168. Identification and Synthesis of two New Organic Sulfur Compounds from the Yellow Passion Fruit (*Passiflora edulis* f. *flavicarpa*)

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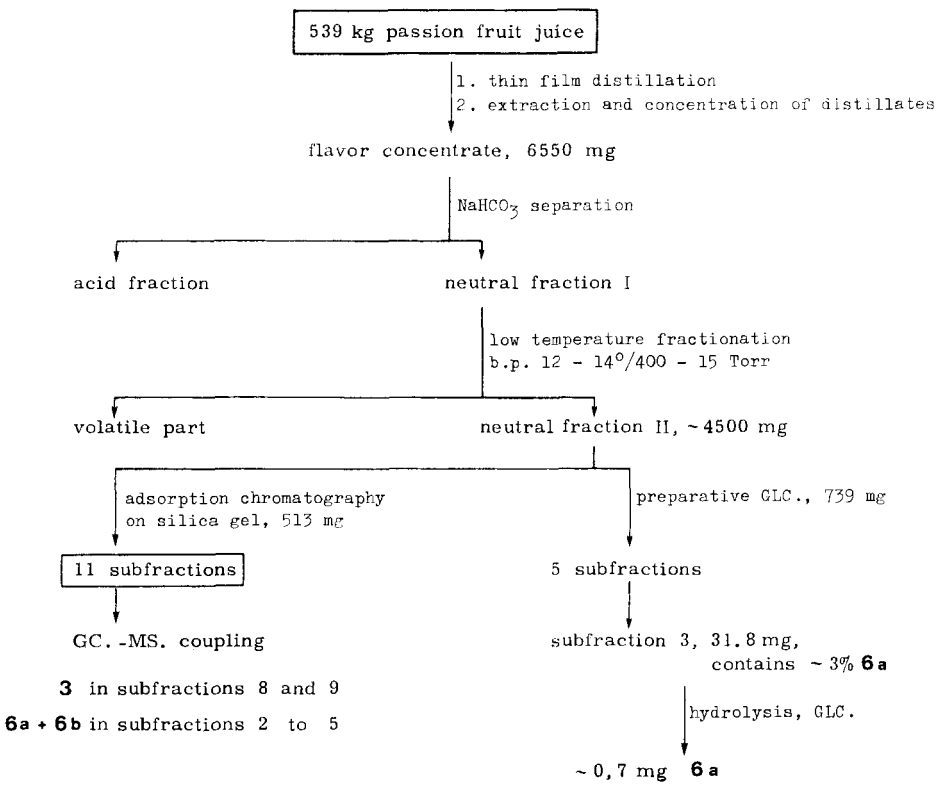
Summary. 3-Methylthio-hexanol (**3**) and a mixture of *cis*- and *trans*-2-methyl-4-propyl-1,3-oxathiane (**6a** and **6b**) have been identified in a flavor concentrate of the yellow passion fruit of Hawaiian origin. Syntheses of these new flavor constituents are described.

Introduction. Pursuing our investigation on the flavor of yellow passion fruit juice previously described [1], we now report the identification and synthesis of two new compounds. A commercially available fruit juice of the yellow passion fruit (*Passi-*

Scheme 1



flora edulis f. *flavicarpa*)[1]) was used for preparing the extract, which was divided into eleven neutral subfractions (in order of increasing polarity), as in [1] (see *Scheme 1* and Exper. Part.). Each subfraction was analysed separately by glass capillary GC. coupled to a mass spectrometer.

1. 3-Methylthio-hexan-1-ol (3). – **3** was found in the fairly polar subfractions 8 and 9. The polar characteristics, the low resolution mass spectrum, and ultramicroscale chemical reactions (hydrolyses, silylation) in conjunction with the mole-

