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SYNTHESIS AND INVESTIGATION OF POTENTIALLY AROMATIC 10 π-ELECTRON SULFUR HETEROCYCLES

by

SHOU-NAN UENG

A dissertation submitted to the Graduate
Faculty in Chemistry in partial fulfillment of the requirements for the degree
of Doctor of Philosophy, City University
of New York.

1978

This manuscript has been read and accepted for the Graduate Faculty in Chemistry in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

7-10-78
date

Klaus Grohmann
Chairman of Examining Committee

10 July 1978
date

David C. Locke
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Supervisory Committee

The City University of New York

ABSTRACT

SYNTHESIS AND INVESTIGATION OF POTENTIALLY AROMATIC 10 π-ELECTRON SULFUR HETEROCYCLES

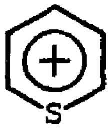
by

SHOU-NAN UENG

Advisor: Professor Klaus Grohmann

It was believed that the inclusion of heteroatoms only slightly perturbs the $(4n+2)\pi$ system, and Hückel's rule also applys to heterocyclic as well as carbocyclic molecules.[20] The formal replacement of carbon-carbon double bonds by sulfur atoms in a given aromatic system results in the formation of the isoelectronically heteroaromatic system.

The three analogues of tropylium cation, 6,[24] 7,[25] and 8[26] are known and shown to be aromatic on the basis of their proton NMR spectra.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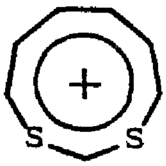
This thesis deals with the synthetic approaches towards several 10 π sulfur heterocycles such as I, II, III and V.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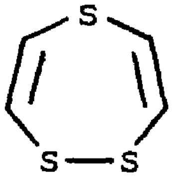
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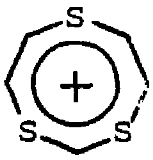
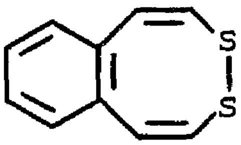
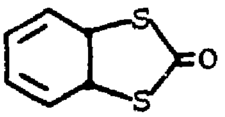

III

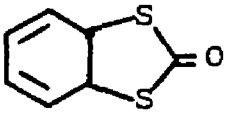

V

These compounds are of interest in order to test the validity of Hückel's rule for 10 π sulfur heterocycles.

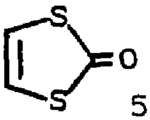
The synthesis of I has been attempted via the key intermediates 52-cis and 52-trans through the Diels-Alder reaction between 55 and 57, through the $(2\pi+2\pi)$ photoaddition between 55 and 70, through the nucleophilic attack of xanthate to benzene oxide-oxepin mixture and through the dehydrobromination of 66.



52-cis ,



52-trans



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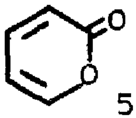

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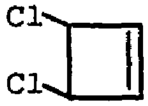

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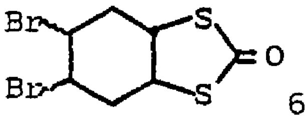
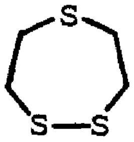


66

The 1,2,5-trithiepin II is the first neutral 10 π-electron sulfur heterocyclic aromatic system has been synthesized. The key features of the synthesis involve the construction of 81, followed by successive introduction of the two double bonds. The introduction of double bonds were performed by the Pummerer reaction[81] of 82 and 94 or by chlorination of 81 followed by dehydrochlorination.



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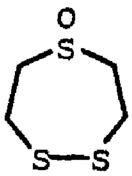

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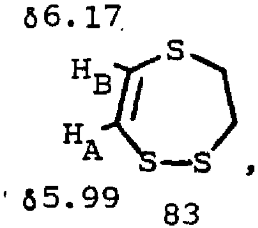

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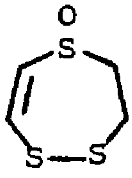

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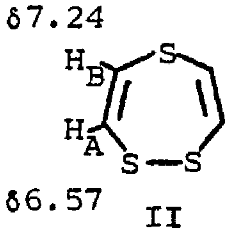
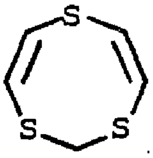


II

With reference to table 6(page 73), while introducing a second double bond into cyclic sulfides changes the olefinic proton chemical shifts only slightly, large downfield shifts of the protons were found in II(downfield shifts for H_A and H_B are 0.58 and 1.07 ppm, respectively) which are consistent with the presence of a diamagnetic ring current in II.

