13. 1,2,3,4,4a,5,8,8a-Octahydro-4β,8aα-dimethylnaphthalen-4aβ-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-4β,8aα-dimethylnaphthalen-4aβ-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.

1. Introduction. – Among the natural products of extremely low threshold values figures perhydro-4β,8aα-dimethylnaphthalen-4aβ-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 *Actinomycetes* 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 foodstuffs (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 μg) 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).

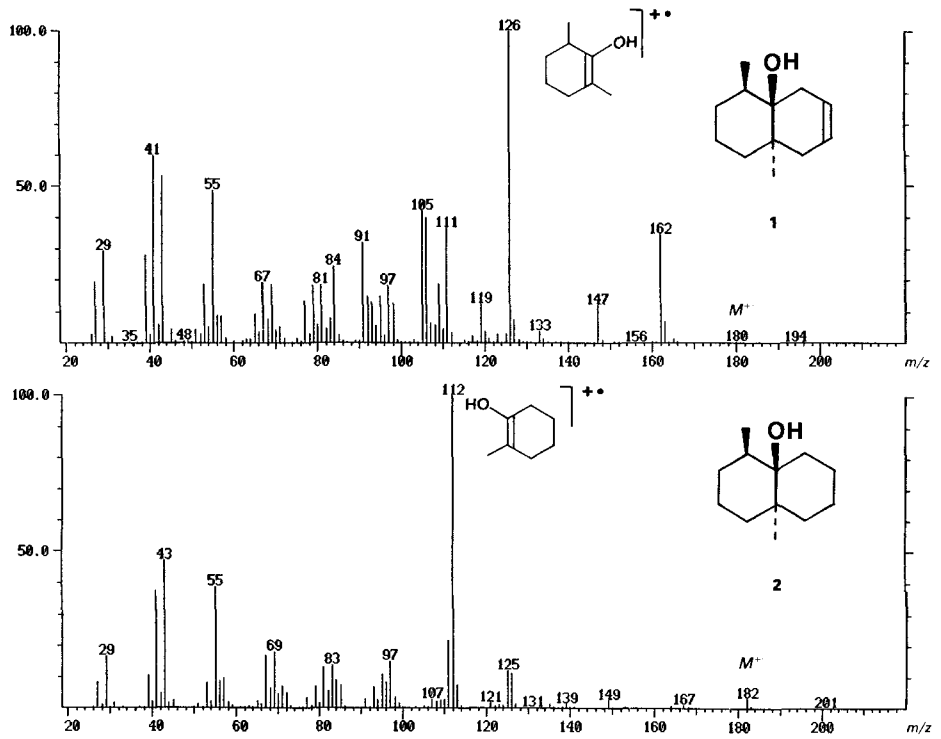


Fig. 1. *Mass spectra* (70 eV) *of dehydrogeosmin* (**1**) *and geosmin* (**2**)

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 diisobutylaluminium 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, CH_2Cl_2, pyridinium *p*-toluenesulfonate (Py·TsOH) (20°, 30 min). *Wolff-Kishner* reduction of **5** (NH_2NH_2, triethylene glycol, KOH, 180°, 1 h)[1]) followed by removal of the isopropylidene group (MeOH, Py·TsOH; 60°, 30 min) furnished the crystalline diol **6** (65% yield from **4**).

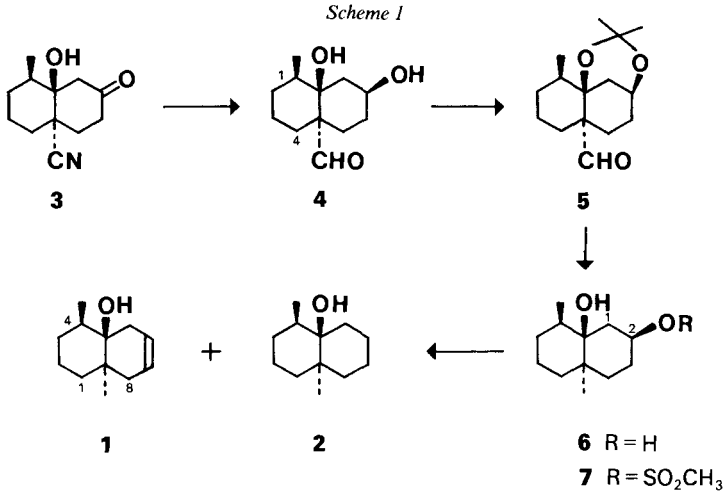
On treatment of **6** with MsCl in CH_2Cl_2/pyridine (20°, 24 h), the secondary OH group was selectively mesylated to give **7** (90% yield). Removal of the methanesulfonyl group of **7** was effected with Zn/NaI in refluxing 1,2-dimethoxyethane (glyme) [5] to give geosmin (**2**)[2]) as the expected reduction product and dehydrogeosmin (**1**) in a ratio of 7:3 (75% yield). The elimination product **1**[3]) was identical with the compound identified in the