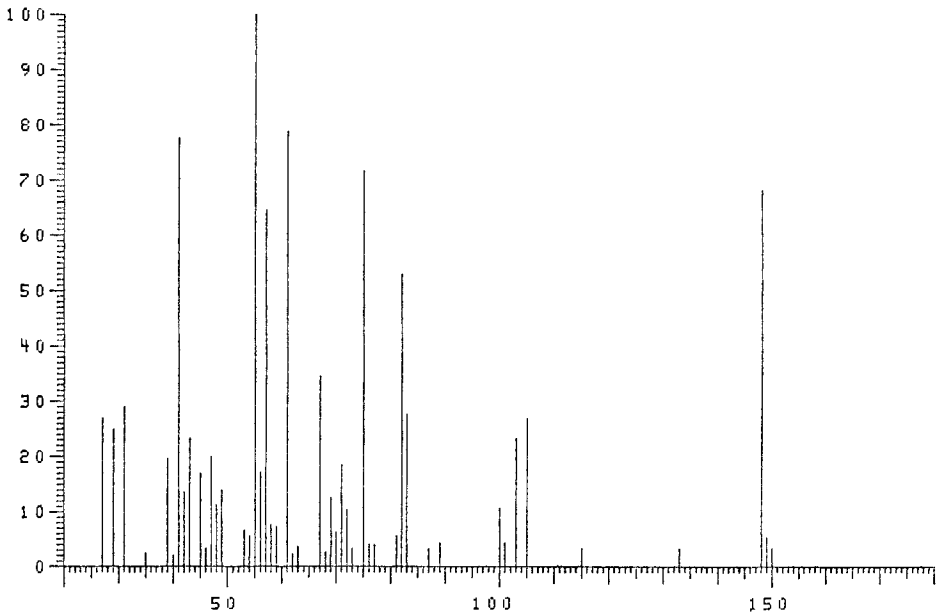


Fig. 1. *Mass spectrum of 3-methylthio-hexan-1-ol* (**3**)

cular ion, *m/e* 148, and the relative intensity (about 5%) of the ion *m/e* 150 suggested one of the two molecular formulas $C_6H_{12}O_2S$ or $C_7H_{16}OS$, with only one of the two possible polar functions -SH or -OH present. The mass spectrum was in agreement with a primary alcool (*m/e* 31) although M^+ was rather strong, and no *M – 18* fragment was visible. A $-SCH_3$ group was possible (*m/e* 100, *M – 48*) and the fragment *m/e* 82 suggested a C_6 chain (), whereas fragments *m/e* 105 and 103 indicated the $-SCH_3$ group to be on C(3).

We therefore synthesized compound **3**, which was identical with the natural compound (GC. retention times on polar and nonpolar phase.) The MS. of the natural and the synthetic compound showed some small differences attributable to impurities in the natural sample.

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[1]) Supplier: Nationwide of Chicago, *Food Brokers Inc.*, 1400 Winston Plaza, Melrose Park, Ill., USA (Origin: Hawaii).

2. 2-Methyl-4-propyl-1,3-oxathianes 6a and 6b. – GC.-MS. coupling of the subfractions 2 to 5 revealed the presence of two further unknown compounds (**6a** and **6b**) with identical mass spectra (see Fig. 2). The molecular ion 160 and the