Therefore, based on this observation, II may be considered an aromatic neutral 10 π-electron sulfur heterocycle.

The routes to synthesize III via 104 and 105 were described.



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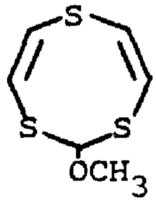

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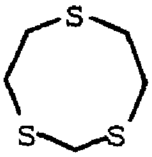

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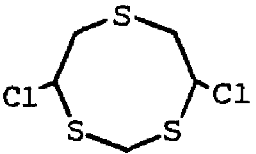

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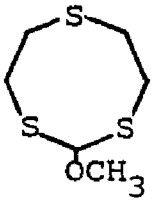

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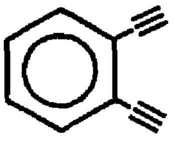
Unexpectedly, decomposition and polymerization took place during the dehydrochlorination of 107 and the Pummerer reaction of the sulfoxide of 106 and 108. Also, an unexpected β-elimination followed by fragmentation was found when 106 was treated with n-butyllithium. All these factors made the synthesis of III not possible.

Starting with 134 followed by the nucleophilic attack of sodium disulfide or of benzyl mercaptan, debenzylation and oxidation was expected to give V, however, at 10°C only naphthalene and sulfur were isolated, indicating a low thermal stability for V (10π), which is comparable to that of 133 (8π).



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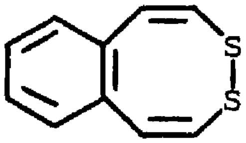
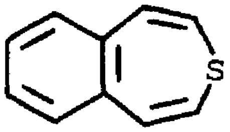


V



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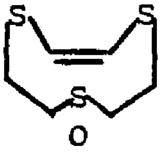
The attempt to synthesize 1,4,7-trithianin 142 via 151 was also described.



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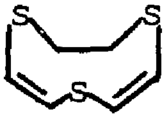

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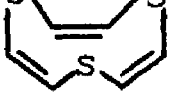

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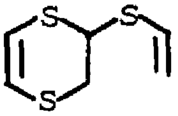

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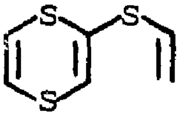

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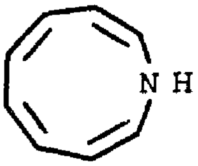
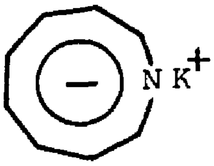
The Pummerer reaction of 151 gave 1:1 mixture of 152 and 156. The formation of 156 from 151 is due to a transannular interaction followed by β-elimination as shown on page 113. Further oxidation and Pummerer reaction on 152 and 156 resulted in polymerization and the formation of 162, respectively.

In summary, among the 10 π-electron heterocyclc system, 1H-azonin 10a,[28] the potassium salt of azonin 13,[30,31] 1,2,5-trithiepin II(this work), and 1,3-dithiepin anion 33,[41] are known and shown to have aromatic character in agreement with Hückel's rule.



10a



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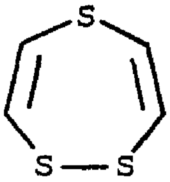

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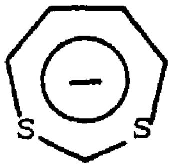

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ACKNOWLEDGEMENT

I wish to express my thanks to Professor Klaus Grohmann for his guidance, understanding, encouragement and patience throughout the entirety of this research. I am also grateful to professors Robert Engel and Joseph Dannenberg for serving on this thesis committee and offering many valuable suggestions and criticisms.

In addition, I would like to thank Professor Robert Lichter and Mrs. Libby Miller for their valuable suggestions as well as Dr. George Furst, Dr. P. Srinivasan and Mr. Mukund Sibi for measuring the ^{13}C NMR spectra.

The partial supports from CUNY FRAP # 11640 and PRF # 09588 are also acknowledged.

