^{13}C-NMR: 201.3 (*s*); 146.8 (*s*); 140.4 (*s*); 135.4 (*s*); 135.2 (*s*); 130.2 (*d*); 129.9 (*s*); 129.8 (*s*); 128.6 (*d*); 38.2 (*s*); 37.8 (*s*); 30.6 (2*q*); 30.1 (2*q*); 29.3 (*q*); 21.5 (*q*); 15.2 (2*q*). MS: 270 (5, $M^{+\bullet}$), 255 (78), 240 (18), 225 (26), 213 (87), 198 (33), 182 (14), 166 (21), 165 (22), 120 (28), 43 (100).

rel-*(2R,3S)-1,2,3,4-Tetrahydro-1,1,2,3,4,4,6,7-octamethylnaphthalene* (**33**). A mixture of (±)-**16** (0.80 g, 3.08 mmol), TsCl (850 mg, 4.46 mmol), and pyridine (4 ml) was kept in the refrigerator for 23 h and at 20° for 24 h. The mixture was then poured into a cold 10% aq. HCl soln. and the tosylate extracted with Et_2O. The org. layer was rapidly washed (cold H_2O, sat. aq. $NaHCO_3$ soln., H_2O, and sat. aq. NaCl soln.), dried (Na_2SO_4), and evaporated to afford 1.20 g of a white solid (max. 2.90 mmol, 65%). The crude tosylate (414 mg, max. 1.0 mmol) was dissolved in THF (20 ml), cooled to 0°, and treated dropwise with 1M $LiBHEt_3$ in THF (2.0 ml, 2.0 mmol).

The soln. was allowed to reach 20°, then heated under reflux (65°), and stirred for 4 h. As the conversion was still low, more $LiBHEt_3$ (2 ml, 2.0 mmol) was added. Finally, 1,2-dimethoxyethane (20 ml) was added, the THF distilled off, and the temp. raised to 100°. The reaction was complete after 40 min, and the mixture was cooled to 10°. Excess hydride was decomposed by careful addition of H_2O (2 ml), 3N aq. NaOH (5 ml), and aq. 30% H_2O_2 soln. (5 ml). Extraction with pentane, washing (H_2O, sat. aq. NaCl soln.), drying (Na_2SO_4), and evaporation gave an oil (375 mg). Bulb-to-bulb distillation (100° (bath)/0.01 Torr) afforded **33** (150 mg, 40% starting from **16**). M.p. 56°. Anal. data: identical with those reported [6].

rel-*(6*R*,7*S*)-5,6,7,8-Tetrahydro-3,5,5,6,7,8,8-heptamethylnaphthalene-2-carbaldehyde* (**34**). See [6]. M.p. 78–80°. ^{13}C-NMR: 192.7 (*d*); 151.3 (*s*); 142.9 (*s*); 137.1 (*s*); 132.3 (*s*); 131.3 (*d*); 130.2 (*d*); 41.0 (2*d*); 38.0 (*s*); 37.4 (*s*); 33.7 (*q*); 33.4 (*q*); 27.6 (*q*); 27.4 (*q*); 19.2 (*q*); 13.3 (*q*); 13.2 (*q*).

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REFERENCES

[1] A. S. Williams, *Synthesis* **1999**, 1707.
[2] G. Fráter, J. A. Bajgrowicz, P. Kraft, *Tetrahedron* **1998**, *54*, 7633.
[3] G. Ohloff, B. Winter, C. Fehr, in 'Perfumes: Art, Science and Technology', Eds. P. M. Müller and D. Lamparsky, Elsevier Applied Science, London, 1991, p. 287.
[4] P. Kraft, J. A. Bajgrowicz, C. Denis, G. Fráter, *Angew. Chem., Int. Ed.* **2000**, *39*, 2980.
[5] W. K. Giersch, K. H. Schulte-Elte (to *Firmenich*), EP 472966, prior. 28.6.1990 (*Chem. Abstr.* **1992**, *117*, 7513).
[6] C. Fehr, J. Galindo, R. Haubrichs, R. Perret, *Helv. Chim. Acta* **1989**, *72*, 1537.
[7] G. Suzukamo (to *Sumitomo Chem. Corp. Ltd.*), EP 71006, prior. 11.6.81 (*Chem. Abstr*. **1983**, *99*, 122073r).
[8] H. Boelens, P. C. Traas, H. J. Takken, *Perfumer and Flavorist* **1980**, *5*, 39.
[9] G. Fráter, U. Müller, P. Kraft, *Helv. Chim. Acta* **1999**, *82*, 1656.
[10] C. Fehr, J. Galindo, *Helv. Chim. Acta* **1995**, *78*, 539 and ref. cit. therein.
[11] a) S. R. Wilson, R. S. Myers, *J. Org. Chem*. **1975**, *40*, 3309; R. E. Ireland, R. H. Müller, A. K. Willard, *J. Am. Chem. Soc*. **1976**, *98*, 2868; b) P. Kraft, W. Eichenberger, G. Fráter, *Eur. J. Org. Chem*. **1999**, 2781.
[12] B. Shive, J. Horeczy, G. Wash, H. L. Lochte, *J. Am. Chem. Soc*. **1942**, *64*, 385.
[13] T. Manimaran, G. P. Stahly, *Tetrahedron: Asymmetry* **1993**, *4*, 1949.
[14] W. Oppolzer, C. Chapuis, G. Bernardinelli, *Helv. Chim. Acta* **1984**, *67*, 1397; B. H. Kim, D. P. Curran, *Tetrahedron* **1993**, *49*, 293 (review).
[15] P. Mangeney, A. Alexakis, J. F. Normant, *Tetrahedron Lett*. **1988**, *29*, 2677.
[16] H. Gerlach, *Helv. Chim. Acta* **1968**, *51*, 1587; H. Gerlach, W. Müller, *Helv. Chim. Acta* **1972**, *55*, 2277.
[17] S. Krishnamurthy, H. C. Brown, *J. Org. Chem*. **1976**, *41*, 3064.
[18] C. Fehr, F. Delay, P.-A. Blanc, N. Chaptal-Gradoz (to *Firmenich*), EP 664286, prior. 08.12.94 (*Chem. Abstr.* **1995**, *123*, 169378y).
[19] C. Fehr, N. Chaptal-Gradoz, J. Galindo, *Chem. Eur. J.* **2002**, *8*, 853.

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