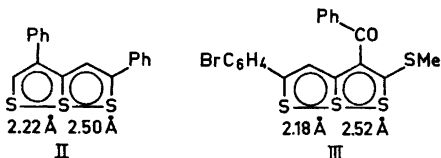
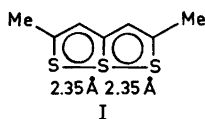


The Sulphur-Sulphur Bonds in Thiothiophthene Derivatives

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X-Ray structure determinations of the thiothiophthene derivatives (I)–(III)

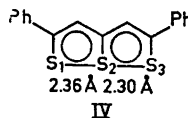


have been reported. The sulphur-sulphur distances are found to be equal in the symmetrical compound (I)¹⁻³ and unequal in the unsymmetrical compounds (II)⁴ and (III),⁵ *i.e.* 2.35 Å in (I), 2.22 and 2.50 Å in (II), and 2.18 and 2.52 Å in (III). The values for (III) are averages of respective distances from two independent molecules. According to the authors "there is good agreement between the two independent molecules with the exception of the 'long' S-S distance", which is 2.47 Å in one and 2.57 Å in the other. Since the standard deviation, σ , in S-S distance is reported to be ± 0.007 Å, it is assumed that this difference of 14 σ is significant.

It has been pointed out by different authors^{5,6} that the results from (I) could be ambiguous since they may represent the average of two-fold disorder of molecules with a "short" and a "long" S-S distance. The molecules lie in special positions, with crystallographic mirror plane passing through the central sulphur and carbon atoms, and the central sulphur atom shows a pronounced anisotropy which may indicate such disorder.

It has been suggested,⁵ therefore, that the "short" S-S distance in the 2.12–2.22

Å range and the "long" S-S distance in the range 2.47–2.57 Å are typical for the thiothiophthene system irrespective of the substituents. A structure investigation of the symmetrical thiothiophthene derivative (IV), for which both S-S distances could be independently determined, has been carried out in order to test this hypothesis, and the preliminary results are given.



The sulphur-sulphur distances are found to be different, *i.e.* $S_1-S_2=2.355 \pm 0.003$ Å and $S_2-S_3=2.297 \pm 0.003$ Å. The difference of 0.06 Å is, however, considerably smaller than the corresponding differences in the unsymmetrical derivatives. It is compatible with the difference observed in the two independently determined "long" S-S distances in compound (III).

This suggests to the author that the two S-S distances in any completely symmetrical thiothiophthene molecule are exactly equal in an isolated molecule, in agreement with the electronic structure which has been calculated for the thiothiophthene ring system.⁷ However, these S-S bonds of total bond order less than unity appear to be unusually sensitive to intermolecular as well as intramolecular environment.

The crystals of 2,5-diphenylthiophthene (IV) are dark purple and belong to the orthorhombic space group $P2_12_12_1$. The cell dimensions are $a=11.955$, $b=15.170$ and $c=7.915$ Å. There are four molecules per unit cell; density, calc. 1.446 g/cm³, found 1.44 g/cm³.

The structure analysis is based on photographic data collected by the equi-inclination Weissenberg technique (CuK α radiation). The intensities of the 1495 observed $hk0-hk7$ and $0kl$ reflections were estimated visually.

Approximate coordinates for the sulphur atoms and the carbon atoms of the thiothiophthene system were found from a three-dimensional Patterson synthesis, and the orientation of the phenyl groups could be roughly estimated by packing considerations. The atomic parameters were refined by least squares methods, and the present R factor is 0.073.

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1. Bezzi, S., Mammi, M. and Garbuglio, C. *Nature* **182** (1958) 247.
2. Bezzi, S., Garbuglio, C., Mammi, M. and Traverso, G. *Gazz. Chim. Ital.* **88** (1958) 1226.
3. Mammi, M., Bardi, R., Garbuglio, C. and Bezzi, S. *Acta Cryst.* **13** (1960) 1048.
4. Hordvik, A., Sletten, E. and Sletten, J. *Acta Chem. Scand.* **20** (1966) 2001, and to be published.
5. Johnson, S. M., Newton, M. G., Paul, I. C., Beer, R. J. S. and Cartwright, D. *Chem. Commun.* **1967** 1170.
6. van den Hende, J. and Klingsberg, E. *J. Am. Chem. Soc.* **88** (1966) 5045.
7. Giacometti, G. and Rigatti, G. *J. Chem. Phys.* **30** (1959) 1633.

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Conversion of α -L-Angiotensinamide to β -L-Angiotensin during Enzymatic Degradation

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Earlier studies by Sjöholm and Yman¹ on the inactivation of α -L-angiotensinamide* by oxytocinase showed a rapid degradation

* We gratefully acknowledge the gift of α -L- and α -D-angiotensin (α -L- and α -D-Asp¹-Val⁶-angiotensin-II), β -L-angiotensin (β -L-Asp¹-Val⁶-angiotensin-II), and α -L-angiotensinamide (α -L-Asp(NH₂)¹-Val⁶-angiotensin-II) from Dr. B. Riniker, CIBA Ltd, Basle.

of the peptide. However, the pressor activity of the incubation mixture always followed a characteristic course, indicating that a biologically active intermediate could have been formed during incubation. The present communication describes the electrophoretic separation of the vaso-pressor components of the mixture obtained after incubation of α -L-angiotensinamide with oxytocinase prepared according to Sjöholm *et al.*^{2,3}

Experimental and results. α -L-Angiotensinamide (2 mg) was dissolved in 300 μ l of sodium phosphate buffer (0.005 M, pH 7.4) and digested with 100 μ l of oxytocinase (dialyzed against 0.001 M phosphate buffer, pH 7.4) at 37°C for 24 h. A control sample, in which the enzyme was replaced by the same amount of water, was treated in the same way. After incubation, 50 μ l of the test and control samples were used for high-voltage electrophoresis on Whatman 3 MM paper, together with references (see Fig. 1). The references were detected with ninhydrin reagent, after which the paper was cut into sections and eluted with 0.9 % sodium chloride for 15 h. The hypertensive activity of the fractions was determined in a male rat, with β -L-angiotensin as reference, in a 4-point assay. In the test sample, biological activity

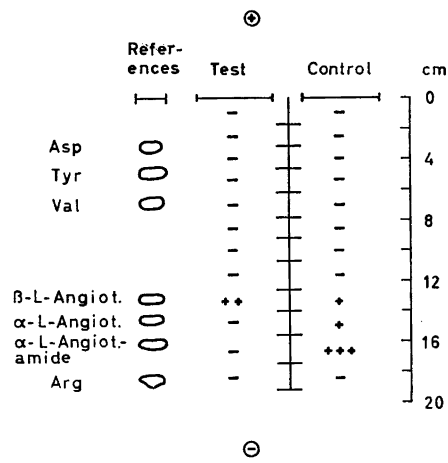


Fig. 1. High-voltage paper electrophoresis (1500 V, 2 h) in formic acid-pyridine buffer (1 ml of pyridine and about 20 ml of formic acid in 2000 ml of water to pH 2.7). The references were stained with ninhydrin reagent. The signs in the areas from the test and control samples denote the amount of biological activity present.