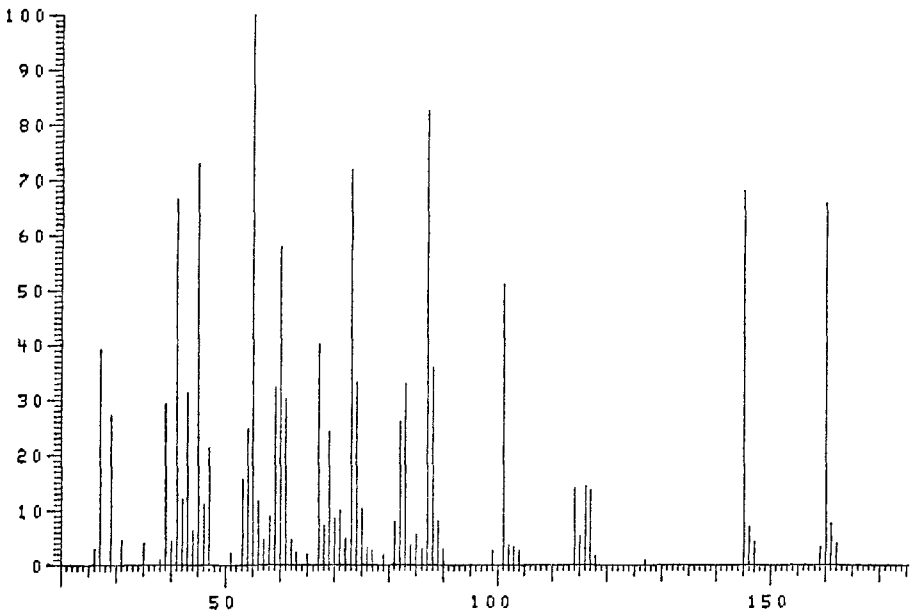


Fig. 2. *Mass spectrum of 2-methyl-4-propyl-1,3-oxathianes* **6a** and **6b**

relative intensity of the $M + 2$ ion (5.5%) suggested two isomers of either $C_8H_{16}OS$ or $C_7H_{12}O_2S$, the intensity of the $M + 1$ ion being in better agreement with $C_8H_{16}OS$. The chromatographic behavior of the two substances **6a** (about 9 parts) and **6b** (about 1 part) required two configurational isomeric structures of weak polarity. Chemical reactions on an ultramicroscale (10–100 ng) demonstrated the absence of ester, thioester and carbonyl functions and of active hydrogen (-OH, -SH).

No decision could be made about the presence of a double bond; no hydrogenation was observed[2]), but catalyst poisoning by a sulfur containing compound was possible. No satisfactory structure containing an ether (–O–) and a sulfide (–S–) group could be constructed from the mass spectrum.

Combination of physico-chemical and chemical separation methods enabled us finally to isolate in a pure state about 700 μg of the main isomer, for which a high resolution NMR. spectrum suggested structure **6** and which was indeed identical with synthetic **6a**. The NMR. spectra of the synthetic diastereoisomers **6a** and **6b** (see Fig. 3 and 4) show clearly that the main product of the 10:1 mixture corresponds to the thermodynamically more stable *cis*-configuration (**6a**) in which the two substi-

[2]) Catalyst: Pd (10%) on activated carbon, 15 min at 200° [2].

