

### 13. 1,2,3,4,4a,5,8,8a-Octahydro-4 $\beta$ ,8 $\alpha$ -dimethylnaphthalen-4a $\beta$ -ol (= Dehydrogeosmin), a Novel Compound Occurring in the Flower Scent of Various Species of *Cactaceae*

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The 1,2,3,4,4a,5,8,8a-octahydro-4 $\beta$ ,8 $\alpha$ -dimethylnaphthalen-4a $\beta$ -ol (= dehydrogeosmin; **1**) has been identified as the olfactorily dominant compound in the flower scents of *Rebutia marsoneri* WERD., *Dolichothele longimamma* (DC.) BR. et R., and *Sulcorebutia kruegeri* (CARD.) RITT. The structure of **1**, which might be of importance to the pollination biology of such *Cactaceae*, is based on spectral data and synthesis.

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**1. Introduction.** – Among the natural products of extremely low threshold values figures perhydro-4 $\beta$ ,8 $\alpha$ -dimethylnaphthalen-4a $\beta$ -ol (**2**) – the so-called geosmin – which emits a very strong earthy-musty odor typical for freshly ploughed soil. Geosmin (**2**) is a metabolite of many *Actinomyces* and of several blue-green algae and is known as an off-flavor contaminant of water supplies as well as a trace constituent of several food-stuffs (compare review given in [1] [2]).

In the course of a broad olfactory evaluation of fragrant flowers, the characteristic musty-earthy odor typical for geosmin (**2**) could be recognized most surprisingly in the flower scents of a series of species belonging to the genera of e.g. *Rebutia*, *Sulcorebutia*, *Dolichothele*, and *Mammillaria*. Searching for the compound responsible for this unusual olfactory aspect in a flower scent, the headspace of a single flower of *Rebutia marsoneri* WERD. native to North Argentina was trapped on charcoal (5 mg) during the time of maximal opening (noon to 2 p.m.). Indeed, the sample thus obtained (ca. 6  $\mu$ g) contained to 35% a compound characterized by a mass fragmentation indicative of a dehydrogeosmin (cf. Fig. 1). Based on the key fragment  $m/z$  126 (100%), considered to originate from a *retro-Diels-Alder* fragmentation, the structure of dehydrogeosmin is proposed to be **1**.

Due to lack of sufficient material, compound **1** could not be isolated in pure form for further spectral characterization. However, it showed the same retention data on a polar and apolar capillary column and the same mass fragmentation as a synthetic sample obtained as outlined below (*Scheme 1*).

It may be assumed that the biogenesis of dehydrogeosmin (**1**), like the one of geosmin (**2**) and cybullol [3], involves degradation of an eudesmane-type sesquiterpene. Dehydrogeosmin (**1**) is olfactorily characterized by the musty-earthy odor of geosmin (**2**) and an additional camphoraceous aspect. Its odor threshold is ca. 10 times higher than that of **2** ( $2 \cdot 10^{-11}$  g/l air vs.  $2 \cdot 10^{-12}$  g/l air).

