224. Investigation of the Head-Space of Roasted Meat
II. Synthesis of Substituted 2,4,5-Trithia-hexanes*)

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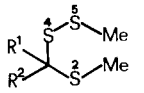
Summary

Substituted 2,4,5-trithiahexanes **1**, a class of substances recently found in roasted meat, have been synthesized *via* two different routes.

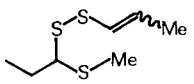
Introduction. – Investigations from this laboratory [1] have shown that compounds of the structural type **1** occur in the head-space of roasted pork meat (NMR. and MS.). In order to prove rigorously the individual structures **1** of the isolates, we have undertaken the syntheses of these compounds by two different approaches *(Schemes 1* and *4)*.



R^1 = H, alkyl
R^2 = alkyl, aryl

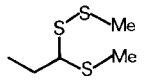
1

Although information on similar structures is scarce, compound **2**, exhibiting the same 2,4,5-positions of sulfur atoms, was isolated [2] from the essential oil of *Asa foetida* which finds some use in perfumery [3]. On the other hand the parent compound **1a** of class **1** is known to occur in cabbage, broccoli and cauliflower [4]. Compound **1c** is formed [5] under the influence of heat, in a model system containing propanal, hydrogen sulfide and methanethiol.



2
(in *Asa foetida* [2])

1a
(in cabbage, broccoli and cauliflower [4])



1c

From the synthetic viewpoint *Brintzinger & Schmahl* [6] report the preparation of compounds similar to **1a** by reaction of chloromethylsulfenyl chloride with thiols. *Block & O'Connor* [7] describe an interesting access to structure **1a**, starting with di-

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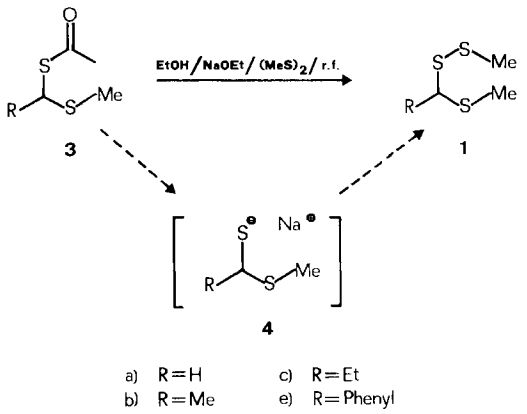
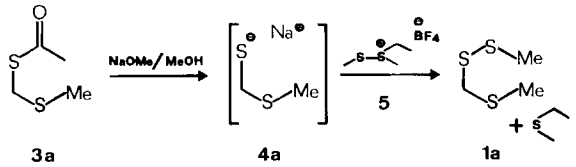
methyl thiolsulfinate. Finally, *Buttery & Seifert* [8] have shown that photolysis of dimethyl disulfide gives rise to 2,4,5-trithiahexane **1a** in low yield.

Synthesis of 2,4,5-trithiahexanes 1 from 2,4-dithiahexan-5-ones 3 (Method A). – Thioacetates **3a, b, c, e**, synthesized according to *Scheme 3*, were directly transformed to the target-compounds **1a, b, c, e**, with an excess of dimethyl disulfide in the presence of catalytic amounts of sodium alcoholate (yields 30–74%). The postulated intermediates of type **4**, initially expected to decompose to the corresponding thioaldehydes and their derivatives, were substantiated in the case **4a** *(Scheme 2)*.

Scheme 1



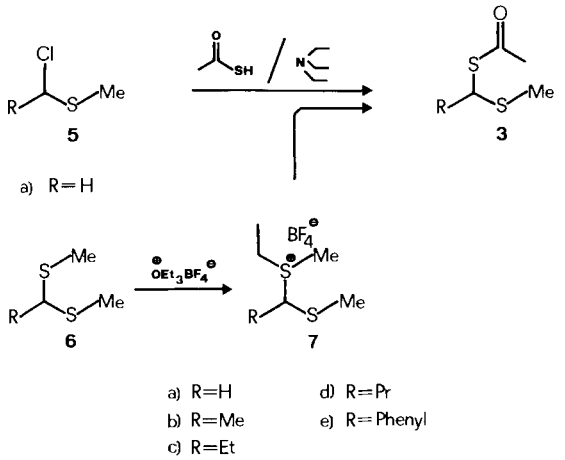
Scheme 2



Methanolysis of **3a** gave a product assumed to be **4a**, because subsequent quenching with the highly reactive, alkylated disulfide **5** [9] yielded **1a** under comparatively mild conditions.

Preparation of the starting materials **3** proved to be troublesome, although they are accessible *via* two different routes *(Scheme 3)*. For example, chloromethylmethylsulfide (**5a**), can easily be transformed to the corresponding thioacetate **3a** with thioacetic acid/triethylamine. Another approach leading to the thioesters **3a–3e** starts from the corresponding thioacetals **6a–6e**, alkylated with *e.g.* triethyloxonium fluoroborate to the intermediates **7a–7e** which are intercepted with thioacetic acid/triethylamine. Similar transformations of branched-chain thioacetals and especially of analogous thioketals to derivatives **3** failed. We were therefore looking for a more general synthetic method for 2,4,5-trithiahexanes **1**.

