Tetrahedron Letters, Vol.31, No.35, pp 4999-5002, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

ONION ESSENTIAL OIL CHEMISTRY. *CIS*- AND *TRANS*-2-MERCAPTO-3,4-DIMETHYL-2,3-DIHYDROTHIOPHENE FROM PYROLYSIS OF BIS(1-PROPENYL) DISULFIDE[1]

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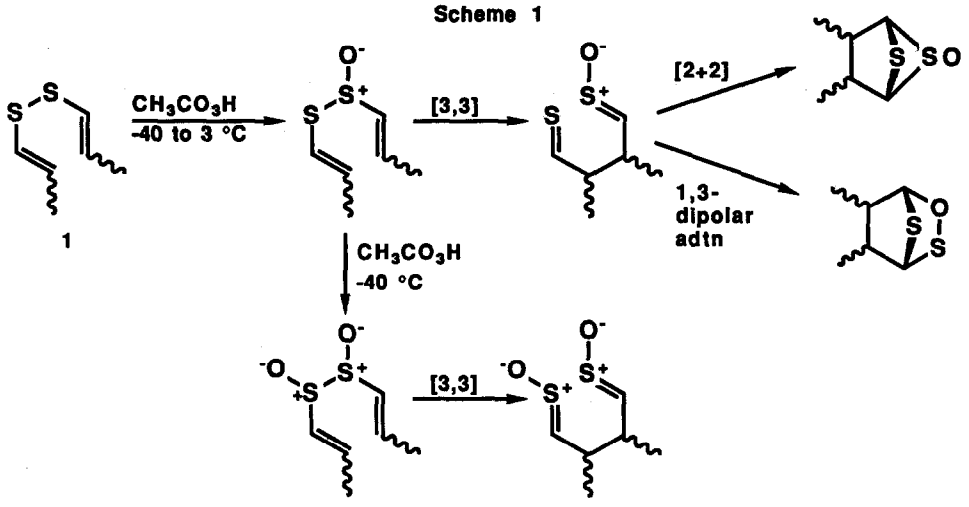
Summary: Heating the onion oil component bis(1-propenyl) disulfide gives *cis*- and *trans*-2-mercapto-3,4-dimethyl-2,3-dihydrothiophene which can lose H_2S upon further heating giving 3,4-dimethylthiophene. A dithio-Claisen rearrangement is proposed for the key step.

We recently reported the formation of unusual unsaturated heterocycles upon pyrolysis of bis(2-propenyl) disulfide, the principle component of the essential oil of garlic.[2] We also reported the novel rearrangements of 1-propenyl 1-propenethiosulfinate and bis(1-propenyl) *vic*-disulfoxide, in the first case to 2,3-dimethyl-5,6-dithiabicyclo[2.1.1]hexane 5-oxides and 5,6-dimethyl-2,7-dithia-3-oxabicyclo[2.2.1]heptanes and in the second case to 2,3-dimethyl-1,4-butanedithial S,S'-dioxide via sulfoxide-accelerated dithio-Claisen reactions, which proceed at temperatures below 0 °C (Scheme 1)[3]. To complement these studies we have now examined the pyrolysis of the antibacterial onion and garlic extract component[4] bis(1-propenyl) disulfide and find that it too affords under mild conditions unusual heterocycles. These previous unknown compounds may play an important role in the characteristic odor and flavor of onions and other alliaceous plants. Our work provides useful information about the little studied dithio-Claisen rearrangement.[5]

When a 1% solution of the isomers of bis(1-propenyl) disulfide[4,6] (**1**) in benzene is kept at 85°C for 3 h, GC and GC-MS analysis reveals the formation in over 85% yield of equal amounts of two new compounds, **2a** and **2b** (Scheme 2), isomeric with the starting material, as well as minor quantities of 3,4-dimethylthiophene (**3**), previously observed as the predominant product formed when **1** is heated to 150-200 °C in the presence of $KHSO_4$.[5b] Prolonged heating at higher temperatures results in the conversion of **2a** and **2b** to **3** (Scheme 3). Attempts to separate **2a** and **2b** by TLC or HPLC were unsuccessful; extensive decomposition occurred under all conditions tried. Compounds **2a** and **2b** could be identified, respectively, as *cis*- and *trans*-2-mercapto-3,4-dimethyl-2,3-dihydrothiophene primarily on the basis of their ^1H and ^{13}C NMR spectra.[7]

