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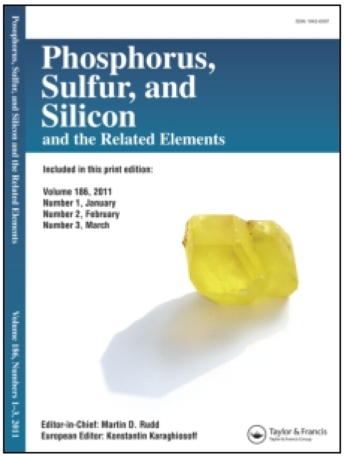

Phosphorus, Sulfur, and Silicon and the Related Elements

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THE REACTION OF UNSATURATED CARBONYL COMPOUNDS WITH "ACTIVATED" SULFUR. PART 3.[1] REACTION COURSE

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(Received 16 April, 1998)

A reaction course of the process which starts from (2*E*,4*E*)-1,5-diphenyl-2,4-pentandien-1-one **1** by reaction with sulfur and triethylamine at room temperature and completes to give phenyl(5-phenyl-2-thienyl)methanone **5**, is proposed and discussed.

Keywords: Sulfurization; cinnamylideneacetophenone; sulfur; trithiepin; tetrathiocin

INTRODUCTION

Recently we reported that when (2*E*,4*E*)-1,5-diphenyl-2,4-pentandien-1-one **1** is allowed to react with sulfur in the presence of triethylamine (TEA) and a suitable solvent at room temperature, the formation of compounds **2–9**, can be observed (Scheme 1).[1,2]

Furthermore, we have found that these reactions proved to be of general effectiveness with 2,4-dienones as it has been shown with the two methoxy derivatives of (2*E*,4*E*)-1,5-diphenyl-2,4-pentandien-1-one, **1a, b**, (3*E*,5*E*)-6-phenyl-3,5-hexadien-1-one **10**, (1*E*,4*E*,6*E*)-1,7-diphenyl-1,4,6-heptatrien-3-one **11** and (1*E*,3*E*,6*E*,8*E*)-1,9 diphenyl-1,3,6,8-nonatetraen-5-one **12**[3] (Formulae **1a, b** and **10–12**).

In this paper we wish to report data acquired on the sequence of the whole process, which leads to the final pheny(5-phenyl-2-thienyl)methanone **5** starting from the initial (2*E*,4*E*)-1,5-diphenyl-2,4-pentandien-1-one 1, by means of spe-

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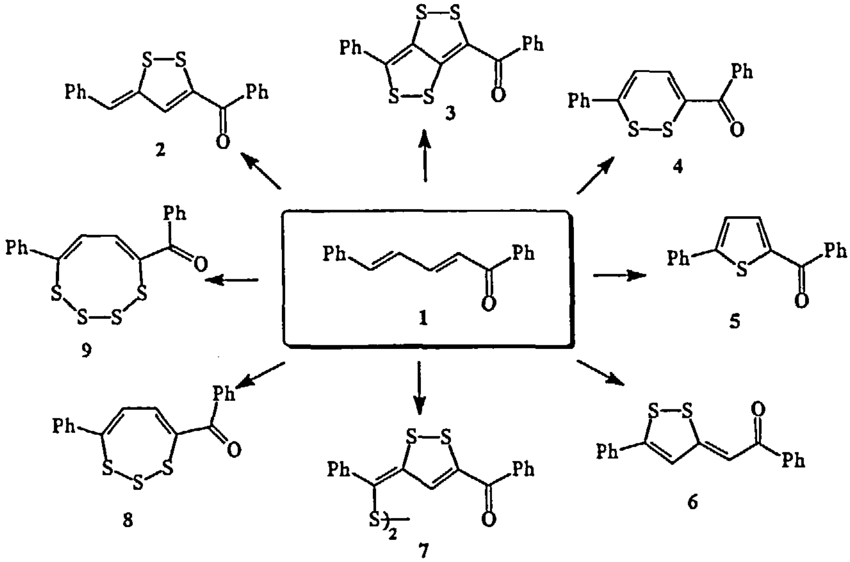
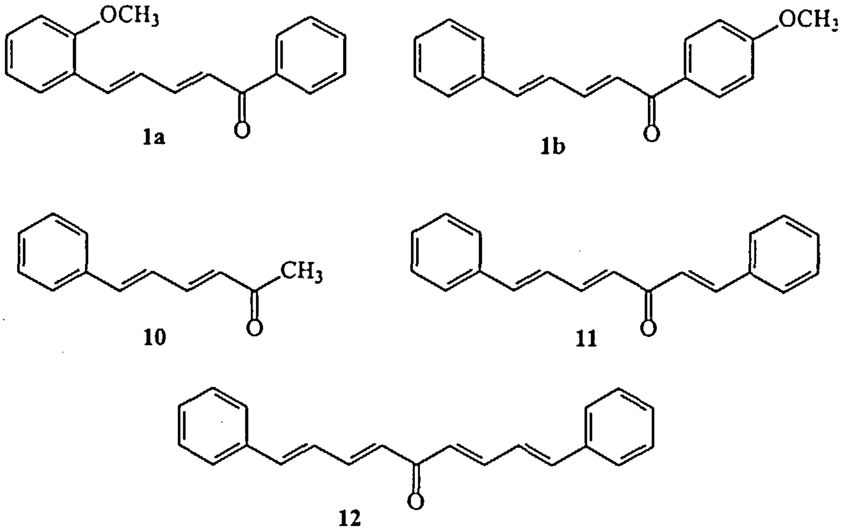
* Corresponding to Author.