Scheme 3

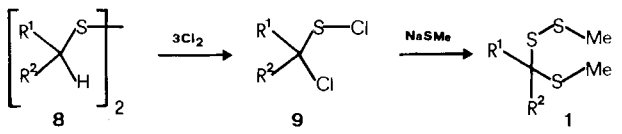


a) R=H

a) R=H d) R=Pr
b) R=Me e) R=Phenyl
c) R=Et

Synthesis of 2,4,5-trithia-hexanes 1 from symmetrical disulfides 8 (Method B). – Disulfides **8** were chlorinated with 3 equivalents of chlorine by the method of *Brintzinger* [6] [10] to give α-chlorosulfenyl chlorides **9**. Subsequent reaction of **9** with 2 equivalents of sodium methylthiolate gave the 2,4,5-trithiahexanes. This method (B) was, from a structural viewpoint (substitution pattern of R^1 and R^2), of much wider application for the synthesis of structures **1** than method A. The *Table* summarizes the different trisulfides **1** synthesized. With the exception of **1a**, all have been detected in roasted pork meat [1].

Scheme 4

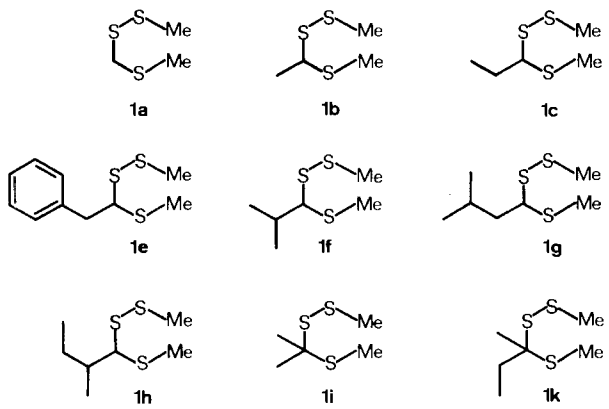


f) R^1 = H, R^2 = *i*-Propyl i) R^1 = Me, R^2 = Me
g) R^1 = H, R^2 = *i*-Butyl k) R^1 = Me, R^2 = Et
h) R^1 = H, R^2 = *s*-Butyl

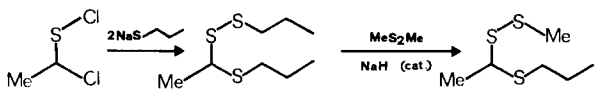
The reaction of α-chlorosulfenyl chloride **9b** with sodium 1-propanethiolate to **10b** *(Scheme 5)* exemplifies that method B is not restricted to methanethiol for the transformations of type **9** → **1**. In addition, we have been able to exchange the propylthio unit of the disulfide part in **10b** by reaction with an excess of dimethyldisulfide in the presence of catalytic amounts of sodium hydride, when trisulfide **11b** was obtained.

Both methods A and B yielded, besides the target-compounds **1**, in every case up to 10% of the corresponding dimers **12**, resulting from an equilibration [9] according to *Scheme 6*. It was not too difficult to separate them from the 2,4,5-trithiahexanes **1** by fractional distillation. In a few selected cases they were isolated and

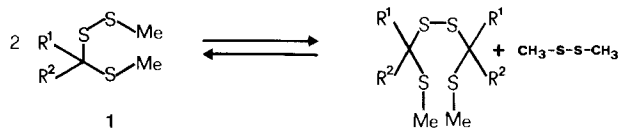
Table



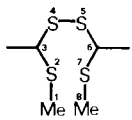
Scheme 5



Scheme 6



fully characterized (see exp. part). When $R^1 \neq R^2$, as in **12b** and **12c**, the product **12** was an approximately 1:1 mixture of the *meso* and *d,l*-forms (*cf.* NMR. data in the exper. part), not separable by preparative GC., although in the case of *e.g.* **12b**, the two isomers exhibit slightly different behaviour on capillary GC-columns.

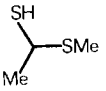


12b

Compound **12b** is a simple representative of a further, new class of compounds, the 2,4,5,7-tetrathiaoctanes, isolated from roasted pork-meat in this laboratory [1].

Discussion. – Structures **1** and **12** are tetrahedralized heteroatomic derivatives of aldehydes and ketones, and belong, from this point of view, to a generalized family of compounds [11], which comprises such diverse constituents as *e.g.* 3,5-dimethyl-1,2,4-trithiolane [12], 2,4,5-trimethyl-3-oxazoline [12] or 2,4,6-trimethyl-

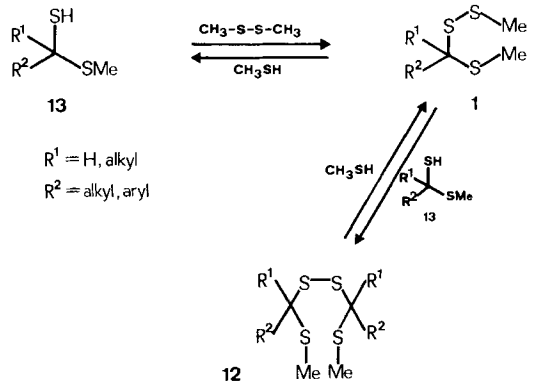
1,3-dithia-5-azacyclohexane ('thialdine') [13], well-known to occur in processed meat. Moreover, 1-methylthioethanethiol (**13b**) was detected in the head-space of beef-broth [13] and isolated [14] as one of the reaction products of acetaldehyde, hydrogen sulfide and methanethiol, three precursors known to be present in heat-treated meat.