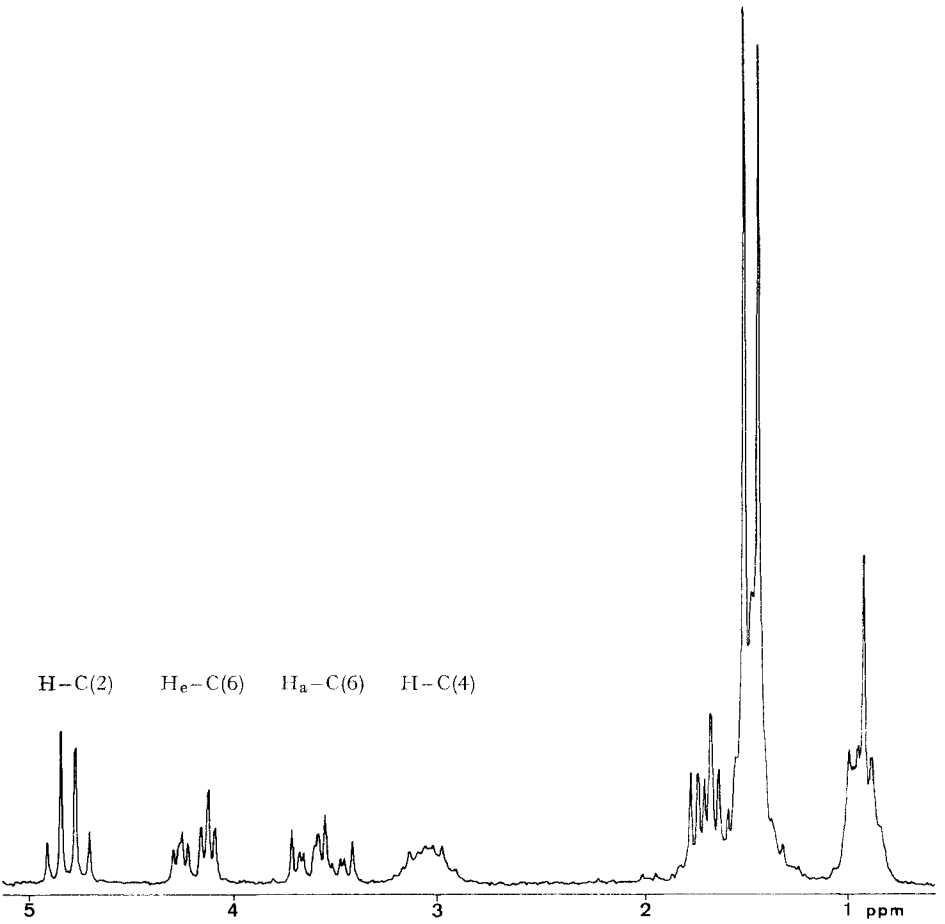


Fig. 3. *90 MHz ^{1}H-NMR. spectrum* (in $CDCl_3$) *of* **6a**

tuents are equatorial. As expected, the axial and equatorial protons on C(6) show a clear difference in their chemical shifts. This difference becomes quite small in the spectrum of the *trans*-isomer (**6b**) in which the relative shifts of the H–C(2) and H–C(4) signals suggest that this compound should exist predominantly in the conformation with the methyl substituent in the axial position. Retention values on polar and nonpolar stationary phase are in agreement with the above *cis-trans* assignment.

Compounds **3** and **6a**/**b** are new substances, which all exhibit interesting organoleptic properties. 3-Methylthio-hexanol (**3**) has a green, fatty and sulfury note, typical of certain exotic fruits, and it imparts the character of fresh fruit to the juice of passion fruits. A homologue of **3**, 3-Methylthio-propanol, has been identified in soy sauce [3], tomato[4] and cabernet wine [5]. **6a** and **b** both have a strong and

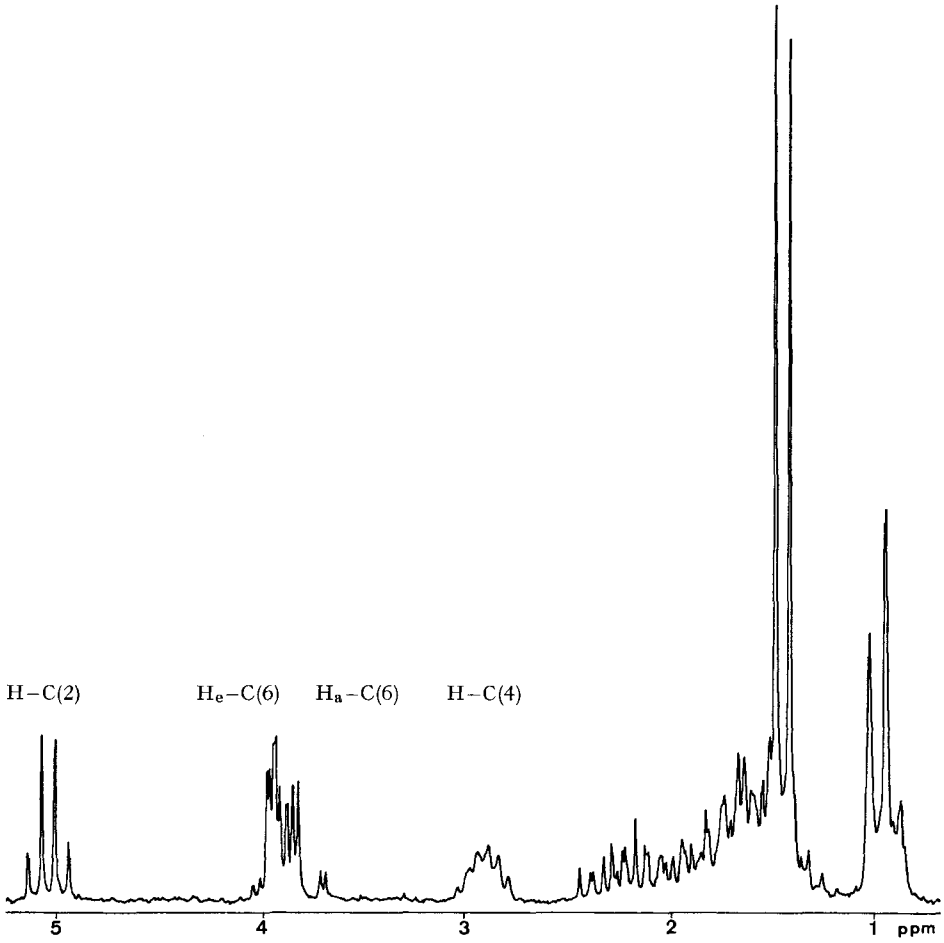
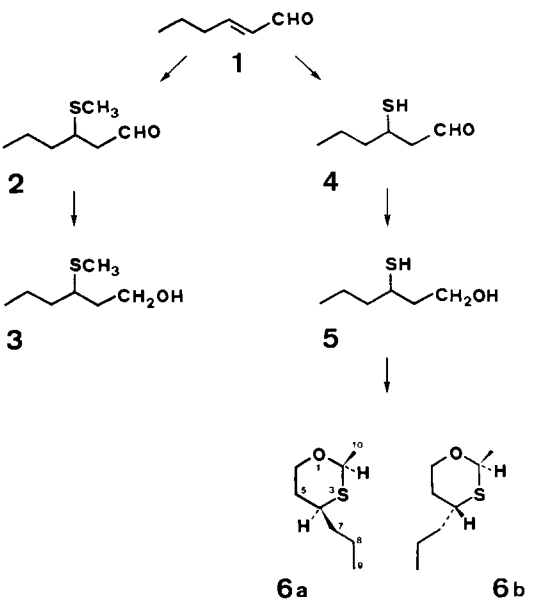