[1]) 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.

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

[3]) The formation of unsaturated compounds from sterically hindered mesylates upon NaI/Zn treatment has ample precedent [5a].

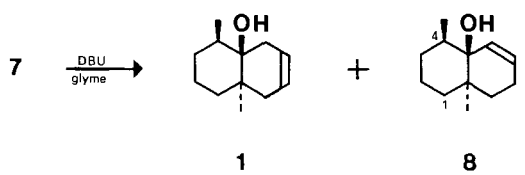
Scheme 1



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

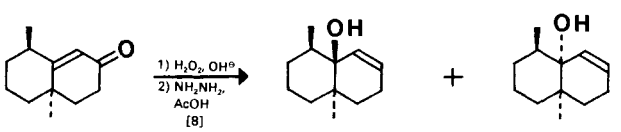
On the other hand, treatment of **7** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing glyme for 5 h afforded a 4:1 mixture of **1** and **8** (78% yield). In contrast to **1**, the isomeric **8** is characterized by a key fragment *m/z* 109 in its MS.

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*[4]). The minor, less polar isomer of the two octalols formed, which were readily separated by chromatography on SiO_2, proved to be identical with the minor isomer obtained on treatment of **7** with DBU *(Scheme 2)*.

Scheme 3



[4]) 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%)