SCHEME 1



FORMULAE 1a, b and 10–12

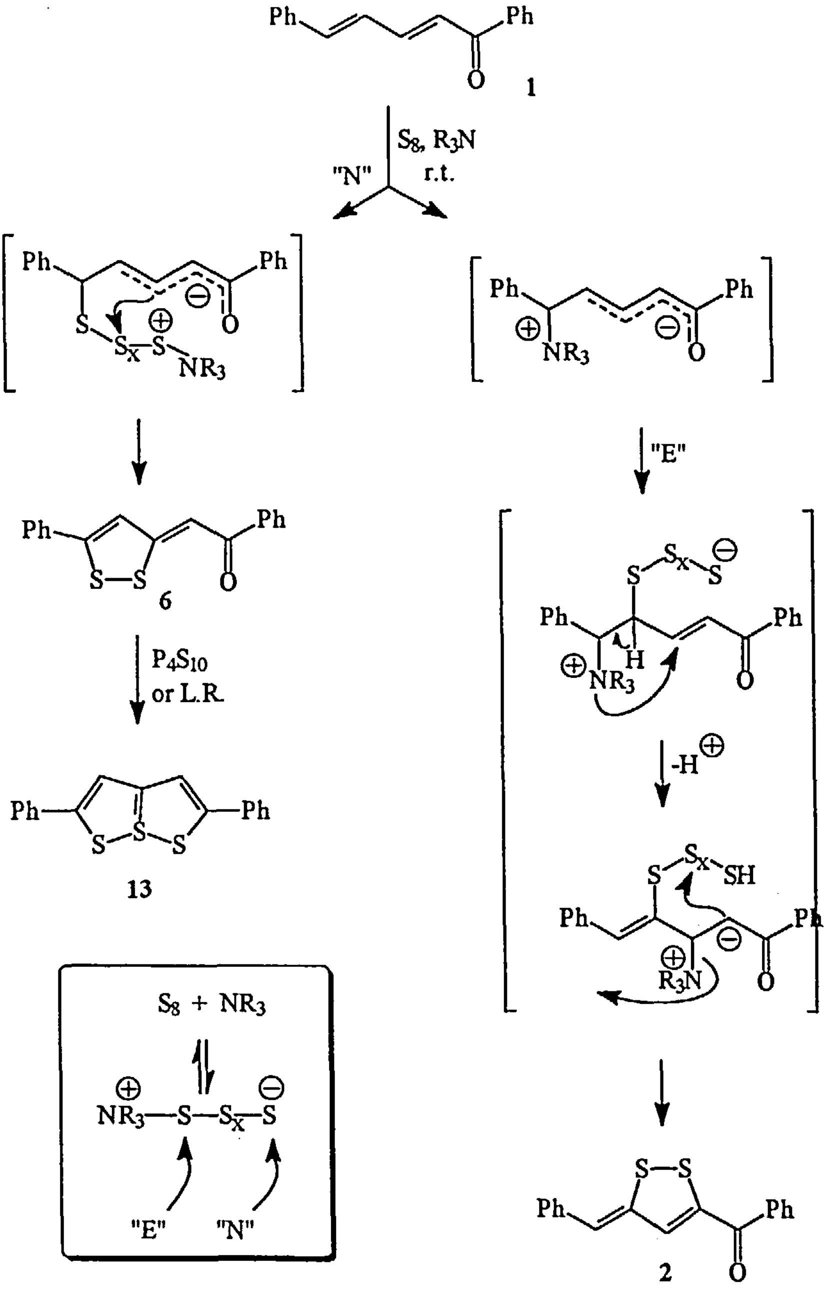
cific tests on previously isolated compounds. These data allow to verify the correlation among these different compounds and the intermediacy of someone of them without which other reaction products can not be obtained.

