266. Investigation on the Head-Space of Roasted Meat. III. Synthesis of 4,6-Dimethyl-2,3,5,7-tetrathiaoctane[1])

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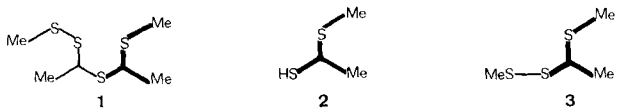
(10.VII.78)

Summary

A synthesis of 4,6-dimethyl-2,3,5,7-tetrathiaoctane (**1**), from 3,5-dimethyl-1,2,4-trithiolane (**6**), is described. Compound **1**, possessing a unique structure was recently found to be a constituent of roasted pork meat.

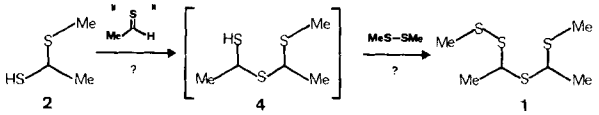
Introduction. – Analytical work performed in this laboratory by *Hřivnáč et al.* [1] has led to the assignment of structure **1** (NMR. and MS. data) to a compound occurring in the head-space of roasted pork meat. Compound **1** strongly resembles at least 2 structures **2** [2] and **3** [1] known from meat analyses *(Scheme 1)*. The building-

Scheme 1



block **2** is incorporated in **3**, as well as in **1**. A reasonable pathway relating **2** and **3** was suggested by us [3]. Generically **1** could be the product of chain expansion of **2** with thioacetaldehyde or precursors thereof, leading to a hypothetical mercaptan intermediate **4** *(Scheme 2)*, which could then be quenched in the same way as suggested for the formation of **3** from **2** [3].

Scheme 2



Structure **1** is the first isolated representative of the 2,3,5,7-tetrathiaoctanes; however, it seems probable that less volatile homologues will be found in the future. This expectation is justified because various 3-substituted 2,4,5-trithiahexanes co-occur in roasted pork-meat [1], compound **3** being structurally the most simple example isolated.

[1]) Part II: see [3].

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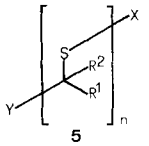
From a formal point of view thioaldehyde and thioketone derivatives of type **5** seem to play a dominant role in heat-treated, sulfur-containing food, such as roasted meat.

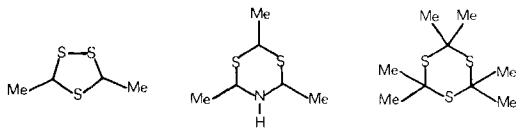


5

n = 1, 2, 3, · · · ?
R^1, R^2 = H, alkyl, · · ·

Nature seems to be mainly concerned with how to start (group Y) and how to terminate (group X) the n-fold sequence of thiocarbonyl-derived units as depicted in **5**. Besides compounds **1**, **2**, **3**, 3 further structures **6** [4], **7** [2] and **8** [5], known from meat-analyses, fitting very well into the framework **5** discussed, can be quoted; the latter examples being an illustration of the many possibilities realized for X and Y in nature.

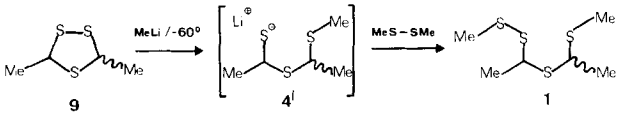
Scheme 3



6 **7** **8**

Synthesis of 4,6-dimethyl-2,3,5,7-tetrathiaoctane (1). – Guided by 'biogenetic' reasoning, such as outlined in *Scheme 2*, we effected a short synthesis of **1** *(cf. Scheme 4)*. Deprotonated 1-methylthiomercaptans are not too prone to degrade into their parts [3]. Therefore we focused our attention on the deprotonated form **4′** of the postulated intermediate **4**.

Scheme 4



9 **4′** **1**

3,5-Dimethyl-1,2,4-trithiolane (**9**) [6] (*ca.* 60% *cis*- and 40% *trans*-isomers by NMR. assignments, *cf. Tjan et al.* [6]) reacted with methyllithium at $-60°$ to give the anticipated intermediate **4′**, which was transformed to **1** in the presence of excess dimethyldisulfide. The product **1** is a mixture of diastereoisomers, readily separated by preparative GC. However, configurational assignment on the basis of their spectral data was not possible. The 3:2 ratio of the *cis* and *trans* starting material **9** seems to be reflected in a 3:2 ratio of isomeric pairs (±)-**1a** and (±)-**1b**. Based on the assumption that the chiral centers in intermediate **4′** remain configurationally stable under the reaction conditions, we tentatively assign the *erythro*-configuration to (±)-**1a** (originating from *cis*-**9**) and the *threo*-configuration to (±)-**1b** (originating from *trans*-**9**).