TO MY PARENTS,
Jung and Ching-Duang
and MY WIFE,
Marina

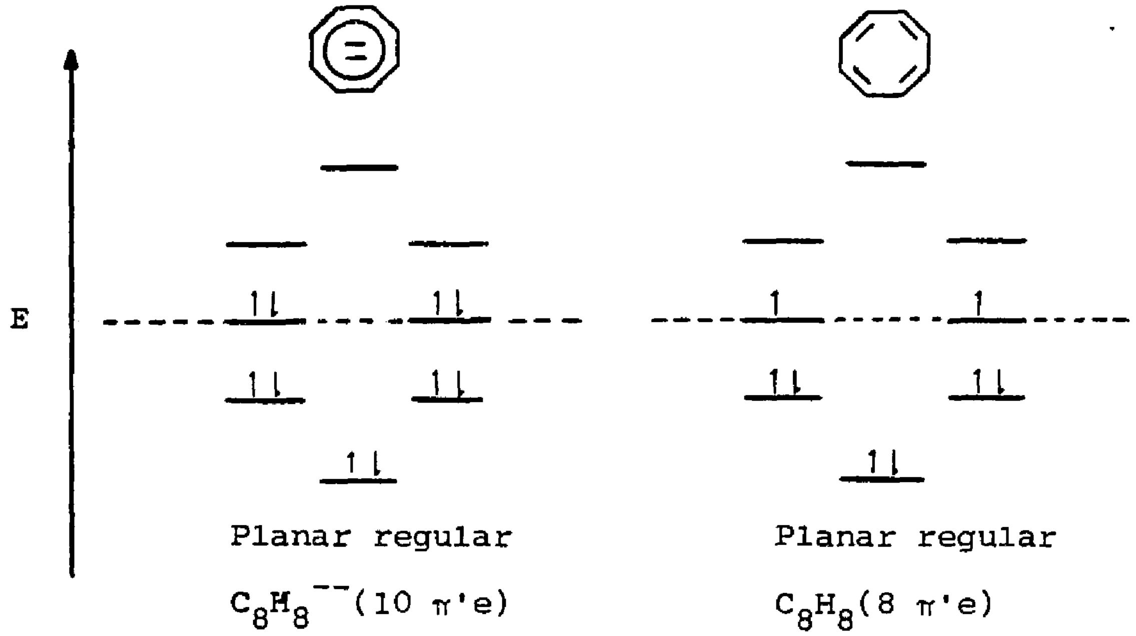
TABLE OF CONTENTS

INTRODUCTION

The controversial term "aromatic character" was introduced by Kekule last century in order to explain the rather unexpected properties of benzene vs the hypothetical molecule cyclohexatriene.[1] R. Willstatter's failure to prepare cyclobutadiene the lower homologue of benzene and his synthesis of cyclooctatetraene[2] which behaved as a typical very reactive polyolefin showed that cyclic conjugation is not sufficient for a molecule to be "aromatic".

E. Huckel,[3] in 1931, performed molecular-orbital calculations which predicted that regular monocyclic planar conjugated polyenes would have a closed-shell configuration of π-electrons if they contained $4n+2$ π-electrons, where n is a positive integer or zero. Molecules possesing this closed-shell electron configuration are predicted to have a certain stability, characterized as "aromaticity".

An unsaturated cyclic or polycyclic molecule or ion may be classified as aromatic if all the annular atoms participate in a regular planar conjugated system such that, in the ground state, all the π-electrons are paired and accommodated in bonding or non-bonding molecular orbitals(closed-shell).



Molecular-orbital energy levels for a closed-shell and an open-shell systems containing 8 and 10 π-electrons

The stability, "aromaticity" associated with these closed-shell molecules can be detected by comparison of their heats of hydrogenation and combustion with those of suitable models. It is also exhibited in their chemical reactivity such as substitution vs addition etc. The validity of Hückel's rule has been beautifully demonstrated in the syntheses and characterizations of $C_5H_5^-$ [4] and $C_7H_7^+$ [5] and the whole series of annulenes.[6]

A more useful criterion for the "aromatic character" was introduced by Pople[7], Elvidge and Jackman[8] as the <u>diamagnetic ring current</u>. It stated that a planar cyclic conjugated molecule containing 4n+2 π-electrons is predicted to sustain a diamagnetic ring current in an applied magnetic field, causing deshielding for the protons outside the plane of the ring and strong shielding for the protons within or above the ring. The magnitude of the shielding-deshielding contribution from the induced ring current in different aromatic compounds has been estimated by using the relationship

$$\sigma_1 = 0.63\ K_b(\frac{a_1}{a_b})^2\ I_1 \tag{1}$$

Where K_b is the shielding constant value given in the table of Johnson and Bovey[9] for the appropriate separation between the center of the ring and the hydrogen nucleus, a_1 is the radius of the ring in question, a_b is the radius of the benzene ring, I_1 is the ratio of the ring current intensities for the compound and benzene and 0.63 is an empirical constant found by Jonathan and co-workers.[10] This has been demonstrated in the case of the carbocyclic conjugated polyenes, called annulenes, the higher homologues of benzene.