RESULTS AND DISCUSSION

The initially formed compounds, someone of which are easily identifiable by their characteristic color, react more or less rapidly. Monitoring the process in the time by TLC, the formation of these compounds can be observed, and then the decrease and final disappearance of some of them was evident. Moreover, under the same experimental conditions, the course of the whole process is affected by the nature of the used solvent, as already observed.[1,2]

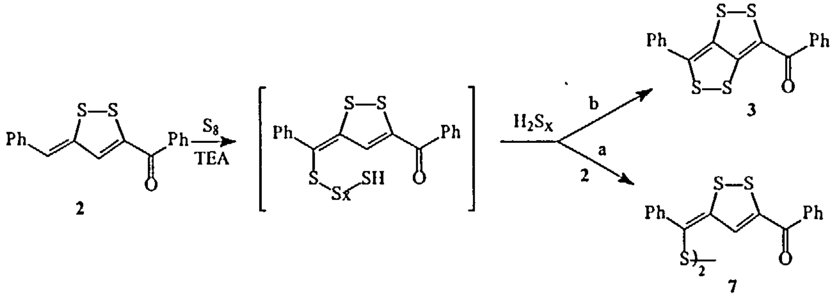
With regard to the chemistry of the whole process, surprisingly, we have found that phenyl{3-[(*E*)-1-phenylmethylidene]-3*H*-1,2-dithiol-5-yl}-methanone **2** is the compound which is initially formed in any of the allowed solvents at room temperature. This clearly derives from an attack of sulfur electrophilic species ("E") on the 2- and 4-positions of the unsaturated ketone **1**.[4] This process can be rationalized considering the evident prevalence of the TEA attack on the 3- and 5-positions of **1** instead of the sulfur nucleophilic species ("N"). The interaction between **1** and TEA promotes the nucleophilicity of its 2- and 4-positions, which can react with "E" species[9] (Scheme 2).

In agreement with this reaction mechanism, no production of the dithiole **2** is observed when the more bulky triisobutylamine (TIBA) is used in the place of TEA in the reaction of **1** and sulfur at room temperature. Even if not favored by these latter adopted reaction conditions, 1-phenyl-2-(5-phenyl-3*H*-1,2-dithiol-3-yliden)-1-ethanone **6** is formed in very low yield, although it would be the natural result of the action of "N" species on the electrophilic 3- and 5-positions of **1**. However, according to our expectation, the yield of the dithiole **6** raised up when the reaction was performed at 60 °C by using TEA or TIBA. The dithiole **6** is quite stable, not only in the usual reaction conditions with TEA, but also when the reaction is conducted in refluxing morpholine[10] or in TIBA at 150 °C. Its sluggishness to the attack of "E" species is obviously ascribable to the poverty of nucleophilicity of its 2- and 4-positions, while the stabilization of its 3- and 5-positions owing to the participation to the dithiole nucleus does not allow their activation towards the nucleophilic attack at room temperature. The dithiole **6** has been revealed by reaction with phosphorous decasulfide or Lawesson's reagent with which it affords 2,5-diphenyl-7λ^4-[1,2]dithiolo[5,1-e][1,2]dithiole **13**.