The mixture of **2a** and **2b** could be methylated (*n*-BuLi; MeI) affording *cis*- and *trans*-2-methylthio-3,4-dimethyl-2,3-dihydrothiophene (**4a** and **4b**) in 55% yield in a 1:4 ratio (Scheme 3). Compounds **4a** and **4b** were stable to storage and could be separated by HPLC on a reverse phase C-18 column (40/60 CH_3CN/H_2O). The assignment of cis and trans stereochemistry to **4a** and **4b**, respectively, is supported by the larger value of the vicinal cou-

Scheme 1

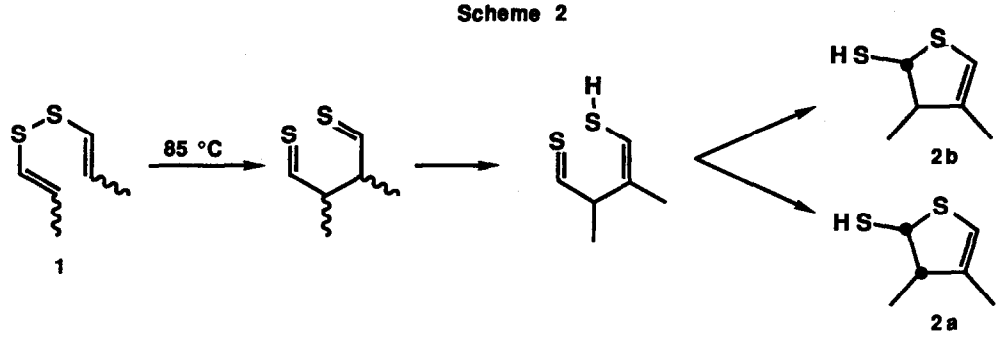


pling constant of the SCHS ring proton in the cis isomer compared to the trans isomer (6.56 vs. 3.04 Hz), as seen in other five membered rings.[8] In addition NOE experiments show that irradiation of the 1.16 ppm methyl doublet ($CHCH_3$) in **4b** gives 18% enhancement of the 4.28 ppm methine doublet (-SCHS-) establishing the cis relationship between these protons and therefore the trans MeSCH-CHMe methyl relationship. In **4a** there was no change in the 4.76 ppm methine doublet intensity upon irradiation of the 1.20 ppm methyl signal. Further characterization of **2a** and **2b** was achieved by conversion (*n*-BuLi; AcCl) into a mixture of two thioacetates (**5a**:**5b** 1:4; IR of S-C=O at 1690 cm^{-1}).

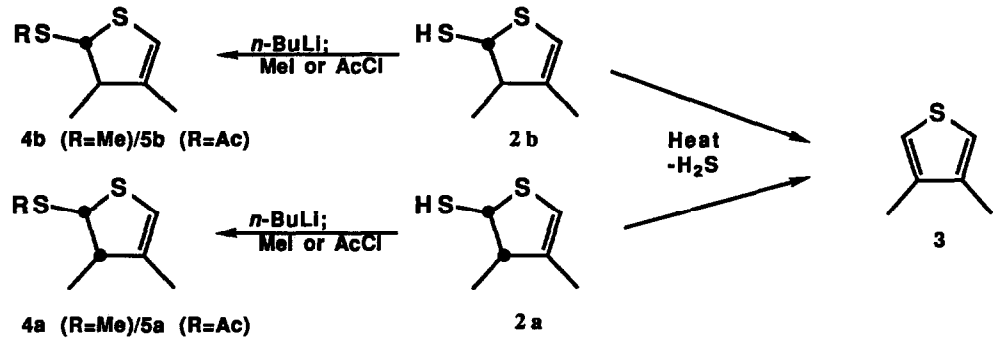
The (E,Z), (E,E), and (Z,Z) isomers of **1** were separated by preparative HPLC (C-18 column; 65/35 CH_3CN/H_2O), identified by ^1H and ^{13}C NMR spectroscopy,[9] and individually subjected to thermolysis in benzene. Analysis by analytical HPLC during the course of the reaction showed that all three isomers gave the same mixture of **2a** and **2b** and that *no isomerization from one isomer of 1 to another occurred under the pyrolysis conditions.* The relative rates of reaction of the three isomers of **1** were found to be E,Z > E,E > Z,Z.