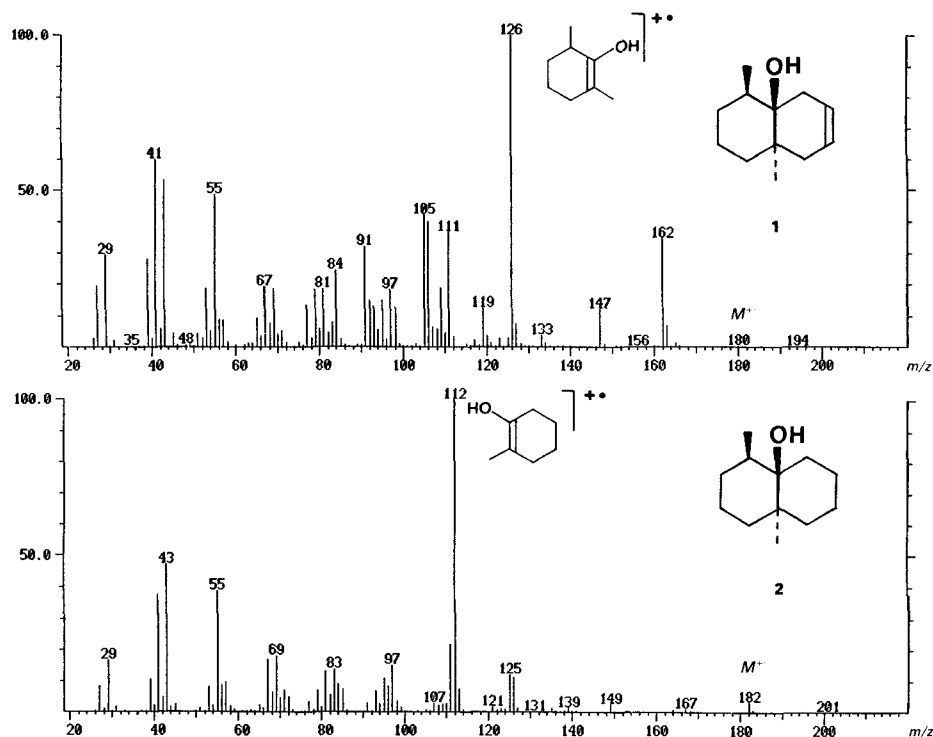


Fig. 1. Mass spectra (70 eV) of dehydrogeosmin (1) and geosmin (2)

**2. Synthesis.** – Originally, the title compound **1** was obtained as a side product on conversion of hydroxy-oxocarbonitrile **3** to geosmin (**2**) in connection with studies on the stereochemical course of the *Robinson* annelation [4]. Reduction of **3** with diisobutylaluminum hydride (DIBAH) in THF/hexane at r.t. for 3 h afforded the dihydroxyaldehyde **4** as a single diastereoisomer (63% yield). The *cis*-configuration of the two OH groups of **4** followed from the ready formation of the cyclic acetal **5** under mild conditions (excess 2-methoxypropene,  $\text{CH}_2\text{Cl}_2$ , pyridinium *p*-toluenesulfonate ( $\text{Py} \cdot \text{TsOH}$ ) ( $20^\circ$ , 30 min). *Wolff-Kishner* reduction of **5** ( $\text{NH}_2\text{NH}_2$ , triethylene glycol, KOH,  $180^\circ$ , 1 h)<sup>1)</sup> followed by removal of the isopropylidene group (MeOH,  $\text{Py} \cdot \text{TsOH}$ ;  $60^\circ$ , 30 min) furnished the crystalline diol **6** (65% yield from **4**).

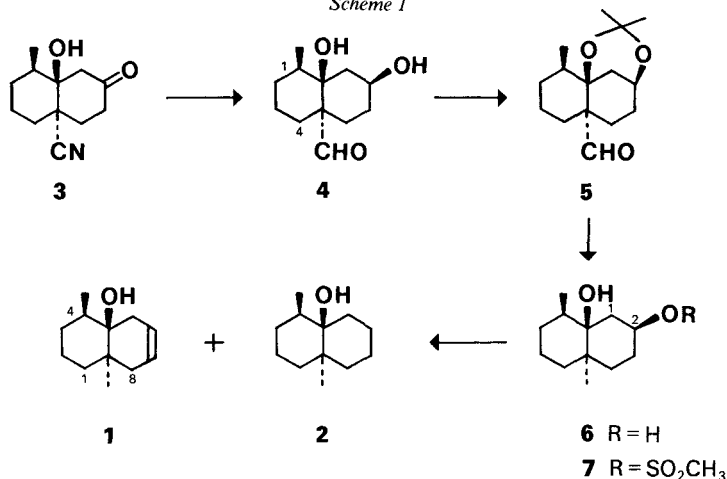
On treatment of **6** with  $\text{MsCl}$  in  $\text{CH}_2\text{Cl}_2$ /pyridine ( $20^\circ$ , 24 h), the secondary OH group was selectively mesylated to give **7** (90% yield). Removal of the methanesulfonyl group of **7** was effected with  $\text{Zn}/\text{NaI}$  in refluxing 1,2-dimethoxyethane (glyme) [5] to give geosmin (**2**)<sup>2)</sup> as the expected reduction product and dehydrogeosmin (**1**) in a ratio of 7:3 (75% yield). The elimination product **1**<sup>3)</sup> was identical with the compound identified in the

<sup>1)</sup> Interestingly, when these conditions were applied to **4**, significant amounts of the corresponding *cis*-decalols were obtained which must arise by a transannular *retro*-aldol/aldol process.