Ph
Ph
O
1
S8, R3N
r.t.
"N"
"E"
NR3
Sx
6
P4S10
or L.R.
13
S8 + NR3
NR3—S—Sx—S
"E"
"N"
-H
SH
R3N
2

SCHEME 2

On the contrary, the dithiole **2** easily reacts with "N" species at its 5-position to give phenyl{3-[(*E*)-1-((5-benzoyl-3*H*-1,2-dithiol-3-ylidene)phenylmethyl-disulfanyl)-1-phenylmethylidene)-3*H*-1,2-dithiol-5–yl}methanone **7** (path a, Scheme 3) and at its 3- and 5-positions to give phenyl(6-phenyl[1,2]dithiolo-[4,3-c][1,2]dithiol-3-yl)methanone **3** (path b, Scheme 3), because these positions are directly conjugated with the carbonyl group. This hypothesis has been verified by allowing to react the dithiole **2** with sulfur and TEA in dimethyl formamide (DMF).

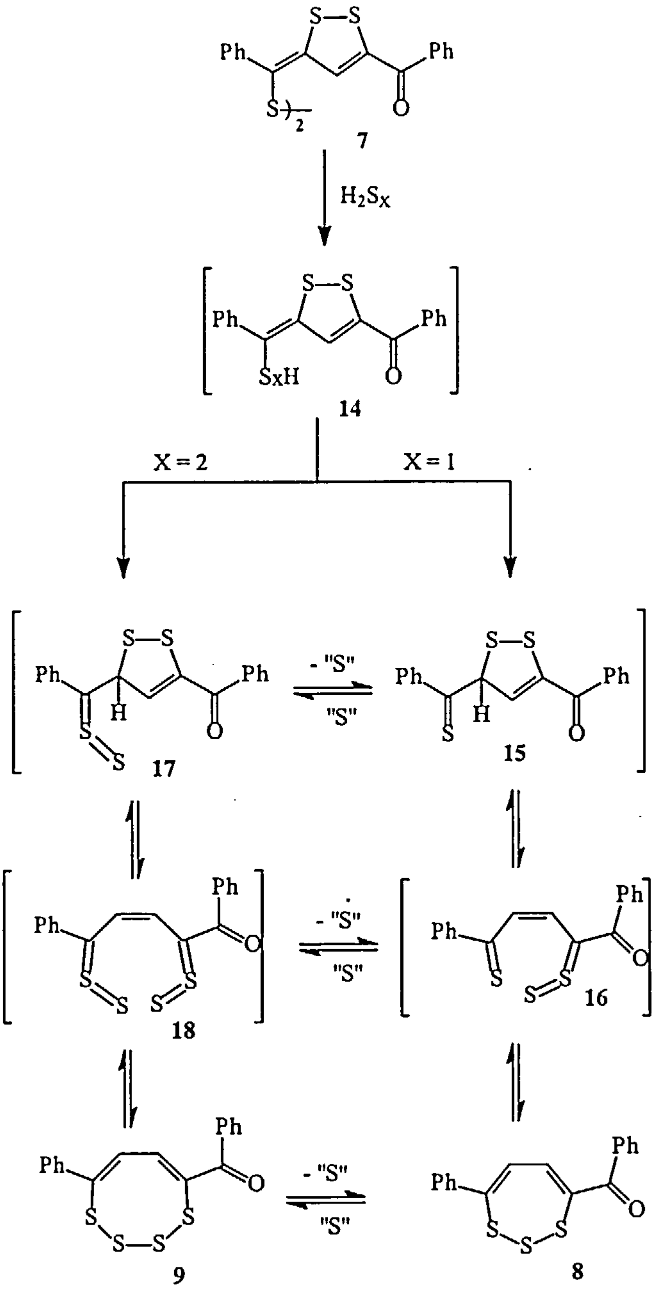


SCHEME 3

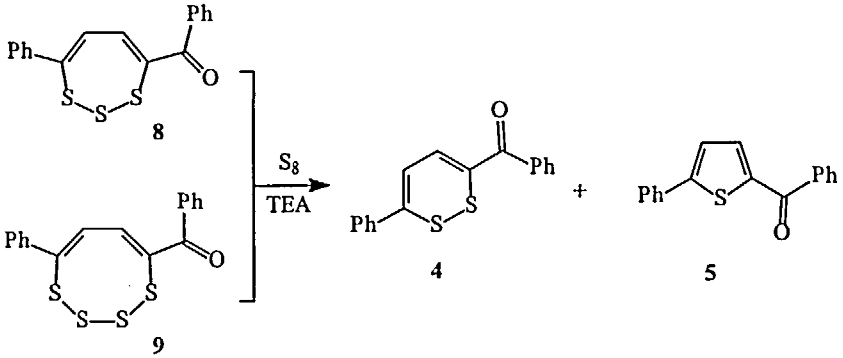
In the reaction conditions, unlike the dithiolodithiole **3**, *the disulfide* **7** *mainly* undergoes a scission process which gives rise to unisolable compound **15** starting from which a series of reactions, such as retro-electrocyclization, intramolecular cycloaddition, sulfur addition and/or extrusion, takes place and leads to phenyl(6-phenyl-1,2-dithiin-3-yl)methanone **4**, phenyl(5-phenyl-2-thienyl)methanone **5**, phenyl(7-phenyl-1,2,3-trithiepin-4-yl)methanone **8**, phenyl(8-phenyl-1,2,3,4-tetrathiocin-5-yl)methanone **9** and some unknown polysulfurated compounds in low amounts[2] (Scheme 4).