13b

It is well established that mercaptans can undergo equilibration reactions with disulfides. Since dimethyl disulfide is a known constituent of meat [15], processes **13** ⇄ **1** ⇄ **12** are highly probable during heat treatment of meat.

Scheme 7



The authors are indebted to Dr. *E. Billeter* and Mr. *J. Märki* for their NMR. services, to Dr. *M. Hrivnac* and Mrs. *L. Sykora* for many preparative GC. and to Dr. *P. Schudel* for his continuing interest in this work. The skillful help of Miss *U. Schärer* and Mr. *Y.-St. Kellenberger* during various syntheses is gratefully acknowledged.

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, *t* = triplet, *qa* = quartet, *m* = multiplet, br. = broad. IR. spectra were measured on a *Perkin-Elmer* 257 spectrometer; characteristic maxima are given in cm^{-1}. Mass spectra were recorded 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 fragment 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).

Method A

1. Syntheses of starting materials; 3-substituted 2,4-dithiahexan-5-ones (3). – 1.1. **3a** *From chloromethylmethylsulfide* (**5a**). A solution of thioacetic acid (6.08 g, 0.08 mol) in 25 ml $CHCl_3$ was stirred and cooled in ice/salt. Triethylamine (8.08 g, 0.08 mol) was added dropwise under argon, when a slightly exothermic reaction was observed. Chloromethylmethylsulfide (**5a**) (7.72 g, 0.08 mol) was added dropwise with stirring to this solution, whereupon a temperaturerise to + 10° was observed. After removal of the cooling bath the temperature rose to + 40°, and a precipitate formed. The reaction mixture was diluted with 10 ml $CHCl_3$ and heated at reflux for 30 min. After cooling to 0°, dilution with 40 ml water, and

acidification with glacial acetic acid to pH = 4, the mixture was extracted with ether (3 × 100 ml). The organic layers were neutralized with saturated $NaHCO_3$-solution, then combined and dried (Na_2SO_4). After evaporation of the solvent at 40°/11 Torr, 12.04 g of crude **3a** were obtained and distilled (*Vigreux*-column) to obtain 7.41 g (68%) of pure (GC., NMR.) 2,4-dithiahexan-5-one (**3a**), b.p. 71–72°/11 Torr. – IR. (liq.): 3000, 2930, 1690, 1420, 1355, 1205, 1130, 1100, 975, 755, 710. – ^{1}H-NMR.: 4.03 (*s*, 2 H, CH_2); 2.40 (*s*, 3 H, $CO-CH_3$); 2.18 (*s*, 3 H, $S-CH_3$). – MS.: 136 (M^+, 5), 43 (100), 61 (42), 45 (34), 46 (13), 35 (10), 94 (5), 63 (3), 77 (1).

1.2. **3a–e** *from dimethylthioacetals* **6a–e** *(general procedure).* A solution of triethyloxonium fluoroborate (47.5 g, 0.25 mol) in 80 ml of abs. CH_2Cl_2 (passed through basic aluminum oxide before use) was added dropwise under argon to a well-stirred solution of dimethyl thioacetals **6a–e**[2]) (0.2 mol) in abs. CH_2Cl_2, keeping the temperature at 30° (cooling). The resulting solutions of salts **7a–e** were subsequently cooled to 0°, and triethylammonium thioacetate[3]) (0.21 mol) in 60 ml abs. $CHCl_3$ was added dropwise at 0°, with good stirring, under argon. The reaction mixture was kept at RT. for 1 h, then ice and diluted acetic acid were added (until the pH was *ca.* 3) and the whole immediately extracted with ether (3 × 100 ml). The organic extracts were washed once with saturated $NaHCO_3$, dried (Na_2SO_4), and the solvent was evaporated at 40°/100 Torr to give the crude thioacetates **3a–e**, which were purified by fractional distillation (*Vigreux*-column).

2,4-Dithiahexan-5-one (**3a**) (46%), b.p. 71–72°/11 Torr. – IR., ^{1}H-NMR. and MS.: *cf.* above under 1.1.

3-Methyl-2,4-dithiahexan-5-one (**3b**) (45,5%), b.p. 69–71°/11 Torr. – IR. (liq.): 3000, 2950, 1690, 1440, 1355, 1135, 1110, 1060, 955, 740, 710. – ^{1}H-NMR.: 4.65 (*qa*, $J = 7$, 1 H, S–CH–S); 2.35 (*s*, 3 H, $CO-CH_3$); 2.18 (*s*, 3 H, $S-CH_3$); 1.65 (*d*, $J = 7$, 3 H, $CH_3-C(S)-S$). – MS.: 150 (M^+,17), 75 (100), 43 (71), 59 (25), 45 (12), 61 (6), 79 (5), 103 (5), 107 (5).