<sup>2)</sup> For other syntheses of geosmin (**2**), see [6] and ref. cit. therein.

<sup>3)</sup> The formation of unsaturated compounds from sterically hindered mesylates upon  $\text{NaI}/\text{Zn}$  treatment has ample precedent [5a].

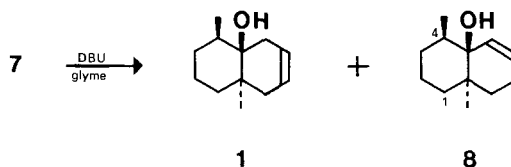
Scheme 1



flower scent of *Rebutia marsoneri*. Furthermore, the transformation  $7 \rightarrow 1 + 2$  establishes that **1** has the same relative configuration as geosmin (**2**).

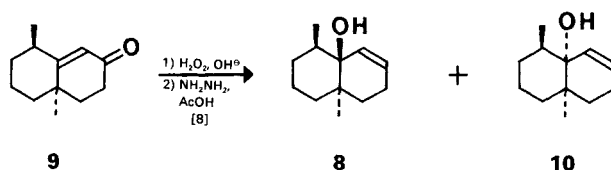
On the other hand, treatment of **7** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing glyme for 5 h afforded a 4:1 mixture of **1** and **8** (78% yield). In contrast to **1**, the isomeric **8** is characterized by a key fragment  $m/z$  109 in its MS.

Scheme 2



In order to confirm the assignment of the position of the double bond of **1** and **8**, the latter compound was synthesized from **9** [7] by an unambiguous route as shown in Scheme 3<sup>4)</sup>. The minor, less polar isomer of the two octalols formed, which were readily separated by chromatography on  $\text{SiO}_2$ , proved to be identical with the minor isomer obtained on treatment of **7** with DBU (Scheme 2).

Scheme 3



<sup>4)</sup> The Wharton rearrangement of a diastereoisomeric mixture of epoxides derived from **9** has already been described by Stothers *et al.* [8], but only the *cis*-isomer **10** had been fully characterized. See also [9].

**3. Remarks.** – In the course of this investigation, the dehydrogeosmin (**1**) was also identified in the flower scent of *Dolichothele longimamma* (DC.) BR. et R. (ca. 5.5%) native to Central Mexico and in that of *Sulcorebutia kruegeri* (CARD.) RITT. (ca. 7.6%)