The NMR. spectra of the synthetic materials (±)-**1a** and (±)-**1b** and the isolated compound are illustrated. The isolate seems to consist of the *erythro*-form of **1** (the

small signal at $\delta = 2.2$ ppm is not conclusive evidence for the co-occurrence of the *threo*-isomer). However, in view of the delicate isolation technique [1] and since no argument is strongly in favour of only one isomer, both isomers (±)-**1a** and (±)-**1b** are probably present in roasted pork meat.

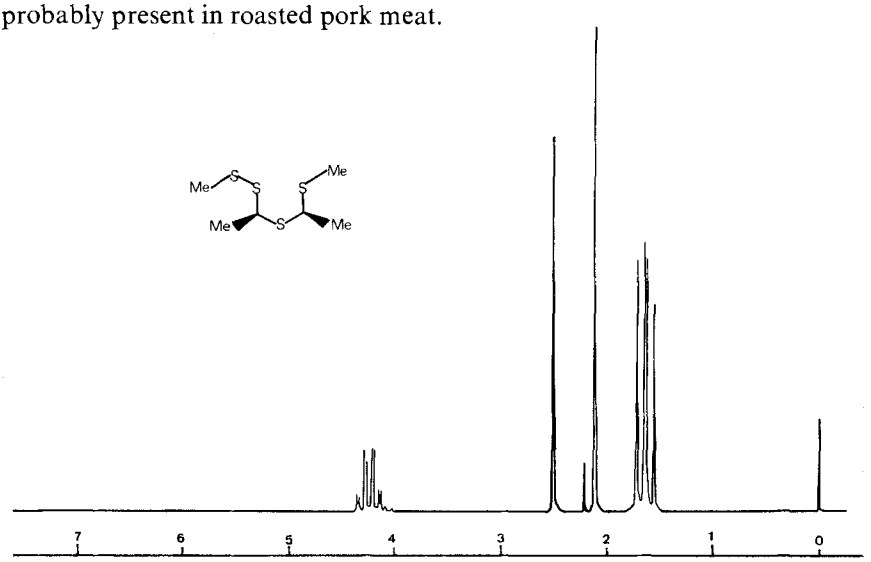


Fig. 1. *^{1}H-NMR. of synthetic* erythro (±)-**1a**

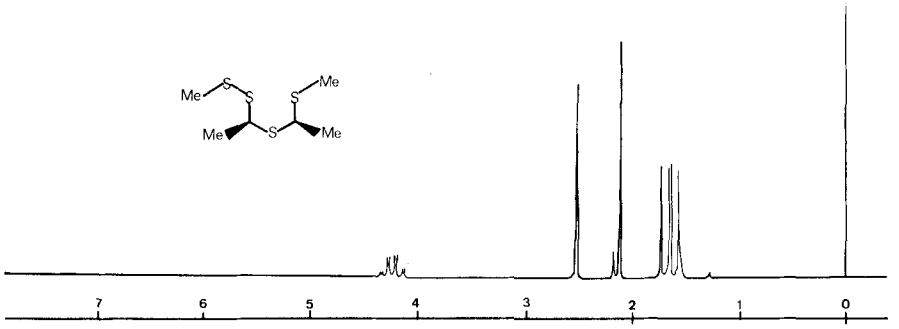


Fig. 2. *^{1}H-NMR. of isolated, natural* erythro (±)-**1a**

Experimental Part

General remarks. – ^{1}H-NMR. spectra were recorded on a *Varian* XL-100A instrument (100 MHz), in $CDCl_3$ with TMS as internal standard (ppm values relative to TMS = 0, *J* in Hz); abbreviations: *s* = singlet, *d* = doublet, *qa* = quartet. MS. were measured on a *Varian* CH-5 spectrometer, using an inlet temperature of 150° and an ionisation energy of 70 eV; the intensity of the molecular ion and of the 8 most intense fragments' ions are given in % of the base peak. Gas liquid chromatography (GC.) was performed on a *Carlo Erba* Fractovap GI instrument, using OV-101, 2% on AW-DMCS, 80–100 mesh (3 mm × 3 m).