3-Ethyl-2,4-dithiahexan-5-one (**3c**) (37%), b.p. 89–90°/11 Torr. – IR. (liq.): 3000, 2950, 1960, 1430, 1380, 1355, 1135, 1110, 960, 820. – ^{1}H-NMR.: 4.55 (*t*, $J = 7$, 1 H, S–CH–S); 2.37 (*s*, 3 H, $CO-CH_3$); 2.17 (*s*, 3 H, $S-CH_3$); 1.92 (*quintet*, $J = 7$, 2 H, CH_2); 1.03 (*t*, $J = 7$, 3 H, CH_3). – MS.: 164 (M^+,4), 43 (100), 89 (54), 41 (51), 45 (23), 73 (16), 61 (12), 47 (11), 75 (8).

3-Propyl-2,4-dithiahexan-5-one (**3d**) (9.5%), b.p. 95–99°/11 Torr. – IR. (liq.): 2980, 2950, 2890, 1690, 1460, 1440, 1380, 1355, 1135, 1110, 955, 770. – ^{1}H-NMR.: 4.65 (*t*, $J = 6.5$, 1 H, S–CH–S); 2.37 (*s*, 3 H, $CO-CH_3$); 2.15 (*s*, 3 H, $S-CH_3$); 2.00–1.20 (*m*, 4 H, CH_2-CH_2); 0.95 (*t*, $J = 7$, 3 H, CH_3).

3-Phenyl-2,4-dithiahexan-5-one (**3e**) (87.5%), b.p. 113°/0.03 Torr. – IR. (liq.): 3050, 2920, 1690, 1600, 1585, 1490, 1455, 1420, 1355, 1130, 1100, 1075, 1030, 955, 840, 705. – ^{1}H-NMR.: 7.50–7.10 (*m*, 5 H, C_6H_5); 5.60 (*s*, 1 H, S–CH–S); 2.30 (*s*, 3 H, $CO-CH_3$); 2.12 (*s*, 3 H, $S-CH_3$). – MS.: 212 (M^+, 3), 137 (100), 123 (77), 43 (57), 121 (55), 165 (37), 45 (26), 77 (16), 91 (9).

2. 3-Substituted 2,4,5-trithiahexanes (1a,b,c,e) from 3a,b,c,e ***(general procedure).*** – The appropriate thioacetate **3a,b,c**, or **e** (0.01 mol) was added to dimethyl disulfide (4.7 g, 0.05 mol) in freshly prepared sodium ethanolate (0.001 mol) in abs. ethanol (20 ml) and heated at reflux for 30 min, under argon. The solution was then cooled to RT., filtered through a layer of basic aluminum oxide and concentrated *in vacuo* at 30°. The crude product **1a,b,c**, or **e** was subjected to a short-path distillation, whereby a complete separation of the considerably higher boiling dimeric compound **12a,b,c**, or **e** was effected. The residues of the first distillation contained **12b** and **12c**; the latter could be obtained pure by short-path distillation at 0.05 Torr/100° (oven temp.). The content of **12b** and **12c** was approximately 10% relative to **1b** and **1c**.

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[2]) Bis(methylthio)methane was obtained according to [16]. Preparation of dimethyl thioacetals **6b–e**. To the freshly distilled aldehyde at −70° was added a catalytic amount (2% by weight) conc. hydrochloric acid followed by 4.5 mol-equiv. of methanethiol. A sharp temperature-rise was observed. The crude mixture (2 phases) was neutralized with saturated Na_2CO_3 solution and extracted with ether. The combined organic phases were dried (Na_2SO_4) and concentrated at 30°/11 Torr. The crude products were distilled (*Vigreux*-column). **6b** (54%), b.p. 40°/11 Torr, n_D^{20} 1.5229; **6c** (76%), b.p. 55°/11 Torr, n_D^{20} 1.5186; **6d** (84%), b.p. 79–80°/11 Torr, n_D^{20} 1.5072; **6e** (92%), b.p. 137–138°/11 Torr, n_D^{20} 1.5973).

[3]) This solution was prepared under argon by slow addition of triethylamine (0.21 mol), dissolved in 30 ml abs. $CHCl_3$ (passed through basic aluminum oxide before use), to a well-stirred solution of thioacetic acid (0.21 mol) in 30 ml abs. $CHCl_3$, kept at 0–10°.

2,4,5-Trithiahexane (**1a**) (62%). – IR. (liq.): 3000, 2950, 1425, 1375, 1310, 1195, 1080, 1060, 970, 960, 820, 750, 705. – ^{1}H-NMR.: 3.87 (*s*, 2 H, S–CH_2–S); 2.50 (*s*, 3 H, S_2–CH_3); 2.23 (*s*, 3 H, S–CH_3). – MS.: 140 (M^+, 13), 61 (100), 45 (29), 35 (13), 46 (12), 47 (8), 63 (6), 79 (6), 93 (4).