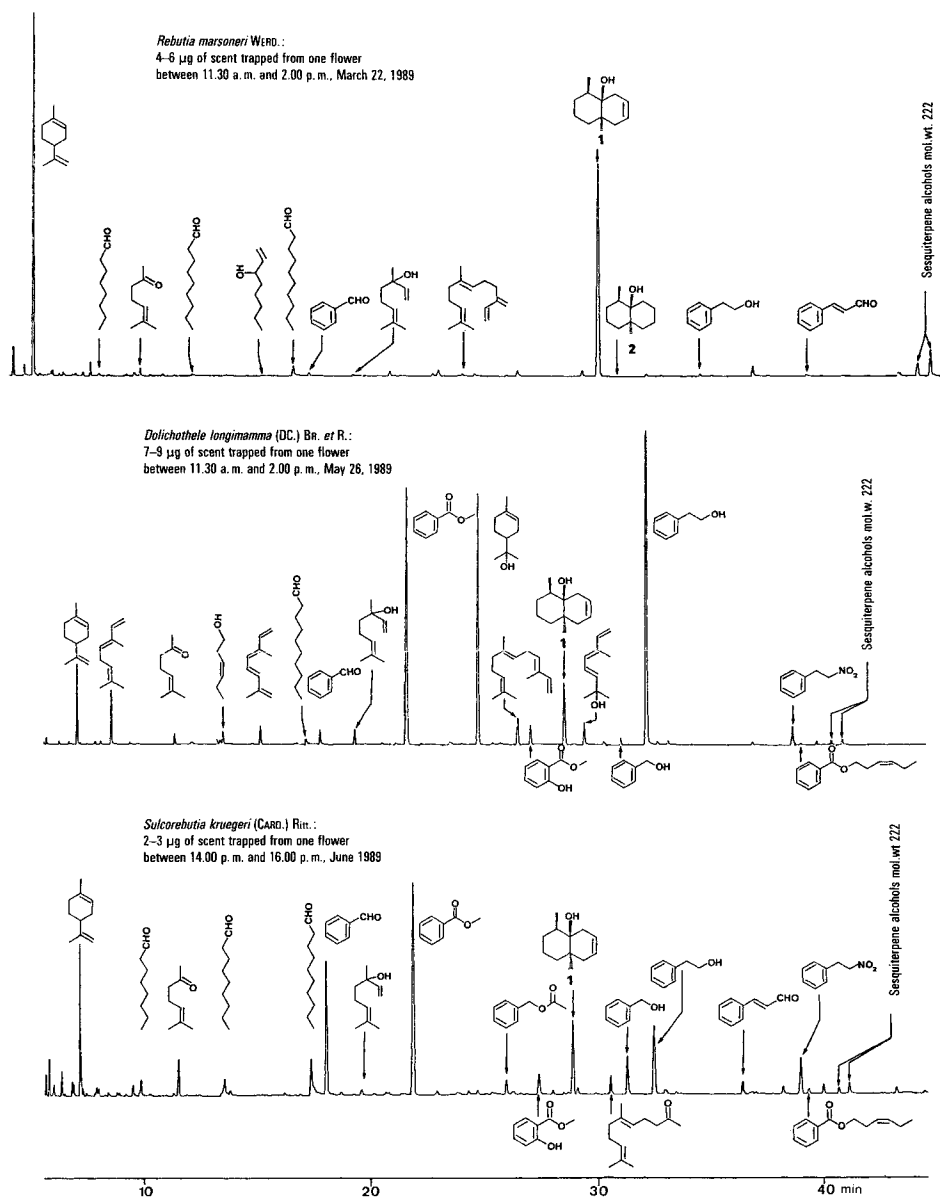


Fig. 2. GC profiles of the trapped scents of *Rebutia marsoneri*<sup>5)</sup>, *Dolichothele longimamma*, and *Sulcorebutia kruegeri*. DB-Wax, 30 m × 0.3 mm i.d., 50–200° with 2.5°/min.

<sup>5)</sup> The somewhat longer retention times are due to the fact that the investigation had to be performed on another specimen of fused-silica capillary column coated with DB-Wax.

native to Bolivia. The GC curves of Fig. 2 show the anal. composition of the three flower scents investigated: they have a similar pattern of constituents. However, their quantitative compositions differ considerably. Interestingly, geosmin (**2**) could only be identified as a trace constituent ( $< 0.01\%$ ) in the flower scent of *Rebutia marsoneri*.

According to the olfactory evaluation of many additional species – **1** is easily detectable by nose down to the level of trace amounts – this compound seems to have a broad distribution within the genera mentioned and related genera, and, interestingly, the flowers of species characterized by the distinct odor of **1** are all of yellow color.

It is certainly most striking that the flower scents of such representatives of the *Cactaceae* family growing under extreme dry and hot conditions are olfactorily dominated by a compound of extreme musty-earthly character which – for the human nose – is always associated with moist/damp places. It would not be too surprising if this new natural product **1** were of significant importance to the pollination biology of such *Cactaceae*.