3,5-Dimethyl-1,2,4-trithiolane (**9**) was prepared following [6] and was a mixture of *cis*- and *trans*-**9** 3:2.

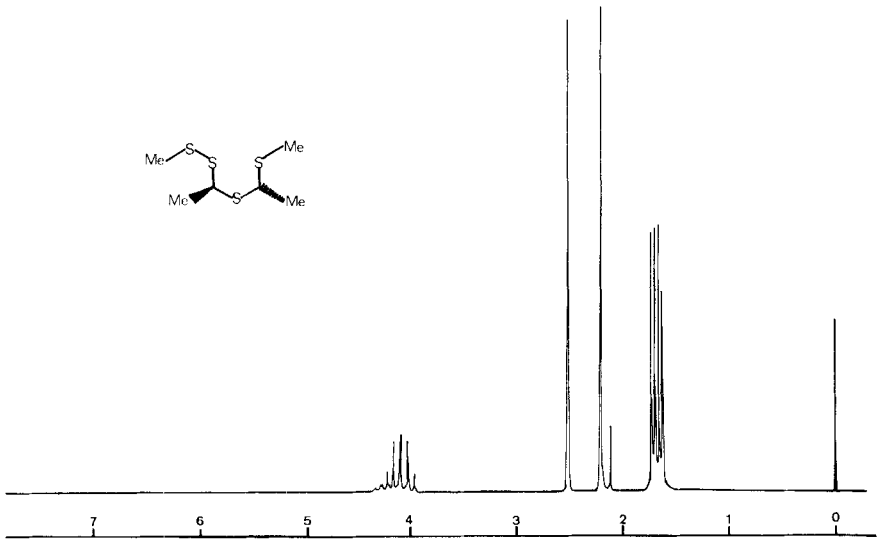


Fig. 3. *^{1}H-NMR. of synthetic* threo (±)-**1b**

4,6-Dimethyl-2,3,5,7-tetrathiaoctane (**1**). 3,5-Dimethyl-1,2,4-trithiolane (**9**) (3.04 g, 20 mmol) in 10 ml abs. ether was added dropwise within 10 min, under argon, to a well stirred 1.8M ethereal solution (11 ml) of freshly prepared CH_3Li at −60°. The solution was stirred at −60° for a further 90 min, then 50 ml of dimethyl disulfide were added with stirring at −50° and this temperature maintained for another 60 min. The cooling-bath was removed and stirring continued for 50 min to reach RT. The reaction mixture was washed to neutrality with saturated NaCl solution (6×25 ml). The organic layer was dried (Na_2SO_4) and evaporated at 60°/11 Torr. The crude product was subjected to a short-path distillation at 0.08 Torr/100° (oven temp.), giving a practically pure 3:2 mixture (3.6 g; 84%) of both possible diastereomers (±)-**1a** and (±)-**1b** (GC., NMR.), the more abundant isomer (±)-**1a** showing a distinctly shorter GC. retention on a packed OV-101 column. Pure (±)-**1a** and (±)-**1b** were obtained by preparative GC. on a OV-101 column.

Erythro-4,6-dimethyl-2,3,5,7-tetrathiaoctane ((±)-**1a**). ^{1}H-NMR.: 4.27 (*qa*, J=7, 1H, S–CH–S); 4.25 (*qa*, J=7, 1H, S–CH–S); 2.53 (*s*, 3H, S_2–CH_3); 2.14 (*s*, 3H, S–CH_3); 1.70 (*d*, J=7, 3H, CH_3); 1.60 (*d*, J=7, 3H, CH_3). – MS.: 214 (M^+, 0), 75 (100), 135 (23), 59 (22), 45 (20), 47 (12), 60 (11), 79 (7), 107 (5).

Threo-4,6-dimethyl-2,3,5,7-tetrathiaoctane ((±)-**1b**). ^{1}H-NMR.: 4.12 (*qa*, J=7, 1H, S–CH–S); 4.06 (*qa*, J=7, 1H, S–CH–S); 2.52 (*s*, 3H, S_2–CH_3); 2.21 (*s*, 3H, S–CH_3); 1.70 (*d*, J=7, 3H, CH_3); 1.66 (*d*, J=7, 3H, CH_3). – MS.: 214 (M^+, 0), 75 (100), 59 (30), 45 (29), 135 (20), 47 (16), 60 (16), 79 (10), 107 (6).

The authors are indebted to Dr. *M. Hřivnáč* and Mrs. *L. Sýkora* for various preparative GC. and to Dr. *P. Schudel* for his stimulating interest in this work.

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