Fig. 4. *90 MHz ^{1}H-NMR. spectrum* (in $CDCl_3$) *of* **6b**

natural fruity odor with a green and slightly burnt note, in particular the *cis*-diastereoisomer, by which the two isomers are easily distinguishable. Both **3** and **6** contain a C_6-chain bearing an oxygen atom at position 1 and a sulfur atom at position 3, for which methionine and linoleic acid could be intermediates in the biogenetic pathway.

3. Synthesis. – **3** was accessible from 2-hexenal by addition of methanethiol and subsequent reduction with sodium borohydride. 2-Hexenal was also the starting material for **6a** and **6b**. After addition of hydrogen sulfide and subsequent reduction with sodium borohydride, the 3-mercapto-hexanol (**5**) obtained was condensed with acetaldehyde to form a mixture of the two diastereoisomers **6a** and **6b** (10:1 ratio) (see *Scheme 2*).

Scheme 2



We are indebted to Mrs. *M. Vuilleumier*, Miss *L. Caimmi* and Mr. *A. Velluz* for valuable technical assistance.

Experimental Part

1. Instrumental. – a) *Gas-chromatography.* Preparative GC.: *Carlo Erba* Fractovap, model GT 200 equipped with a catharometer. *Col. A*, 5% Apiezon L on Chromosorb G-HP 80–100 mesh, length 2.7 m, i.d. 8 mm. Packed column: *F+M*, model 400 equipped with FI-detector and a home-made catharometer. *Col. B*, 5% Carbowax 20 M on Chromosorb GAW-DMCS 80–100 mesh, length 2.7 m, i.d. 4 mm. Glass capillary columns: *Carlo Erba* Fractovap GI 450. *Col. C*, coated with Ucon HB 5100, length 53 m, i.d. 0.31 mm[3]). *Col. D*, coated with Apiezon L, length 50 m, i.d. 0,3 mm[3]). Typical GC. conditions: sample size 10–100 µg, injection without split, injection port temp 200°, column starting temp. 60°, temp. progr. (ΔT) 2°/min, inlet pressure 1 kg/cm². – In all cases He was used as carrier gas. For quantitative measurements we employed a *Hewlett-Packard* integrator model 3370 B. – Retention indices (I) were calculated according to the method given by *Kováts & Wehrli* [6].

b) *Mass spectrometry.* GC.-MS. coupling: GC.-oven *Carlo Erba* Fractovap GI 450 equipped with a glass capillary column coated with Ucon HB 5100, length 33 m, i.d. 0.31 mm[3]), connected *via* a single stage jet separator of the *Becker-Ryhage* type to an *ATLAS* CH4-B mass spectrometer. Temp. of connecting line and separator 200–250°, ion source temp. 250°, electron energy 70 eV. The total ion current was measured with an electron impact detector operating at 17.5 eV. The spectra of the synthetic reference samples were measured on an *ATLAS* CH4 instrument operating under similar conditions. Relative intensities are expressed as % of the most abundant peak (100%).