In the proton NMR spectrum the vinylic protons of non-conjugated cyclic olefins usually absorb in the range δ4.6-5.7; and the protons of cyclic conjugated polyolefins absorb around δ5.4-5.8. The protons of the non-aromatic cyclooctatetraene, for example, absorb at δ5.69. With benzene, however, the protons are strongly deshielded by the secondary magnetic field, and absorb at δ7.19. Other annulenes and aromatic ions have also been studied by proton NMR, and the results are summarized in Table 1.

Table 1 Proton NMR spectra of annulenes and aromatic ions

Compound	π'e	δ	Remarks
Cyclopentadienyl anion	6	5.34	Aromatic [4]
Benzene	6	7.19	Aromatic[1]
Tropylium cation	6	9.09	Aromatic[5]
Cyclooctatetraene	8	5.69	Not aromatic[3]
(10)Annulene 1'&1"	10	isomer 1' 5.67	Not aromatic[12]
		isomer 1" 5.86	Not aromatic
1,6-Methano(10) annulene 2	10	7.2(outer)	Aromatic[13]
		-0.5(methylene)	
(14)annulene	14	A. 5.58; B. 6.07	Two isomers at RT[14]
		A. 7.6(outer)	At -60°C, aromatic
		0.0(inner)	
(18)annulene	18	8.9(outer)	At RT, aromatic[15]
		-1.8(inner)	
		4.55	at 110°C
Cyclooctatetraenyl dianion 4	10	5.62	Aromatic[16]
Cyclononatetraenyl anion 3(all cis)	10	6.18	Aromatic[16]
Cyclononatetraenyl anion 3'(t,c,c,c)	10	-3.52(inner)	Aromatic
		6.4-7.0(outer,6H)	
		7.27(outer,2H)	
Bicyclo(5.4.1)dodecapentaenyl cation 5'	10	8.3-9.6(ring H)	Aromatic[17]
		-1.8- -0.3 (methylene H)	

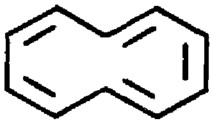
Two systems isoelectronic with benzene are cyclopentadienyl anion[4] and tropylium cation.[5] Both of these have been synthesized and shown by proton NMR spectroscopy to have aromatic character. The observed chemical shifts for the protons in these ions are affected by both the diamagnetic anisotropy and the charge. A positive charge caused a general downfield shift, while a negative charge causes a general upfield shift.

Variation of chemical shifts with charge has a linear relationship with the charge density. Günther[11] studied the observed chemical shifts for five aromatic ions, $C_3H_3^+$, $C_5H_5^-$, $C_7H_7^+$, $C_8H_8^=$ and $C_9H_9^-$, and indicated that

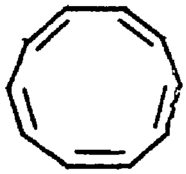
$$\Delta\sigma = 10.7\ \Delta\rho \qquad (2)$$

The quantity $\Delta\sigma$ represents the downfield or upfield chemical shift(ppm) difference from benzene and $\Delta\rho$ represents the difference in the π-electron density per carbon atom in the ion relative to benzene. The discrepancy between equation (1) and (2) could be explained by the fact that the charge density has a greater effect on the proton chemical shift than the variation of the ring size current.