3-Methyl-2,4,5-trithiahexane (**1b**) (74%), b.p. 93–95°/13 Torr; n_D^{20} 1.5693. – IR. (liq.): 3000, 2950, 1440, 1370, 1310, 1260, 1165, 1050, 955, 730, 695. – ^{1}H-NMR.: 3.95 (*qa*, *J* = 7, 1 H, S–CH–S); 2.50 (*s*, 3 H, S–S–CH_3); 2.23 (*s*, 3 H, C–S–CH_3); 1.65 (*d*, *J* = 7, 3 H, S–C(CH_3)–S). – MS.: 154 (M^+, 0), 75 (100), 59 (27), 47 (26), 41 (26), 45 (25), 79 (12), 49 (9), 60 (9).

3,6-Dimethyl-2,4,5,7-tetrathiaoctane (**12b**). Purified by preparative GC. Mixture of *meso*-compound and racemate (7.5%). – IR. (liq.): 2980, 2920, 1440, 1365, 1160, 1045, 955, 730, 690. – ^{1}H-NMR.: 2.98 and 2.99 (2*qa*, *J* = 7, 2 H, HC–S–S–CH); 2.10 and 2.12 (2*s*, 6 H, 2 S–CH_3); 1.83 and 1.82 (2*d*, *J* = 7, 6 H, 2 C–CH_3). – MS.: 214 (M^+, < 1), 75 (100), 59 (14), 41 (10), 47 (10), 45 (9), 60 (5), 135 (4), 76 (4).

3-Ethyl-2,4,5-trithiahexane (**1c**) (60%), b.p. 99–100°/13 Torr; n_D^{20} 1.5578. – IR. (liq.): 2970, 2920, 1450, 1430, 1375, 1305, 1280, 1220, 1155, 1090, 1070, 950, 905, 810, 770, 730. – ^{1}H-NMR.: 3.72 (*d* × *d*, *J* = 8 and 7, 1 H, S–CH–S); 2.50 (*s*, 3 H, S–S–CH_3); 2.20 (*s*, 3 H, C–S–CH_3); 2.25–1.45 (*m*, 2 H, CH_2); 1.10 (*t*, *J* = 7, 3 H, CH_3). – MS.: 168 (M^+, 0), 89 (100), 41 (89), 45 (48), 61 (41), 79 (18), 47 (18), 73 (16), 39 (15).

3,6-Diethyl-2,4,5,7-tetrathiaoctane (**12c**). Purified by preparative GC. Mixture of *meso*-compound and racemate (6%). – IR. (liq.): 2980, 2940, 1450, 1430, 1375, 1280, 1220, 1150, 1090, 1075, 960, 905, 810, 730. – ^{1}H-NMR.: 3.79 and 3.77 (2*d* × *d*, *J* = 8 and 7, 2 H, 2 S–CH–S); 2.21 and 2.18 (2*s*, 6 H, 2 S–CH_3); 2.17–1.55 (*m*, 4 H, 2 CH_2); 1.06 (*t*, *J* = 7, 6 H, 2 CH_3). – MS.: 242 (M^+, < 1), 41 (100), 89 (97), 45 (38), 73 (25), 61 (23), 47 (19), 79 (15), 90 (15).

3-Phenyl-2,4,5-trithiahexane (**1e**). Purified by preparative TLC. (29.5%). – IR. ($CHCl_3$): 3070, 3000, 2930, 1590, 1490, 1450, 1420, 1305, 1180, 1160, 1080, 1050, 1030, 960, 890. – ^{1}H-NMR.: 7.65–7.20 (*m*, 5 H, C_6H_5); 4.88 (*s*, 1 H, S–CH–S); 2.30 (*s*, 3 H, S–S–CH_3); 2.10 (*s*, 3 H, C–S–CH_3). – MS.: 216 (M^+, < 1), 137 (100), 121 (55), 122 (15), 77 (9), 168 (8), 91 (7), 103 (4), 153 (3).

3. Conversion of 2,4-dithiahexan-5-one (3a) to 2,4,5-trithiahexane (1a) with methylthiomethylethylsulfoniumtetrafluoroborate (5). – Thioacetate **3a** (2.86 g, 21 mmol) was added to a solution of sodium methanolate (21 mmol) in abs. methanol (10 ml) – freshly prepared from 0.5 g Na – and heated under argon, at reflux, for 1 h to give **4a**. Sulfonium salt **5**[4]), in $CHCl_3$, was introduced dropwise into the well-stirred solution of **4a** under argon. The reaction mixture was concentrated at 30° *in vacuo*. The residue was diluted with 30 ml water and extracted with ether (3 × 40 ml). The combined organic layers were dried (Na_2SO_4), and the solvent was evaporated at 50°/100 Torr to give 1.53 g of crude 2,4,5-trithiahexane (**1a**). A small sample purified by preparative GC. was identical (IR., ^{1}H-NMR., MS., GC.) with a reference sample, prepared as mentioned under 2.