We are grateful to Mr. *Hp. Schumacher*, Botanical Garden of the City of St. Gallen for allowing to collect the flower scents of the species described. Furthermore, valuable discussions with Dr. *J. Schmid* (MS), Dr. *E. Billeter* (NMR), and Mr. *J. Märki* (NMR) of our analytical department are kindly acknowledged.

### Experimental Part

*General.* See [10]. GC: Carlo Erba GC 6000 Vega Series instrument equipped with a SE-30 glass capillary column ( $28\text{ m} \times 0.3\text{ mm}$ ), He as carrier gas (70 kPa); temp. programming: samples were injected at  $90^\circ$ ; after 2 min,  $6^\circ/\text{min} \rightarrow 120^\circ$ , then  $20^\circ/\text{min} \rightarrow 240^\circ$ .

*Sampling of the Flower Scents.* To collect the flower scent of the individual species of *Cactaceae*, an adsorption filter was placed as close as possible in the center of the respective flower. The filters employed contained a thin layer of 5 mg of charcoal embedded between two grids fused into the wall of a glass tube (65 mm, 3 mm i.d.<sup>6)</sup>). To prevent an additional dilution of the scent by air circulation, the flower including the filter was surrounded by a glass funnel adapted in its size and shape to the flower (3–5 cm in diameter, ca. 4 cm length). Transport of volatiles from the so-called headspace of flower to the charcoal trap was achieved by sucking the fragrant air with the aid of a small battery-operated pump (flow rate 60–80 ml/min). After ca. 2 h (cf. Fig. 2), the adsorbed volatiles were recovered by extraction with  $\text{CS}_2$  ( $3 \times 10\text{ }\mu\text{l}$ ) according to Grob and coworkers [11] [12] who thoroughly described the successful preparation, handling, and extraction of such charcoal traps. For the investigation by GC/MS, 2- $\mu\text{l}$  portions of the resulting eluates (20  $\mu\text{l}$ ) were used. GC: Carlo Erba FTV 4160 with fused silica capillary column (DB-Wax J&W,  $30 \times 0.3\text{ mm}$ ). MS: Varian MAT, models CH-5 and 212 (70 eV).

( $\pm$ )-Perhydro-7 $\beta$ ,8 $\alpha\beta$ -dihydroxy-1 $\beta$ -methylnaphthalene-4 $\alpha\alpha$ -carbaldehyde (**4**). To a soln. of 330 mg (1.59 mmol) of **3** [4] in 10 ml of dry THF were added, at  $0^\circ$  under  $\text{N}_2$ , 8.25 ml of 1M DIBAH (8.25 mmol) in hexane within 3 min. The resulting soln. was warmed up, stirred at r.t. for 3 h, and then poured into an ice-cold, premixed soln. of 30 ml of 2M aq. (+)-L-tartaric acid and 10 ml of 2N NaOH. The mixture was stirred at  $0^\circ$  for 40 min and then extracted with  $\text{Et}_2\text{O}$  ( $3 \times 150\text{ ml}$ ). The combined org. extracts were dried ( $\text{MgSO}_4$ ), filtered, and evaporated: 214 mg (63%) of crystalline **4**. M.p.  $125\text{--}127^\circ$ . TLC (hexane/AcOEt 3:1):  $R_f$  0.16. IR ( $\text{CHCl}_3$ ): 3600w, 3450m, 2700w, 1720s.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 0.90 (d,  $J = 6.5$ ,  $\text{CH}_3$ ); 1.13–1.27 (m, 1 H); 1.34–1.95 (m, 9 H); 1.98 (dd,  $J = 3.5, 14.5$ , H–C(8)); 2.05 (dd,  $J = 15.5, 4, 1\text{ H}$ ); 2.05 (dt,  $J = 14.5, 2$ , H–C(8)); 2.71 (br. s, OH); 3.68 (br. s, OH); 4.18–4.24 (m,  $w_{\text{H}}$   $\approx 8$ , H–C(7)); 9.48 (s, CHO); irradiation at: 0.90 (d)  $\rightarrow$  1.90 (dd,  $J = 4.5, 12$ ,  $\text{H}_{\text{ax}}\text{--C}(1)$ ); 4.21 (m)  $\rightarrow$  1.98 (d,  $J = 14.5$ ,  $\text{H}_{\text{ax}}\text{--C}(8)$ ) and 2.05 (dd,  $J = 2, 14.5$ ,  $\text{H}_{\text{eq}}\text{--C}(8)$ ). MS: 194 (4,  $[\text{M} - \text{H}_2\text{O}]^+$ ), 176 (7), 166 (41), 148 (100), 81 (51), 55 (65), 43 (95), 41 (79).