Among the [10]Annulenes, the parent molecule has been isolated at subzero temperatures in two distinct geometric forms, <u>1</u>' and <u>1</u>".[12]

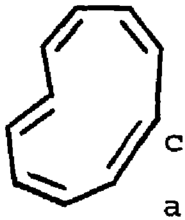


1



δ5.67

1'

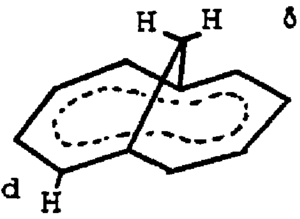


centered at δ5.86

1"

The proton NMR spectrum of 1' remained temperature independent over a range of -40 to -160°C(singlet, δ 5.67). The proton NMR spectrum of 1" was temperature dependent between -40 and -100°C(centered at δ 5.86) and demonstrated that 1" was frozen in a conformation at -100°C and that all the protons achieved equivalence at around -40°C. Above -40°C, both 1' and 1" were thermally converted into cis and trans-9,10-dihydronaphthalene, respectively. No ring current is indicated by their proton NMR spectra. Therefore, [10]Annulene is not aromatic. [10]Annulene with the all-cis relationship has 135° bond angles. If two trans-linkages are present the angle strain disappears, but severe steric interactions between the hydrogen atoms within the ring forces the ring out of planarity.

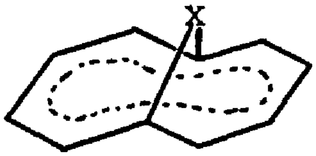
Although the two "internal" hydrogen atoms in [10]-Annulene would prevent the molecule from reaching a planar configuration, models indicate that near-planar systems result if these two hydrogen atoms are replaced by a methano or hetero-bridge. Several bridged compounds 2[13] have been synthesized and on the basis of their proton NMR shown to have aromatic character.



δ-0.5

centered at δ7.2

2

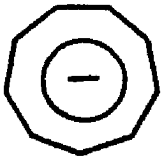


X= O centered at δ7.48

= NH centered at δ7.62

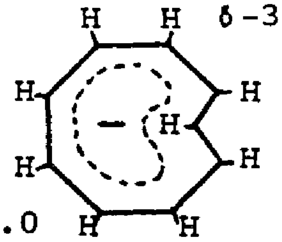
2'

Isoelectronic with cyclodecapentaene are cyclononatetraenyl anion 3 and 3' [16], cyclooctatetraenyl dianion 4[16] and cycloundecapentaenyl cation 5. The anions 3, 3' and 4, unlike the neutral molecule, have been shown to have aromatic character and posses a definite ring current. Although 5 is still unknown, its bridged analogue 5' has been prepared and is aromatic[17] on the basis of its proton NMR spectrum.



δ6.18

3

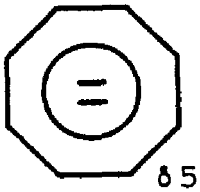


δ-3.53(t)

δ7.27(d)

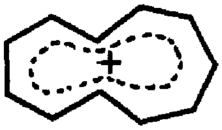
δ6.4-7.0

3'

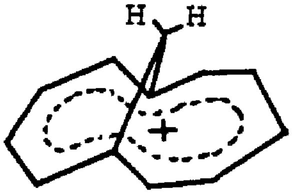


δ5.62

4



5 (unknown)

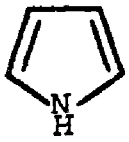


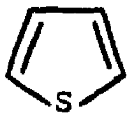
δ-1.8- δ-0.3
(methylene protons)

δ8.3-9.6
(ring protons)

5'

Once the predictive value of Hückel theory was recognized, application of the 4n+2 rule was naturally extended to heterocyclic systems as well. The well known heterocyclic compounds furan, pyrrole and thiophen are isoelectronic with benzene. Considering the bonding orbitals (s and p for the N and O heterocycles, s, p and d for the S) and the relative electronegativities,[18] π-electron delocalization and aromaticity are expected to increase in the order furan, pyrrole and thiophene. This indeed to be the case.[19]