Based on the above studies we suggest that **2a** and **2b** are formed from **1** via a concerted dithio-Claisen [3,3]-sigmatropic rearrangement followed by thioenolization and intramolecular addition of SH to CH=S (Scheme 3) similar to known cyclizations involving 1,4-diketones.[10] The absence of interconversion of isomers of **1** under the reaction conditions precludes a homolytic route to **2a/2b** (e.g. Scheme 4). Pyrolysis of bis(2-methyl-1-propenyl) disulfide, which is unable to undergo thioenolization after dithio-Claisen rearrangement, led to a complex mixture with no major product. Attempts to effect the intramolecular addition of the SH group in **2a** and **2b** to the double bond under either free radical (UV irradiation; thermolysis in the presence of AIBN) or acid-catalyzed conditions were unsuccessful, leading instead to formation of thiophene **3**. We believe that thiophene **3**, one of the significant contributors to the aroma of garlic, leek,[11a] and cooked or fried onions,[11] is formed in these plants from **2a/2b** by loss of H_2S.

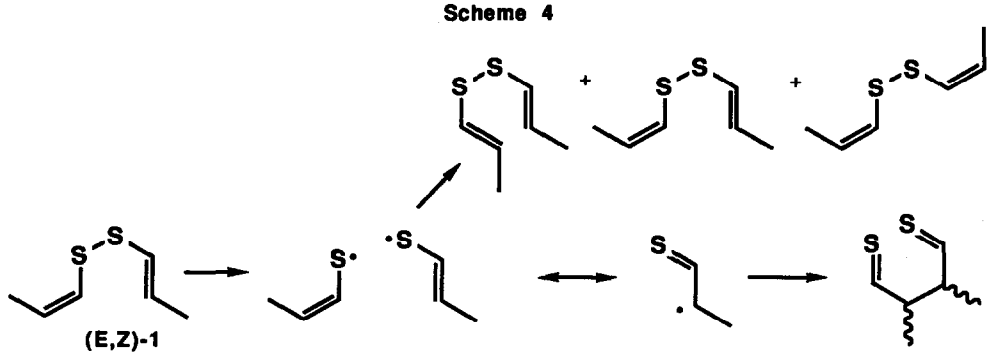
Scheme 2



Scheme 3



Scheme 4



Acknowledgment: We gratefully acknowledge support from the donors of the Petroleum Research Fund, administered by the ACS, the Herman Frasch Foundation, the National Science Foundation, Société Nationale Elf Aquitaine, and the McCormick Company.

References and Notes

1. Presented at the NATO Advanced Study Institute on Reactive Sulfur-Containing Intermediates in Chemistry and Biology, Maratea, Italy, June 1989 and at the 2nd International Conference on Heteroatom Chemistry (ICHAC-2), Albany, NY July 1989.

2. Block, E.; Iyer, R.; Grisoni, S.; Saha, C.; Belman, S.; Lossing, F. P. *J. Am. Chem. Soc.* **1988**, *110*, 7813.

3. Bayer, T.; Wagner, H.; Block, E.; Grisoni, S.; Zhao, S.H., Neszmelyi, A. *J. Am. Chem. Soc.* **1989**, *111*, 3085. Block, E.; Bayer, T. *J. Am. Chem. Soc.* **1990**, *112*, 4584.

4. Hiramitsu, T. *Jpn. Kokai Tokkyo Koho JP 01,117,856 [89,117,856] (Cl. C07C149/00)*, **10 May 1989** (*Chem. Abstr.* **1989**, *111*, 194106t).

5. a) Morgenstern, J.; Mayer, R. *J. Prakt. Chem.* **1966**, *34*, 116. b) Boelens, H.; Brandsma, L. *Recl. Trav. Chim.* **1972**, *91*, 141. c) Campbell, M.M.; Evgenios, D.M. *J. Chem. Soc., Perkin Trans. I.* **1973**, 2866. d) Larsson, F.C.V.; Brandsma, L.; Lawesson, S.-O. *Recl. Trav. Chim.* **1974**, *93*, 258. e) Tamaru, Y.; Harada, T.; Yoshida, Z. *J. Am. Chem. Soc.* **1978**, *100*, 1923. f) Schwab, A. W.; Gilardi, R.D.; Flippen-Anderson, J.L. *Phosphorus Sulfur* **1981**, *10*, 123.