( $\pm$ )-Perhydro-4 $\alpha\alpha$ ,8 $\beta$ -dimethylnaphthalene-2 $\beta$ ,8 $\alpha\beta$ -diol (**6**). To a soln. of 112 mg (0.53 mmol) of **4** in 4 ml of dry  $\text{CH}_2\text{Cl}_2$  were added 0.39 g (5.4 mmol) of 2-methoxypropene (freshly distilled), followed by 12 mg of Py  $\cdot$  TsOH.

<sup>6)</sup> Brechbühler AG, CH-8952 Schlieren, Switzerland.

The soln. was stirred at r.t. for 30 min, then poured into 50 ml of cold 0.1M NaHCO<sub>3</sub>, and extracted with Et<sub>2</sub>O (2 × 100 ml). The combined org. extracts were dried (MgSO<sub>4</sub>), filtered, and evaporated: **5** as a colorless oil. TLC (hexane/AcOEt 3:1): *R<sub>f</sub>* 0.51. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.89 (*d*, *J* = 6.5, CH<sub>3</sub>); 1.42, 1.53 (2 *s*, (CH<sub>3</sub>)<sub>2</sub>C); 4.32 (br. *t*, *w*<sub>1/2</sub> ≈ 10, 1 H); 9.47 (*s*, CHO).

To crude **5** in 3 ml of triethylene glycol, 0.5 ml of hydrazine (99%) were added. The soln. was heated to 110° and then kept at 110° for 30 min. After addition of 0.3 g of solid KOH, the temp. was raised to 180° and then maintained for 1 h. The soln. was cooled, diluted with H<sub>2</sub>O, and poured into ice-H<sub>2</sub>O. After acidification with 1N H<sub>2</sub>SO<sub>4</sub>, the mixture was extracted with Et<sub>2</sub>O (3 × 75 ml). The combined org. extracts were dried (MgSO<sub>4</sub>), filtered, and evaporated. TLC (hexane/AcOEt 3:1): 2 spots at *R<sub>f</sub>* 0.62 and 0.23. For complete removal of the (CH<sub>3</sub>)<sub>2</sub>C group, the oily residue was heated in 3 ml of MeOH with 10 mg of Py·TsOH at 60° for 30 min. Chromatography of the evaporated soln. on SiO<sub>2</sub> (7 g) with hexane/AcOEt 4:1 afforded 68 mg (65%) of crystalline **6**. M.p. 102–103°. Crystallization from hexane raised the m.p. to 104–105°. TLC (hexane/AcOEt 3:1): *R<sub>f</sub>* 0.23. IR (CHCl<sub>3</sub>): 3610w, 3475m, 1018m. <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>): 0.83 (*d*, *J* = 6.5, CH<sub>3</sub>); 0.90–1.08 (*m*, 1 H), overlapped by 1.02 (*s*, CH<sub>3</sub>); 1.24–2.08 (*m*, 12 H); 2.97 (*s*, OH); 3.47 (*d*, *J* = 6.5, OH); 4.12 (*m*, *w*<sub>1/2</sub> = 10, 1 H). MS: 198 (3, *M*<sup>+</sup>), 126 (100).