These processes have been verified by allowing the disulfide **7** to react with sulfur and TEA in solvents such as pyridine, DMF or hexamethylphosphoric triamide (HMPA). In these conditions sulfides **8** and **9** were initially formed and isolated, but when the reaction mixture was allowed to react by prolonging the reaction time, then sulfides **8** and **9** were converted into the dithiin **4** and the thiophene **5**. These latter can be obtained also by reaction of sulfides **8** and **9** with sulfur and TEA in DMF (Scheme 5).

The obtaining of compounds **4**, **5**, **8** and **9** indicates that an opening process of the dithiole ring of **7** takes place and this probably leads to the thiosulfine **16** like other different rings containing S-S group.[11] In our reactions this opening proc-



SCHEME 4



SCHEME 5

ess is assisted by the neighboring thiocarbonyl group giving the conjugated thiosulfine **16** which undergoes the electrocyclic closure affording trithiepin **8**. The tetrathiocin **9** contains a sulfur atom more than the thiosulfine **16** and its formation can arise from the acceptance of a sulfur atom, generated in reaction conditions of production of "activated" sulfur, by the thiono group of the thiosulfine **16** as Saito[12] proposed for the formation of its α,β-unsaturated thiosulfines from the corresponding thioketones or by the trithiepin **8** as Bartlett and Ghosh[13] proposed for the formation of their pentathiepans from a trithiepine. Alternatively, it can be supposed that the scission of the C-S bond, rather than of the S-S bond of **7**, beside the production of compounds **2** and **3**,[2] afford **17** and then the dithiosulfine **18** through an opening process of the same dithiole ring which leads to **16**.