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[3]) Supplier: *H. & G. Jaeggi*, Laboratorium für Gas-Chromatographie, CH–9043 Trogen, Switzerland.

c) *NMR.-spectrometry.* 60 MHz ^{1}H-spectra were measured on a *Hitachi-Perkin-Elmer* R-20B instrument. 90 MHz ^{1}H-spectra were obtained on a *Bruker* HX 90/15″ instrument operating in FT-mode. $CDCl_3$ was used as solvent and δ-values are given in ppm downfield from TMS. Abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quadruplet, *m* = multiplet, br. = broad, *J* = coupling constant (Hz).

Further abbreviations: RT. = room temperature.

2. Isolation of compounds 3 and 6. a) – *Extraction and pre-separation* (*Scheme 1*). The flavor concentrate was obtained from 539 kg commercial passion fruit juice[1]) of Hawaiian origin as previously described [1], total 6.55 g (about 12 ppm). From 6.1 g of this concentrate in *n*-propyl chloride the acids were extracted with aqueous 5% $NaHCO_3$-solution at 0°. The neutral part was concentrated and distilled in a *Fisher* MS 150 type column[4]) (~10 plates). Removal of a volatile head fraction (~40 mg, bath temp. 12–14°, pressure 400 – 15 Torr) gave ~4.5 g of residue (neutral fraction II). 513 mg of the neutral fraction II were separated into 11 subfractions by descending dry-column chromatography in a Teflon tube [7] (column size: i.d. 15.7 mm, length 250 mm, packing 20.8 g silica gel *Merck* HR deactivated with 20% H_2O, development time 100 min, solvent *n*-propyl chloride + 1% methanol). The column was cut into eleven 20 mm zones and these were extracted with propyl chloride and propyl chloride/methanol 10:1. Concentration of these extracts yielded fractions of 13, 83, 99, 50, 15, 24, 45, 65, 39, 11, and 4.8 mg respectively. Further separation of these subfractions followed by GC., the final step being carried out in glass capillary columns coupled to a mass spectrometer.

b) *Isolation of 3-Methylthio-hexanol* (**3**). Coupled GC.-MS. of subfractions 8 and 9 revealed the presence of the sulfur containing compound **3** (conc. *ca* 0.1% in 8), I_{Ucon} *ca.* 1640 (col. C), which is about 10 units shorter than that of geraniol, which always accompanied **3**. – MS.: see Fig. 1.

c) *Isolation of* cis- *and* trans-*2-Methyl-4-propyl-1,3-oxathiane* (**6a** and **6b**). GC.-MS. showed **6a** and **6b** were present in the subfractions 2 to 5 and in the total neutral fraction II, of which *ca.* 0.1% is **6a**. Retention indices, measured on glass capillary columns, were about 1120 and 1140 on column D and 1380 and 1410 on column C. By preparative GC. on column A, 739 mg neutral fraction II were separated, and 31.8 mg of a subfraction 3 (between $I_{Aplezon}$ 1090 and 1200), containing ~3% substance **6a** were collected in traps packed with purified Porapak Q. GC. conditions: inj. 50–70 µl, temperature program 100–214°, ΔT 3°/min, 170 ml He/min. The trapping tubes were rinsed with propyl chloride, methanol and again propyl chloride.

Most of the accompanying substances in this subfraction 3 were esters and so, knowing from previous micro tests that compound **6** was not hydrolysable, we saponified it with 20% methanolic KOH-solution for 4 h at RT. The propyl chloride extract washed to neutrality still showed three main peaks, which were well separated on polar GC. columns. About 700 µg of **6a** ($I_{Carbowax}$ *ca.* 1530) was collected in a capillary tube at the GC. outlet. GC. conditions: column B, temperature programm 80–200°, ΔT 3°/min, 30 ml He/min. The capillary tube was rinsed with $CDCl_3$ directly into the NMR. tube.