(±)-1,2,3,4,4a,5,8a-Octahydro-4β,8αα-dimethylnaphthalen-4αβ-ol (**1**) and (±)-Perhydro-4β,8αα-dimethylnaphthalen-4αβ-ol (= Geosmin, **2**). To a soln. of 51 mg (0.26 mmol) of **6** in 4 ml of CH<sub>2</sub>Cl<sub>2</sub>/pyridine 4:1 (*v/v*) were added dropwise 117 mg (1 mmol) of MsCl. The resulting soln. was stirred at r.t. for 24 h, then poured onto ice/20 ml 1N HCl and extracted with AcOEt (2 × 100 ml). The combined org. extracts were washed with brine, dried (MgSO<sub>4</sub>), and evaporated. Chromatography on SiO<sub>2</sub> (6 g) with hexane/AcOEt 2:1 afforded 64 mg (90%) of **7**. M.p. 83–86° (dec.). TLC (hexane/AcOEt 3:1): *R<sub>f</sub>* 0.18.

A mixture of 30 mg (0.11 mmol) of **7**, 195 mg (1.3 mmol) of NaI, 197 mg (3 mmol) of Zn powder, and 3 ml of glyme was heated in an oil bath at 90–95° for 4 h. After cooling, the mixture was filtered through *Celite* and the flask rinsed with Et<sub>2</sub>O and H<sub>2</sub>O. The combined filtrates were extracted with Et<sub>2</sub>O (2 × 100 ml). The org. extracts were dried (MgSO<sub>4</sub>) and evaporated. Filtration through a pad of SiO<sub>2</sub> (3.5 g) with pentane/Et<sub>2</sub>O 8:1 afforded 15 mg (75%) of a colorless oil. Cap. GC (*SE-30*) showed three peaks at *t<sub>R</sub>* 8.4 (30%), 8.6 (1%), and 8.85 min (69%), corresponding to **1**, **8**, and 2 resp. Prep. GLC (*SE-30*) gave pure **1**.

Data of **1**: TLC (pentane/Et<sub>2</sub>O 5:1): *R<sub>f</sub>* 0.40. IR (CHCl<sub>3</sub>): 3600w, 998m, 878m. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.88 (*d*, *J* = 6.5, CH<sub>3</sub>); 0.97 (*s*, CH<sub>3</sub>); 1.09–1.16 (*m*, 1 H); 1.35–1.75 (*m*, 8 H); 1.92–2.02 (*m*, 1 H); 2.06–2.16 (*m*, 2 H); 5.53–5.61 (*m*, 1 H); 5.66–5.74 (*m*, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.84 (*q*); 21.31 (*t*); 21.42 (*q*); 30.73 (*t*); 34.59 (*t*); 34.82 (*d*); 35.32 (*t*); 36.35 (*s*); 38.08 (*t*); 73.41 (*s*); 123.70 (*d*); 126.35 (*d*). MS: *Fig. 1*.

Data of **2**: TLC (pentane/Et<sub>2</sub>O 5:1): *R<sub>f</sub>* 0.44. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.78 (*d*, *J* = 6.5, CH<sub>3</sub>); 1.03 (*s*, CH<sub>3</sub>). MS: *Fig. 1*. Data identical with those of an authentic sample (kindly provided by Dr. A. Hochstetler, Givaudan Corporation, Clifton, USA).

Reaction of **7** with DBU. A mixture of 55 mg (0.20 mmol) of **7**, 7 ml of glyme and 200 mg (ca. 1.3 mmol) of DBU was heated in an oil bath at 100° for 5 h under N<sub>2</sub>. The soln. was poured into ice-H<sub>2</sub>O containing 120 mg (2 mmol) of AcOH and extracted with Et<sub>2</sub>O (2 × 75 ml). The combined org. extracts were dried (MgSO<sub>4</sub>) and evaporated. Chromatography on SiO<sub>2</sub> (4 g) with pentane/Et<sub>2</sub>O 8:1 afforded 28 mg (78%) of a colorless oil. Capillary GC (*SE-30*) showed two peaks at *t<sub>R</sub>* 8.4 and 8.6 min in a 4:1 ratio, corresponding to **1** and **8**, resp. The product ratio was confirmed by <sup>1</sup>H-NMR. No attempts were made to separate the two isomers. *R<sub>f</sub>*, *t<sub>R</sub>*, and <sup>1</sup>H-NMR signals of the minor **8** were identical with those of a pure sample prepared as outlined below.