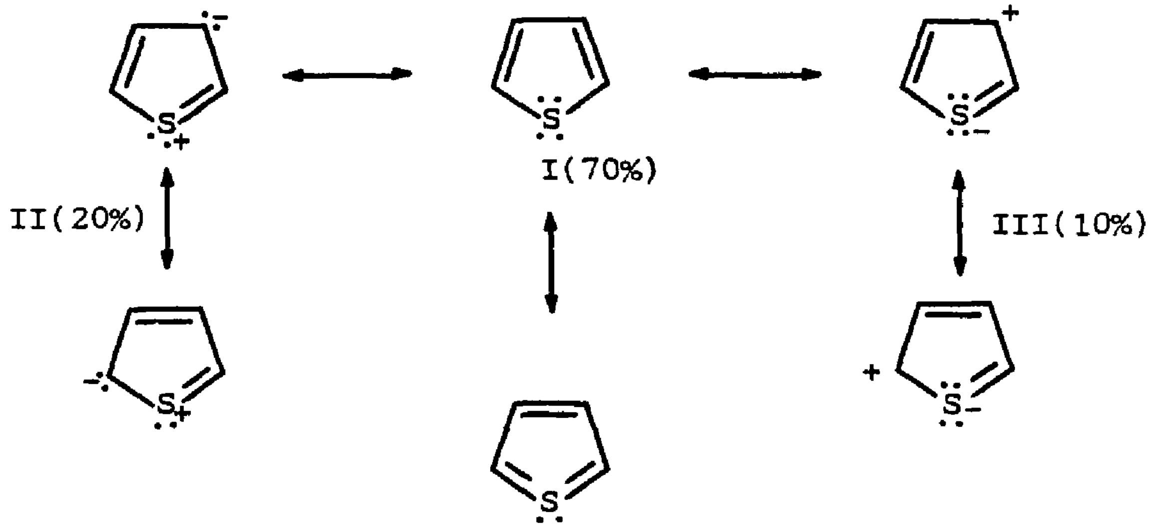




ELECTRONEGATIVITY	O	N	S	C
	(3.44)	(3.04)	(2.55)	(2.52)

Schomaker and Pauling,[20] comparing bond lengths, resonance energy values*, and dipole moments in pyrrole, furan and thiophene, concluded that in thiophene the sulfur appeared to expand its valence shell to some extend to ten electrons in place of the usual octet characterizing oxygen and nitrogen. Thus, the following structures are considered important contributors to the resonance hybrid of thiophene.

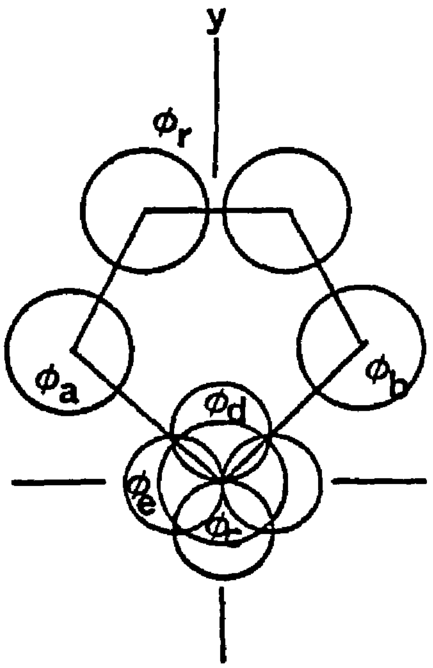
*Resonance energy: The difference in energy between the actual molecule and the structurally related model of lowest energy which contains alternating single and double bonds.[21]

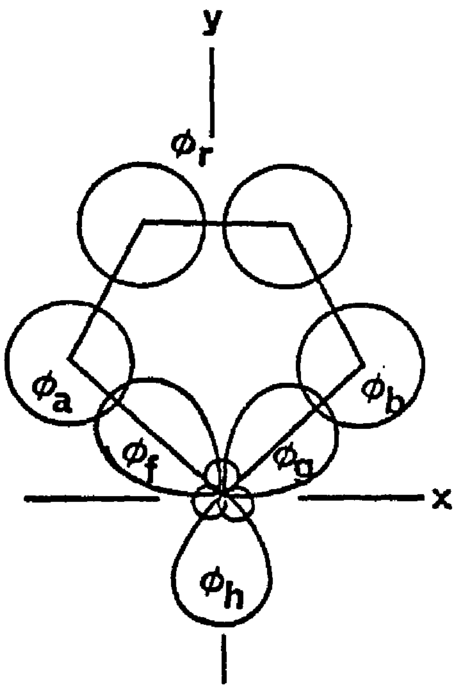


IV
(10%)

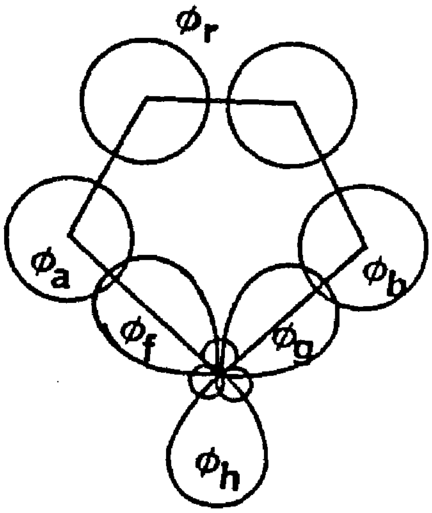
The structures III and IV involve the sulfur d orbitals. The added stabilization resulting from this delocalization accounts for the close similarity of this compound to benzene.