However, in spite of all made attempts, we have not been able until now, in our reaction conditions, to confirm the intermediacy of thiosulfines **16** or **18** by cycloaddition reactions,[14] probably because the interference of the TEA or nucleofilic species present in the reaction mixture on the added dipolarophiles. The corresponding bicyclic systems **8a** and **9a** (Formulae **8a**, **9a**), which are in better agreement with literature data,[15] could be considered preferred in comparison with sulfides **8** and **9**; nevertheless, beside the determining NMR spectra,[1] the results based on PM3 calculations show that compound **8** is about 26,1 Kcal/mol^{-1} more stable than **8a** and compound **9** is about 30.1 Kcal/mol^{-1} more stable of **9a**.

The dithiin **4**, like the tetrathiocin **9**,[16] tends to extrude sulfur to give **5** owing to its antiaromatic character[17]and consequently there is great amount of thiophene **5** along with small amounts of **4** and **8** in the final solution. Therefore,

8a **9a**

FORMULAE 8a, 9a

thiophene **5** appears to be the final compound of the whole process which initiates from **1** by reaction with sulfur and TEA at room temperature.

In conclusion, the obtaining of the thiophene **5** and dithiole **6**, in addition to trithiapentalene **13**, from the reaction of **1** with sulfur in refluxing morpholine[10] finds an explanation in the reactions performed at room temperature and 60 °C. The absence of **13** in the two latter cases must clearly be ascribed to the most drastic conditions required for the attack to the carbonyl group of **6** by "N" species.

EXPERIMENTAL

All melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. ^{1}H NMR Spectra were recorded on a Bruker WP 80 FT spectrometer using tetramethylsilane as internal standard and deuterochloroform as solvent, unless otherwise stated. IR spectra were recorded on a Perkin Elmer 281 and Synthesis 2000 spectrophotometer as potassium bromide discs, or neat. UV spectra were measured on a HP 8452 A spectrophotometer in dichloromethane solutions. EI and FAB mass spectra were recorded on a VG ZAB-2SE spectrometer. Analytical thin layer chromatographic separation were performed on aluminium plates pre-coated with Merck silica gel 60-F_{254}. Chromatographic separations of reaction mixtures were performed by means of column gravity or flash chromatography using Merck silica gel 60 and in some cases by means of centrifugally enhanced preparative thin layer chromatography (CEPTLC) using plates coated with Merck silica gel 60-PF_{254}. Mixtures of cyclohexane-ethyl acetate were used as eluents.

Starting materials

(2E, 4E)-1,5-diphenyl-2,4-pentandien-1-one **1**,[18] compounds **2–6**[2] and **7**,[1] **12**[1] and **13**[1]were prepared as previously reported. The identification of samples from different experiments was secured by mixed mps and/or superimposable IR and UV spectra.

Reactions of the unsaturated ketone 1 with sulfur and TIBA

a. A mixture of the unsaturated ketone **1** (0.69 g, 3 mmol), sulfur (0.96 g, 30 mg/at) and TIBA (5.5 g, 10 mmol) in pyridine (20 ml) was allowed to stand under stirring at room temperature and the reaction course was followed by TLC, but no valuable reaction was observed until 72 hr.
b. When the same reaction was carried out at 60 °C, TLC showed the presence of the dithiole **6** after 24 hr. The solvent and amine were then removed under vacuum and the residue was extracted with acetone (3 × 10 ml). The removal of the acetone from extracts gave a residue which was crystallized from ethanol to afford **6** (0.10, 8%) as light yellow crystals whose properties are in agreement with those reported.[2]
c. When the same reaction was carried out at 150 °C for 3 hr, two phases were formed. After cooling, the liquid phase was separated from the dense brown oil, which latter was treated with cyclohexane to give a yellow solid. The recrystallization from ethanol gave the dithiole **6** (0.18 g, 20.6%). The dithiole **6** was identified through the formation of the trithiapentalene **13** obtained by reaction with an excess of phosphorous decasulphide in toluene.[19]

Reaction of the unsaturated ketone 1 with sulfur and TEA at 60°C

A mixture of the unsaturated ketone **1** (0.46 g, 2 mmol), sulfur (0.64 g, 20 mg/at) and TEA (6 ml) in pyridine (10 ml) was heated at 60 °C and the reaction course was followed by TLC. After 2 hr, TLC showed the presence of dithioles **2** and **6**, but after 6 hr the dithiole **2** disappeared and the presence of compounds **3, 6** and **7** was observed. The mixture was then directly chromatographed by using cyclohexane as initial eluent until all pyridine was eluted. Upon addition of increasing amounts of ethyl acetate to cyclohexane, the following fractions were eluted in the order: the dithiolodithiole **3** (0.10 g, 13%), dithiole **6**(0.16 g, 27%) and disulfide **7** (0.12 g, 18%).