(±)-1,2,3,4,4a,7,8,8a-Octahydro-4β,8αα-dimethylnaphthalen-4αβ-ol (**8**). Enone **9** [7] was converted to a 9:1 mixture **10/8** following [8]: 45% yield. Chromatography of the crude product on SiO<sub>2</sub> with pentane/Et<sub>2</sub>O 10:1 afforded **8** as colorless oil. TLC (pentane/Et<sub>2</sub>O 5:1): *R<sub>f</sub>* 0.42. IR (CHCl<sub>3</sub>): 3600m, 3470w, 1640w. <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>): 0.92 (*d*, *J* = 6.5, CH<sub>3</sub>); 0.95 (*s*, CH<sub>3</sub>); 1.00–2.22 (*m*, 12 H); 5.70–5.82 (*m*, 1 H); 5.95 (*dt*, *J* = 10, 2, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.82 (*q*); 19.29 (*q*); 20.70 (*t*); 23.14 (*t*); 30.14 (*t*); 31.47 (*t*); 32.12 (*d*); 33.61 (*t*); 36.47 (*s*); 72.28 (*s*); 129.90 (*d*); 130.70 (*d*). MS: 180 (30, *M*<sup>+</sup>), 165 (62), 162 (34), 147 (63), 110 (55), 109 (100), 105 (56), 91 (89).

Continued elution of the column with pentane/Et<sub>2</sub>O 5:1 afforded (±)-1,2,3,4,4a,7,8,8a-Octahydro-4β,8αα-dimethylnaphthalen-4αα-ol (**10**). M.p. 43–45°. TLC (pentane/Et<sub>2</sub>O 5:1): *R<sub>f</sub>* 0.27. IR (CHCl<sub>3</sub>): 3605m, 1025m, 973m. <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>): 0.99 (*d*, *J* = 6.5, CH<sub>3</sub>); 1.03 (*s*, CH<sub>3</sub>); 1.08–2.24 (*m*, 12 H); 5.72–5.92 (*m*, 2 H). MS: 180 (12, *M*<sup>+</sup>), 110 (73), 109 (100).

## REFERENCES

- [1] G. Ohloff, in 'Progress in the Chemistry of Organic Natural Products', Eds. W. Herz, H. Grisebach, and G. W. Kirby, Springer-Verlag, Wien, 1978, pp. 483–484.
- [2] J. A. Maga, *Food Rev. Int.* **1987**, 3, 269.
- [3] a) W. A. Ayer, M. G. Paice, *Can. J. Chem.* **1976**, 54, 910; b) W. A. Ayer, L. M. Browne, S. Fung, *ibid.* **1976**, 54, 3276; c) W. A. Ayer, L. M. Browne, *Tetrahedron* **1981**, 37, 2199.
- [4] C. Nussbaumer, presented at the 'Herbstversammlung der Schweizerischen Chemischen Gesellschaft', October 21, 1988, Bern, in preparation.
- [5] a) Y. Fujimoto, T. Tatsuno, *Tetrahedron Lett.* **1976**, 17, 3325; b) P. Kočovský, V. Černý, *Collect. Czech. Chem. Commun.* **1979**, 44, 246.
- [6] a) G. Revial, *Tetrahedron Lett.* **1989**, 30, 4121; b) P. Gosselin, D. Joulain, P. Laurin, F. Rouessac, *ibid.* **1989**, 30, 2775.
- [7] S. R. Wilson, R. N. Misra, *J. Org. Chem.* **1980**, 45, 5079.
- [8] L. M. Browne, R. E. Klinck, J. B. Stothers, *Org. Magn. Reson.* **1979**, 12, 561.
- [9] W. C. Still, M. J. Schneider, *J. Am. Chem. Soc.* **1977**, 99, 948.
- [10] C. Nussbaumer, G. Fráter, *Helv. Chim. Acta* **1987**, 70, 396.
- [11] K. Grob, *J. Chromatogr.* **1973**, 84, 255.
- [12] K. Grob, F. Zürcher, *J. Chromatogr.* **1976**, 117, 285.