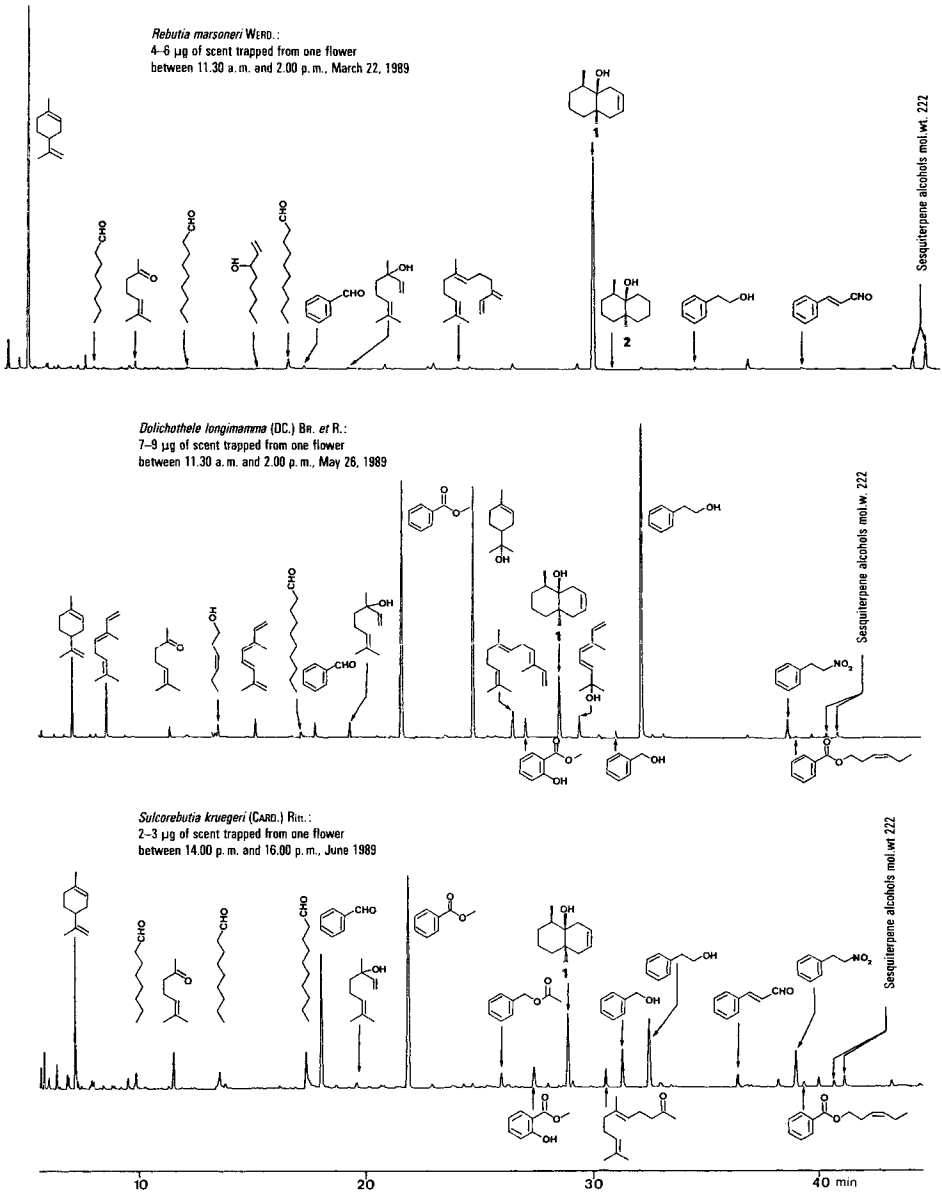


Fig. 2. *GC profiles of the trapped scents of* Rebutia marsoneri[5]), Dolichothele longimamma, *and* Sulcorebutia kruegeri. *DB-Wax*, 30 m × 0.3 mm i.d., 50–200° with 2.5°/min.

[5]) 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-earthy 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 m × 0.3 mm), He as carrier gas (70 kPa); temp. programming: samples were injected at 90°; after 2 min, 6°/min → 120°, then 20°/min → 240°.

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.[6]). 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 CS_2 (3 × 10 µl) 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-µl portions of the resulting eluates (20 µl) were used. GC: *Carlo Erba FTV 4160* with fused silica capillary column (*DB-Wax J&W*, 30 × 0.3 mm). MS: *Varian MAT*, models *CH-5* and 212 (70 eV).

(±)-Perhydro-7β,8aβ-dihydroxy-1β-methylnaphthalene-4aα-carbaldehyde (**4**). To a soln. of 330 mg (1.59 mmol) of **3** [4] in 10 ml of dry THF were added, at 0° under 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° for 40 min and then extracted with Et_2O (3 × 150 ml). The combined org. extracts were dried ($MgSO_4$), filtered, and evaporated: 214 mg (63%) of crystalline **4**. M.p. 125–127°. TLC (hexane/AcOEt 3:1): R_f 0.16. IR ($CHCl_3$): 3600*w*, 3450*m*, 2700*w*, 1720*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*d*, *J* = 6.5, 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 (*td*, *J* = 15.5, 4, 1 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*, $w_{1/2} \approx 8$, H–C(7)); 9.48 (*s*, CHO); irradiation at: 0.90 (*d*) → 1.90 (*dd*, *J* = 4.5, 12, H_{ax}–C(1)); 4.21 (*m*) → 1.98 (*d*, *J* = 14.5, H_{ax}–C(8)) and 2.05 (*dd*, *J* = 2, 14.5, H_{eq}–C(8)). MS: 194 (4, $[M - H_2O]^+$), 176 (7), 166 (41), 148 (100), 81 (51), 55 (65), 43 (95), 41 (79).

(±)-Perhydro-4aα,8β-dimethylnaphthalene-2β,8aβ-diol (**6**). To a soln. of 112 mg (0.53 mmol) of **4** in 4 ml of dry CH_2Cl_2 were added 0.39 g (5.4 mmol) of 2-methoxypropene (freshly distilled), followed by 12 mg of Py·TsOH.