Reaction of the dithiole 2 with sulfur and TEA

a. A mixture of the dithiole **2** (0.45 g, 0.15 mmol), sulfur (0.96 g, 30 mg/at) and TEA (3 ml) in DMF (10 ml) was allowed to stand under stirring at room temperature and the reaction course was followed by TLC. After 0.5 hr, TLC showed the presence of compounds **3** and **7** together with unreacted **2,** but the reaction mixture was left for additional 7.5 hr. The reaction mixture was then poured into water, extracted with benzene (3 × 5 ml) and extracts were dried over sodium sulfate. The removal of the solvent gave a residue which was subjected to CEPTLC to afford in order of elution the dithiolodithiole **3** (0.11 g, 20.2%), initial dithiole **2** (0.12 g, 26.7%) and disulfide **7** (0.14 g, 28.9%). Trace amounts of compounds **4** and **5** were also observed, but not isolated.

b. The same reaction was also carried out in acetonitrile or pyridine. TLC showed that after 3 hr compounds **3** and **7** were present in moderate yields and after 48 hr the yield of **7** increased considerably.

Reaction of the disulfide 7 with sulfur and TEA

a. A mixture of the disulfide **7** (0.5 g, 0.75 mmol), sulfur (2.4 g, 75 mg/at) and TEA (4 ml) in DMF (10 ml) was allowed to stand under stirring at room temperature and the reaction course was followed by TLC. After 24 hr the reaction mixture was poured into water and the resulting solid was filtered and dissolved in dichloromethane. The organic solution was washed, dried over sodium sulfate and evaporated under reduced pressure to give a residue. The chromatography of the residue afforded in order of elution sulfides **8** (0.18 g, 3.6%) and **9** (0.24 g, 4.9%) along with minor amounts of compounds **4** and **5.**

b. When the same reaction was allowed to stand for 48 hr, TLC showed the remarkable decrease of compounds **8** and **9** and the appearance of compounds **4** and **5.**

c. In pyridine or HMPA the reaction gave the same products, but in different reaction times.

Reactions of sulfides 8 and 9 with sulfur and TEA

A mixture of the tetrathiocin **9** (0.18 g, 0.5 mmol) sulfur (0.32 g, 10 mg/at) and TEA (2 ml) in DMF (5 ml) was allowed under stirring to stand at room temperature for 24 hr. The reaction mixture was then poured into water and the resulting solid was filtered and dissolved in dichloromethane. The organic solution was washed, dried over sodium sulfate and evaporated under reduced pressure to give a residue. The chromatography of the residue afforded in order of elution compounds **4** and **5** together with small amounts of **8** and **9**.

A mixture of the trithiepin **8**, sulfur and TEA in the same above stoichiometric ratio was allowed to stand under stirring at room temperature for 24 hr. The above work up gave compounds **5** and **4** and small amounts of **8**.

Acknowledgements

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[4] It is well known that the sulfur in the presence of phosphines,[5] amines[6] and ammonia[7] acts as a "nucleo-electrophilic thiation reagent"[8] since these nucleophiles open the sulfur eight membered ring affording nucleophilic and electrophilic species, also at room temperature.

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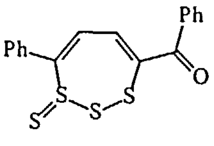

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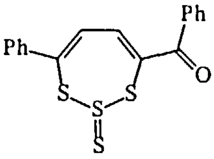

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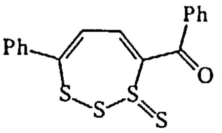

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