Method B

1. Starting dialkyldisulfides 8. – *Diisobutyldisulfide* (**8f**) is commercially available (*Fluka*). *5,6-Dithia-2,9-dimethyldecane* (**8g**) and *5,6-dithia-3,8-dimethyl-decane* (**8h**) were prepared from 1-bromo-3-methylbutane and 1-bromo-2-methylbutane respectively, as follows: thioacetic acid (114 g, 1.5 mol) was slowly added under argon to an efficiently stirred solution of triethylamine (151.5 g, 1.5 mol) in 700 ml 1,2-dimethoxyethane, when a temperature rise to 45° was observed. After cooling to RT., the appropriate bromo compound (226.5 g, 1.5 mol), in 100 ml 1,2-dimethoxyethane, was added dropwise, with good stirring, within 30 min. The mixture was then heated at reflux for 1 h. After cooling to RT. and dilution with 500 ml water, the crude material was extracted with ether (5 × 200 ml). The organic layers were washed with water (3 × 150 ml), combined, dried (Na_2SO_4) and concentrated at 30°/15 Torr. The crude thioacetates were fractionated (*Vigreux*-column), to obtain the pure thioacetates.

3-Methylbutyl S-thioacetate (87.8%), b.p. 62°/13 Torr; n_D^{20} 1.4585. – IR. (liq.): 1690, 1470, 1385, 1350, 1130, 965, 950. – ^{1}H-NMR.: 2.90 (*t*, *J* = 7, 2 H, S–CH_2); 2.32 (*s*, 3 H, CO–CH_3); 1.90–1.20 (*m*, 3 H, CH–CH_2); 0.90 (*d*, *J* = 6, 6 H, 2 CH_3). – MS.: 146 (M^+, 2), 43 (100), 70 (31), 86 (24), 55 (14), 41 (14), 69 (10), 61 (5), 103 (4).

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[4]) Preparation of *methylthiomethylethylsulfonium tetrafluoroborate* (**5**): triethyloxonium tetrafluoroborate (3.99 g, 21 mmol), dissolved in 12 ml abs. $CHCl_3$ (passed through basic aluminum oxide), was added dropwise under argon to a well-stirred solution of dimethyl disulfide (1.97 g, 21 mmol) in 4 ml abs. $CHCl_3$. The resulting solution of **5** was used directly.

2-Methylbutyl S-thioacetate (83.4%), b.p. 61°/13 Torr; n_D^{20} 1.4621. – IR. (liq.): 1690, 1460, 1420, 1375, 1350, 1130, 1105, 950. – ^{1}H-NMR.: 2.85 (*d* × *d*, *J* = 7 and 4, 2 H, S–CH_2); 2.33 (*s*, 3 H, CO–CH_3); 1.80–0.70 (*m*, 6 H, CH_3–CH_2–CH); 0.90 (*d*, *J* = 7, 3 H, CH_3). – MS.: 146 (M^+, 1), 43 (100), 70 (41), 41 (11), 71 (11), 55 (8), 57 (7), 72 (5), 42 (4).

Each of the thioacetates (83.7 g, 0.573 mol) was heated at reflux under argon for 1 h in NaOH (57.32 g, 1.433 mol), 280 ml water and 570 ml methanol. The mixture was cooled to RT., 570 ml pentane were added, and I_2 (72.77 g, 0.287 mol) was introduced portionwise, with cooling and efficient stirring. After 2 h at RT., the organic layer was separated, and the aqueous phase was extracted with pentane (4 × 200 ml). The combined organic extracts were washed with 0.1N $Na_2S_2O_3$ (2 × 100 ml) and concentrated at 40°/11 Torr. The resulting crude disulfides were fractionated (*Vigreux*-column) to obtain pure materials.

5,6-Dithia-2,9-dimethyldecane (**8g**) (94.4%), b.p. 62–63°/0.04 Torr; n_D^{20} 1.4855. – IR. (liq.): 1465, 1380, 1360, 1215, 1160. – ^{1}H-NMR.: 2.70 (*t*, *J* = 7, 4 H, 2 S–CH_2); 1.95–1.30 (*m*, 6 H, 2 CH_2–CH); 0.90 (*d*, *J* = 6, 12 H, 4 CH_3). – MS.: 206 (M^+, 21), 43 (100), 71 (59), 41 (20), 55 (11), 136 (9), 102 (5), 70 (5), 69 (5).

5,6-Dithia-3,8-dimethyldecane (**8h**) (96.6%), b.p. 70–72°/0.06 Torr; n_D^{20} 1.4880. – IR. (liq.): 1460, 1375, 1265, 1230, 1190, 1150, 965. – ^{1}H-NMR.: 2.73 (*d* × *d*, *J* = 7 and 5, 4 H, 2 S–CH_2); 2.00–0.70 (*m*, 12 H, 2 CH_3–CH_2–CH); 0.95 (*d*, *J* = 6, 6 H, 2 CH_3). – MS.: 206 (M^+, 18), 43 (100), 71 (80), 41 (27), 55 (10), 136 (9), 56 (4), 101 (3), 69 (3).