[6]) *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 $NaHCO_3$, and extracted with Et_2O (2 × 100 ml). The combined org. extracts were dried ($MgSO_4$), filtered, and evaporated: **5** as a colorless oil. TLC (hexane/AcOEt 3:1): R_f 0.51. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*d*, J = 6.5, CH_3); 1.42, 1.53 (2 *s*, $(CH_3)_2C$); 4.32 (br. *t*, $w_{½} \approx 10$, 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_2O, and poured into ice-H_2O. After acidification with 1N H_2SO_4, the mixture was extracted with Et_2O (3 × 75 ml). The combined org. extracts were dried ($MgSO_4$), filtered, and evaporated. TLC (hexane/AcOEt 3:1): 2 spots at R_f 0.62 and 0.23. For complete removal of the $(CH_3)_2C$ 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_2 (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_f 0.23. IR ($CHCl_3$): 3610*w*, 3475*m*, 1018*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.83 (*d*, J = 6.5, CH_3); 0.90–1.08 (*m*, 1 H), overlapped by 1.02 (*s*, CH_3); 1.24–2.08 (*m*, 12 H); 2.97 (*s*, OH); 3.47 (*d*, J = 6.5, OH); 4.12 (*m*, $w_{½}$ = 10, 1 H). MS: 198 (3, $M^{+\cdot}$), 126 (100).

(±)-1,2,3,4,4a,5,8,8a-Octahydro-4β,8aα-dimethylnaphthalen-4aβ-ol (**1**) *and (±)-Perhydro-4β,8aα-dimethylnaphthalen-4aβ-ol* (= Geosmin, **2**). To a soln. of 51 mg (0.26 mmol) of **6** in 4 ml of CH_2Cl_2/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 ($MgSO_4$), and evaporated. Chromatography on SiO_2 (6 g) with hexane/AcOEt 2:1 afforded 64 mg (90%) of **7**. M.p. 83–86° (dec.). TLC (hexane/AcOEt 3:1): R_f 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_2O and H_2O. The combined filtrates were extracted with Et_2O (2 × 100 ml). The org. extracts were dried ($MgSO_4$) and evaporated. Filtration through a pad of SiO_2 (3.5 g) with pentane/Et_2O 8:1 afforded 15 mg (75%) of a colorless oil. Cap. GC *(SE-30)* showed three peaks at t_R 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_2O 5:1): R_f 0.40. IR ($CHCl_3$): 3600*w*, 998*m*, 878*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*d*, J = 6.5, CH_3); 0.97 (*s*, CH_3); 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). ^{13}C-NMR (100 MHz, $CDCl_3$): 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_2O 5:1): R_f 0.44. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.78 (*d*, J = 6.5, CH_3); 1.03 (*s*, CH_3). 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_2. The soln. was poured into ice-H_2O containing 120 mg (2 mmol) of AcOH and extracted with Et_2O (2 × 75 ml). The combined org. extracts were dried ($MgSO_4$) and evaporated. Chromatography on SiO_2 (4 g) with pentane/Et_2O 8:1 afforded 28 mg (78%) of a colorless oil. Capillary GC *(SE-30)* showed two peaks at t_R 8.4 and 8.6 min in a 4:1 ratio, corresponding to **1** and **8**, resp. The product ratio was confirmed by ^{1}H-NMR. No attempts were made to separate the two isomers. R_f, t_R, and ^{1}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,8aα-dimethylnaphthalen-4aβ-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_2 with pentane/Et_2O 10:1 afforded **8** as colorless oil. TLC (pentane/Et_2O 5:1): R_f 0.42. IR ($CHCl_3$): 3600*m*, 3470*w*, 1640*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.92 (*d*, J = 6.5, CH_3); 0.95 (*s*, CH_3); 1.00–2.22 (*m*, 12 H); 5.70–5.82 (*m*, 1 H); 5.95 (*dt*, J = 10, 2, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 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, $M^{+\cdot}$), 165 (62), 162 (34), 147 (63), 110 (55), 109 (100), 105 (56), 91 (89).

Continued elution of the column with pentane/Et_2O 5:1 afforded *(±)-1,2,3,4,4a,7,8,8a-Octahydro-4β,8aα-dimethylnaphthalen-4aα-ol* (**10**). M.p. 43–45°. TLC (pentane/Et_2O 5:1): R_f 0.27. IR ($CHCl_3$): 3605*m*, 1025*m*, 973*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.99 (*d*, J = 6.5, CH_3); 1.03 (*s*, CH_3); 1.08–2.24 (*m*, 12 H); 5.72–5.92 (*m*, 2 H). MS: 180 (12, $M^{+\cdot}$), 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.