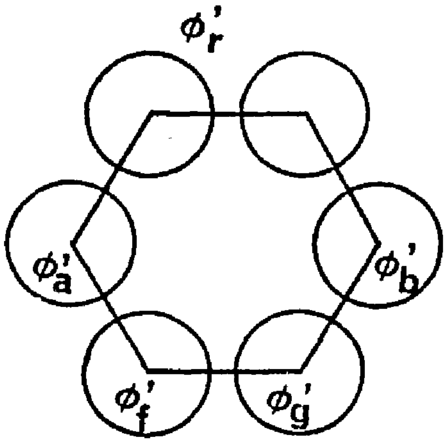
This essentially qualitative valence-bond representation of thiophene was translated into a quantitative study by Longuet-Higgins[22] in 1949 with the aid of the M.O. method. The model of thiophene is presented below. The x and y axes are shown, the z-axis being perpendicular to the plane of the molecule. The $2p_z$ atomic orbitals of the C atoms were denoted as ϕ_a and ϕ_b, the three atomic orbitals $3p_z$, $3d_{yz}$ and $3d_{xz}$ of the S atom which are conjugated with ϕ_a and ϕ_b are denoted as ϕ_c, ϕ_d, and ϕ_e, respectively.





By a linear combination of ϕ_c, ϕ_d, and ϕ_e, it was demonstrated that the $3p_z$ orbital and two 3d orbitals of sulfur could be hybridized to give three hybrid pd^2 orbitals, ϕ_f, ϕ_g, and ϕ_h, two of which(ϕ_f and ϕ_g) have the proper energy and symmetry characteristics required for entering into conjugation with the $2p_z$ orbitals of the neighbouring ring carbons. Since, moreover, these two sulfur hybrid orbitals are defined to be mutually non-orthogonal,[22] the analogy with benzene becomes clear; both are systems in which six electrons are associated with six atomic orbitals. The third pd^2 orbital(ϕ_h), which is orthogonal to the other two is mainly 3d in character and is of too high energy for it to be occupied in the ground state. Due to the numerical calculations within the HMO framework, the ϕ_f and ϕ_g orbital may simply be replaced by carbon $2p_z$ orbitals. The atomic orbital model for the benzene analogue of the thiophene is shown below.

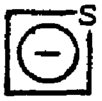
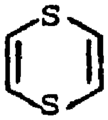
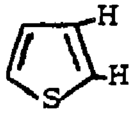
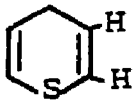
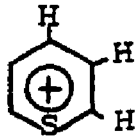
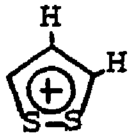
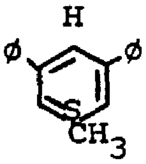




Denote the atomic orbitals ϕ'_a, ϕ'_b, ϕ'_r corresponding to ϕ_a, ϕ_b, ϕ_r and the $2p_z$ orbitals of the two C atoms which replace the sulfur may be denoted as ϕ'_f, ϕ'_g. A very close similarity in resonance energies, bond orders, bond lengths and dipole moments has been found through further MO calculation.[22] Hence, based upon this model developed by Longuet-Higgins, the formally bivalent sulfur atom(atoms) can be considered to be electronically equivalent to -CH=CH- group(groups), and formal replacement of a carbon-carbon double bond in a given aromatic system should result in the formation of an isoelectronically heteroaromatic system.

So far, only thiophene and thiapyrylium cation 6,[24] the 1,2-dithiolium cation 7[25] the 1,3-dithiolium cation 8,[26] are known example of this postulation.

Attempts to prepare sulfur analogue thiacyclobutene anion of cyclopentadienyl anion has not succeeded[23] so far. The three analogues of the tropylium cation, 6,[24] 7,[25] and 8[26] have been synthesized and shown to have aromatic character on the basis of their proton NMR spectra. The proton NMR data for 6 π-electron sulfur and related system are shown below (Table 2).