Diisopropyldisulfide (**8i**) and *di(*sec.*butyl)disulfide* (**8k**) were obtained in the following way from propane-2-thiol and from butane-2-thiol, respectively. About ⅔ of the total I_2 (76.2 g, 0.3 mol) was added portionwise within 90 min to a well-stirred mixture of the thiol (0.6 mol), 670 ml pentane and 670 ml water. Then NaOH (24 g, 0.6 mol) in 100 ml water was introduced, as well as the remainder of I_2. Stirring was continued for a further 2 h, the phases were separated, and the aqueous layer was extracted with pentane (4 × 200 ml). The combined organic phases were washed with a 10% solution of $Na_2S_2O_3$ (4 × 100 ml) and evaporated at 30°/13 Torr. The resulting, crude disulfides were fractionated (*Vigreux*-column) to obtain the pure disulfides.

Diisopropyldisulfide (**8i**) (88%), b.p. 54–55°/13 Torr; n_D^{20} 1.4921. – IR. (liq.): 1450, 1380, 1365, 1230, 1155, 1050. – ^{1}H-NMR.: 3.00 (*septet*, *J* = 7, 2 H, 2 S–CH); 1.30 (*d*, *J* = 7, 12 H, 4 CH_3). – MS.: 150 (M^+, 39), 43 (100), 108 (44), 41 (24), 66 (14), 110 (8), 59 (6), 74 (5), 93 (3).

*Di(*sec.*butyl)disulfide* (**8k**) (93%), b.p. 84–85°/13 Torr; n_D^{20} 1.4926. – IR. (liq.): 1450, 1370, 1285, 1275, 1210, 1140, 1050, 1010, 995, 950, 790. – ^{1}H-NMR.: 2.73 (*sextet*, *J* = 7, 2 H, 2 S–CH); 2.00–1.35 (*m*, 4 H, 2 CH_2); 1.25 (*d*, *J* = 7, 6 H, 2 CH_3); 0.97 (*t*, *J* = 7, 6 H, 2 CH_3). – MS.: 178 (M^+, 33), 57 (100), 41 (58), 122 (55), 39 (16), 55 (10), 59 (9), 45 (7), 61 (5).

2. 3-Substituted 2,4,5-trithiahexanes 1f–k from disulfides 8f–k *via* α-chlorosulfenyl chlorides 9f–k *(general procedure).* – A solution of the appropriate disulfide **8f–k** (0.14 mol) in 70 ml CCl_4 was cooled to −30°, and about 10 g of Cl_2 were slowly introduced with good stirring. Then the temperature was raised to −10/−12°, and the remaining ⅔ (19.8 g) of the total Cl_2 were slowly added at this temperature, whereby a solid precipitated. At the end of the reaction the mixture was allowed to warm to RT. (strong evolution of HCl). After 1 h at RT., most of the solvent was evaporated at 20°/15 Torr to give the crude α-chlorosulfenyl chloride **9f–k**, which then was cooled to 0° and used directly. Sodium methanthiolate (0.56 mol) in abs. methanol (200 ml) – freshly prepared from sodium methanolate/methanol and methanethiol – was added dropwise under argon, with good stirring, at 0–10°. The mixture was stirred at RT. for a further 1 h then poured onto a mixture of 250 ml water and 130 ml saturated $NaHCO_3$ solution. After extraction with ether (5 × 200 ml), the organic layers were washed with 130 ml water, combined and dried (Na_2SO_4). The solvent was evaporated *in vacuo*. The crude products **1f–k** were distilled (*Vigreux*-column).

3-Isopropyl-2,4,5-trithiahexane (**1f**) (35%), b.p. 54°/0.04 Torr; n_D^{20} 1.5470. – IR. (liq.): 2970, 2920, 1460, 1420, 1380, 1360, 1305, 1175, 1160, 950, 745. – ^{1}H-NMR.: 3.67 (*d*, *J* = 4, 1 H, S–CH–S–S); 2.47 (*s*, 3 H, S–S–CH_3); 2.25 (*s*, 3 H, S–CH_3); 2.60–2.10 (*m*, 1 H, C–CH–C); 1.10 (*t*, *J* = 6, 6 H, CH_3–C–CH_3). – MS.: 182 (M^+, < 1), 55 (100), 103 (77), 45 (25), 39 (12), 61 (12), 47 (9), 79 (8), 87 (8).

3-Isobutyl-2,4,5-trithiahexane (**1g**) (33%), b.p. 75–76°/0.075 Torr; n_D^{20} 1.5372. – IR. (liq.): 2950, 2920, 1470, 1430, 1380, 1365, 1305, 1260, 1165, 950, 890, 730. – ^{1}H-NMR.: 3.77 (*t*, *J* = 8, 1 H, S–CH–S–S); 2.45 (*s*, 3 H, S–S–CH_3); 2.15 (*s*, 3 H, S–CH_3); 2.00–1.40 (*m*, 3 H, CH–CH_2); 0.90 (*d*, *J* = 5, 6 H, CH_3–C–CH_3). – MS.: 196 (M^+, 0), 61 (100), 117 (70), 41 (48), 75 (42), 43 (32), 45 (30), 69 (21), 79 (10).