3. Synthesis. – a) *3-Methylthio-hexanol* (**3**). To a stirred mixture of 100 g 2-hexenal (1.0 mol) and 2.3 g trimethylamine 40% in H_2O, 48 g gaseous methanethiol (1.2 mol) were introduced (ammonia condenser) over 1.75 h at 10–20°, and the mixture was further stirred at 20° for 1 h. The product was dissolved in ether, washed with 10% aqueous H_2SO_4-solution and H_2O, dried with $MgSO_4$, filtered and evaporated to yield about 150 g of crude product, b.p. 87–88°/10 Torr, yielding 129 g of *3-methylthio-hexanal* (**2**). – NMR.: 0.91 (3H, br. *t*); 1.5 (4H, br. *m*); 2.0 (3H, *s*); 2.57 (2H overl. *m*); 2.95 (1H, br. *m*); 9.65 (1H, *t*, *J* = 2). – MS.: M^+ 146 (41): *m/e*: 70 (100), 55 (86), 41 (79), 42 (61), 61 (46), 48 (46), 75 (33), 27 (33), 118 (19).

To a stirred solution of 113 g of **2** (0.755 mol) in 230 ml methanol and 230 ml water, 22 g $NaBH_4$ (0.58 mol) in 80 ml H_2O were added dropwise at 0–5° during 30 min. After 30 min of

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[4]) *Fischer*, Labor- und Verfahrenstechnik, Heerstrasse 35–37, D–53 Bonn-Bad Godesberg, Germany.

additional stirring at 10°, 350 ml 10% aq. H_2SO_4 were added. After extraction with petroleum ether, the solution was washed and dried, the solvent evaporated leaving a crude product which was distilled: b.p. 61–62°/10.01 Torr; yield 103 g of pure *3-methylthio-hexanol* (**3**). – NMR.: 0.91 (3H, br. *t*); 2.0 (3H, *s*); 2.7 (1H, br. *m*); 3.76 (2H, *t*, J = 6). – MS. see Fig. 1.

b) *2-Methyl-4-propyl-1,3-oxathianes* (**6a** *and* **6b**). Hydrogen sulfide was bubbled into a stirred solution of 88 g 2-hexenal (0.9 mol) and 1.0 g hydroquinone in 200 ml tetrahydrofurane at 25–30°. The excess H_2S was absorbed in ammonia. After 4 h the addition was complete, and the mixture was cooled to 15°. A small sample of *3-mercaptohexanal* (**4**) was isolated. MS.: M^+ 132 (16); *m/e*: 55 (100), 41 (85), 42 (75), 70 (51), 27 (45), 29 (40), 39 (38), 61 (33), 99 (14), 114 (12).

After neutralization of residual H_2S with 40% aq. NaOH-solution reduction was directly effected using 10 g $NaBH_4$ (0.26 mol, in 40 ml H_2O) added dropwise over 2 h to the cooled mixture at 15°. Then the mixture was dissolved in 400 ml H_2O, extracted with ether, the ether extract washed with H_2O, with 5% aq. H_2SO_4, and again with H_2O. The dried and concentrated crude product was distilled through a *Vigreux* column, 84.2 g *3-mercaptohexanol* (**5**) being collected in a main fraction. – NMR.: 0,9 (3H, br. *t*); 2,9 (1H, br. *m*); 3,74 (2H, *t*, J = 7). – MS.: M^+ 134 (8); *m/e*: 55(100), 41 (73), 57 (64), 61 (50), 100 (41), 31 (40), 67 (34), 47 (30).

A solution of 84 g **5** (0.625 mol) and 1.25 g *p*-toluenesulfonic acid in 250 ml di-isopropyl ether were heated to reflux with a water separator, and 30.5 g acetaldehyde (0.7 mol) were introduced dropwise during 1 h. After $2^1/_2$ h of further reflux, the mixture was washed with 5% Na_2CO_3-solution and water, dried with $MgSO_4$ and concentrated. From 104 g crude product 85 g of *pure* **6a** and **6b** in a proportion of 10 : 1, b.p. 85–86°/12 Torr (*Vigreux* column) were obtained. The two isomers were separated by distillation in a Normag 100 cm spinning band column[5]) (40 plates), b.p. 26–28°/0.22 Torr.

6a: NMR. see Fig. 3, MS. see Fig. 2.

6b: NMR. see Fig. 4, MS. see Fig. 2.

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