6. Brandsma, L.; Schuijl, P.J.W. *Recl. Trav. Chim.* **1969**, *88*, 519.

7. **2a**, ^{1}H NMR ($CDCl_3$) δ 5.77 (s, 1 H), 4.87 (dd, 1 H), 2.89 (dq, 1 H), 1.99 (d, J = 8.24 Hz, 1 H), 1.76 (s, 3 H), 1.17 (d, J = 6.67 Hz, 3 H); ^{13}C NMR δ 135.6, 117.5, 57.9, 49.6, 15.95, 12.25; EI GC-MS (retention time 11.1 min) 148 (M+2; 2%), 146 (M^+, 25%), 113 (100%), 111 (95%), 97 (78%), 79 (41%), 45 (96%); **2b** ^{1}H NMR ($CDCl_3$) δ 5.65 (s, 1 H), 4.28 (dd, 1 H), 2.70 (dq, 1 H), 2.37 (d, J = 7.27 Hz, 1 H), 1.75 (s, 3 H), 1.10 (d, J = 6.78, 3 H); ^{13}C NMR δ 135.2, 115.4, 54.4, 53.8, 15.9, 12.3; GC-MS (retention time 9.5 min) 148 (M+2; 3%), 146 (M^+, 25%), 113 (100%), 111 (80%), 97 (66%), 79 (40%), 45 (93%); **4a**, ^{1}H NMR ($CDCl_3$) δ 5.75 (s, 1 H, =CH), 4.76 (d, J = 6.56 Hz, 1 H, -SCHS-), 3.02 (m, 1 H, CHMe), 2.13 (s, 3 H, SCH_3), 1.75 (s, 3 H, $=CCH_3$), 1.20 (d, J = 7.43 Hz, 3 H, $CHCH_3$); ^{13}C NMR δ 136.3, 116.7, 63.1, 48.9, 16.5, 15.7, 14.1; GC-MS (retention time 14.7 min) 162 (M+2, 3%), 160 (M^+, 24%), 113 (100%), 112 (30%), 97 (37%), 79 (41%), 45 (77%), 39 (33%); **4b** ^{1}H NMR ($CDCl_3$) δ 5.60 (s, 1 H, =CH), 4.28 (d, J = 3.04 Hz, 1 H, -SCHS-), 2.75 (dq, 1 H, CHMe), 2.15 (s, 3 H, SCH_3), 1.75 (s, 3 H, $=CCH_3$), 1.16 (d, J = 6.78 Hz, 3 H, $CHCH_3$); ^{13}C NMR δ 135.9, 115.2, 62.6, 53.2, 16.5, 15.6, 14.0; GC-MS (retention time 13.3 min) 162 (M+2, 3%), 160 (M^+, 27%), 113 (100%), 112 (28%), 97 (37%), 79 (43%), 45 (77%), 39 (35%).

8. Hauser, F. M.; Rhee, R.P. *J. Org. Chem.* **1981**, *46*, 227.

9. Spinning band distillation of methyl (E,Z)-1-propenyl sulfide (**i**) affords fractions enriched in either (E)-**i** (higher bp; ^{1}H NMR $J_{HC=CH}$ = 15.4 Hz) or (Z)-**i** (lower bp; ^{1}H NMR $J_{HC=CH}$ = 9.2 Hz). Cleavage and oxidation (I_2 or H_2O_2) of the fraction enriched in (E)-**i** gave **1** enriched in one isomer which we assign as (E,E)-**1** (^{1}H NMR δ 6.0 (m, 4 H), 1.78 (dd, J = 6.7, 1.2 Hz, 6 H); ^{13}C NMR δ 130.5, 124.5, 18.1). Similarly cleavage and oxidation of the fraction enriched in (Z)-**i** gave **1** enriched in another isomer which we assign as (Z,Z)-**1** (^{1}H NMR δ 6.05 (dq, J = 9.5, 1.7 Hz, 2 H), 5.69 (dq, J = 6.8, 9.5 Hz, 2 H), 1.70 (dd, J = 6.8, 1.7 Hz, 6 H); ^{13}C NMR δ 128.7, 128.0, 14.4). Pure (E,Z)-**1** was obtained by HPLC separation of mixed isomers of **1** (^{1}H NMR δ 5.95 (m, 3 H), 5.70 (m, 1 H), 1.71 (dd, J = 6.4, 1.1 Hz, 3 H), 1.70 (dd, J = 6.9, 1.5 Hz, 3 H); ^{13}C NMR δ 130.7, 128.5, 124.8, 127.9, 18.1, 14.4).

10. March, J. "Advanced Organic Chemistry" 3rd Edition, John Wiley & Sons, NY 1985, p 791.

11. a) Tokarska, B.; Karwowska, K. *Nahrung* **1983**, *27*, 443. b) Boelens, M.; de Valois, P.J.; Wobben, H.J.; van der Gen, A. *J. Agr. Food Chem.* **1971**, *19*, 984. c) Brodnitz, M.H.; Pollock, C.L.; Vallon, P.P. *J. Agr. Food Chem.* **1969**, *17*, 760. d) Galetto, W.G.; Hoffman, P.G. *J. Agric. Food Chem.* **1976**, *24*, 852.

(Received in USA 7 August 1989; accepted 25 June 1990)