*3-*sec.*Butyl-2,4,5-trithiahexane* (**1h**) (32%), b.p. 58–60°/0.05 Torr; n_D^{20} 1.5432. – IR. (liq.): 2970, 2920,

1450, 1420, 1375, 1305, 1155, 950, 740. – ^{1}H-NMR.: 3.75 (*d*×*d*, *J* = 4 and 2, 1 H, S–CH–S–S); 2.47 (*s*, 3 H, S–S–CH_3); 2.25 (*s*, 3 H, S–CH_3); 2.20–0.80 (*m*, 9 H, CH_3–CH_2–CH–CH_3). – MS.: 196 (M^+, 0), 61 (100), 41 (92), 69 (83), 117 (64), 45 (53), 75 (42), 79 (11), 101 (8).

3,3-Dimethyl-2,4,5-trithiahexane (**1i**) (17.5%), b.p. 47–48°/0.03 Torr; n_D^{20} 1.5540. – IR. (liq.): 2980, 2930, 1430, 1375, 1360, 1300, 1150, 1105, 1070, 950. – ^{1}H-NMR.: 2.46 (*s*, 3 H, S–S–CH_3); 2.15 (*s*, 3 H, S–CH_3); 1.65 (*s*, 6 H, CH_3–C–CH_3). – MS.: 168 (M^+, 0), 89 (100), 41 (30), 49 (27), 73 (18), 59 (17), 45 (13), 61 (8), 47 (7).

3-Methyl-3-ethyl-2,4,5-trithiahexane (**1k**) (26%), b.p. 50–55°/0.04 Torr; n_D^{20} 1.5550. – IR. (liq.): 2980, 2920, 1440, 1375, 1365, 1300, 1140, 1085, 1030, 950, 800. – ^{1}H-NMR.: 2.45 (*s*, 3 H, S–S–CH_3); 2.08 (*s*, 3 H, S–CH_3); 1.85 (*qa*, *J* = 8, 2 H, CH_2); 1.55 (*s*, 3 H, CH_3–C(S)–S_2); 1.00 (*t*, *J* = 8, 3 H, CH_3). – MS.: 182 (M^+, 0), 103 (100), 55 (86), 59 (17), 87 (15), 45 (11), 61 (10), 79 (5), 135 (3).

3. 5-Methyl-4,6,7-trithiadecane (10b). – Diethyl disulfide (48.8 g, 0.4 mol) was chlorinated following the general procedure outlined under 2. The intermediately formed α-chlorosulfenyl chloride was treated with sodium propanethiolate in methanol, strictly following the general procedure. The crude product was worked up, as mentioned in 2, and distilled (*Vigreux*-column) to give 76.6 g (45%) of 5-methyl-4,6,7-trithiadecane (**10b**), b.p. 65–70°/0.02 Torr. A pure sample was obtained by preparative GC. – IR. (liq.): 2980, 2940, 2890, 1450, 1380, 1290, 1230, 1155, 1050, 900. – ^{1}H-NMR.: 3.89 (*qa*, *J* = 7, 1 H, S–CH–S–S); 2.90–2.40 (*m*, 4 H, 2 S–CH_2); 2.00–1.30 (*m*, 4 H, 2 CH_2); 1.63 (*d*, *J* = 7, 3 H, S–C(CH_3)–S–S); 1.00 (*t*, *J* = 7, 6 H, 2 CH_3). – MS.: 210 (M^+, < 1), 103 (100), 61 (49), 43 (43), 41 (20), 59 (12), 45 (8), 60 (8), 75 (4).

4. 5-Methyl-4,6,7-trithiaoctane (11b). – Sodium hydride (0.5 g) and dimethyldisulfide (252 g) were heated at 30–40° under argon, for 30 min, with good stirring, then 5-methyl-4,6,7-trithiadecane (**10b**) (25.2 g, 0.12 mol) was added. The mixture was heated at 100–110° for 4.5 h. The solution was poured into 1N HCl then extracted with ether (3 × 150 ml). The extracts were combined, dried (Na_2SO_4) and concentrated *in vacuo*. The crude material **11b** was distilled (*Vigreux*-column)to give 15.52 g (71%) of pure (GC.) 5-methyl-4,6,7-trithiaoctane (**11b**); b.p. 58–60°/0.15 Torr; n_D^{20} 1.5467. – IR. (liq.): 2970, 2920, 1440, 1365, 1300, 1235, 1155, 1040, 950. – ^{1}H-NMR.: 4.00 (*qa*, *J* = 7, 1 H, S–CH–S–S); 2.90–2.40 (*m*, 2 H, S–CH_2); 2.50 (*s*, 3 H, S–S–CH_3); 1.67 (*d*, *J* = 7, 3 H, CH_3–C(S)–S_2); 2.00–1.30 (*m*, 2 H, CH_2); 1.00 (*t*, *J* = 7, 3 H, CH_3). – MS.: 182 (M^+, < 1), 61 (100), 103 (83), 43 (54), 41 (28), 59 (21), 75 (16), 45 (14), 60 (11).

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