Compound	δ	π-e'	Comment
	-----	6	Unknown
	5.99	8	Antiaromatic ?
	7.04 7.17	6	Aromatic
	5.55 5.90		---------
	9.20 8.90 10.0	6	Aromatic
	8.88(d,J=5 Hz) 10.57(d,J=5 Hz)	6	Aromatic
	10.25(s) 9.07(s)	6	Aromatic
	6.18(t,J= 1.7 Hz) 4.03(d,J=1.7 Hz)	6	

While it is relatively easy to detect diamagnetic ring current [6] in carbocyclic system and possible to assess the effect of the charge on aromatic ions,[11] the measurement of ring current in heterocyclic system poses a considerable difficulties and is not free of ambiguity.[28] This is because the specific influence of the heteroatom, sulfur, on the chemical shift.

Further complication in separating the factors affecting proton chemical shifts arise from the investigation of the heteroaromatic ions. As indicated before, three factors can be identified a) diamagnetic ring current b) effect of heteroatom(diamagnetic anisotropy, electronegativity) c) charge distribution.

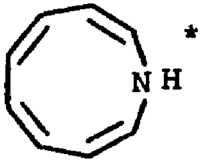
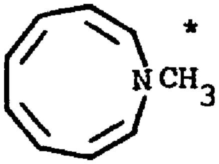
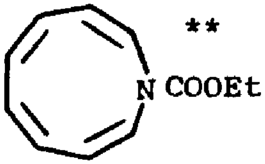
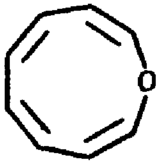
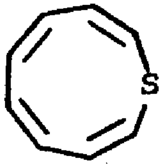
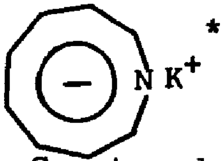
Therefore, only the chemical shift comparison of closely related system will provide the experimental data concerning the effect of heteroatom vs the diamagnetic ring current vs charge distributions.

The synthesis and investigation of 10 π-electron heterocyclic systems has met with only limited success so far. As stated previously, replacement of carbon-carbon double bonds by heteroatoms(S,N, or O) in a given aromatic system should result in the formation of isoelectronically heteroaromatic system.

Among the 9-membered ring heteroaromatic compounds, the analogues of cyclodecapentaene, aza(9)annulene 10,[28] oxa(9)annulene 11 [26] and thia(9)annulene 12 are potentially aromatic species. In terms of their possible aromaticity, compound 10, 11, and 12 have an advantage over the (10)-annulene is that a planar 9-membered ring is less strained than a planar 10-membered ring. Table 3 showed the proton NMR spectra of 9-membered ring heteroatom systems.

Compound 11 has been synthesized by Anastassiou and Masamune [26] and was shown not to be aromatic on the basis of its proton NMR spectrum. By contrast, 1H-azonin 10a [28] shows aromatic character based on comparisons of proton NMR and UV data for 10a to that of 11 and cyclononatetraenyl anion. Compound 10b demonstrated only a small degree of aromatic character; this could be arise from unfavorable steric interactions between the substituent on the nitrogen atom and the α-protons. Compound 10c [29] shows no apparent ring current presumably because the lone pair is less available for donation into the π-system. Masamune [30] and Anastassiou [31] claimed that 13, obtained from the treatment of 10c with potassium t-butoxide, is aromatic and planar.

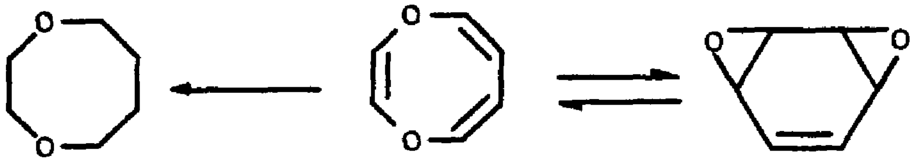
Table 3 Proton NMR spectra of 9-membered ring heteroatom systems

Compound		π'e	ring proton α	 β	 γ + δ	
			δ value	δ value	δ value	
10a	 *	10	7.07(d,J=11.0 Hz)	6.00(br d,J=11.0 Hz)	7.97-6.70(m)	Aromatic
10b	 *	10	5.85(d,J=10.5 Hz)	4.88(dd,J=10.5,4.3Hz)	6.13-5.94(m)	Not aromatic
10c	 **	10	6.37(d,J=9.6 Hz)	5.32(d,J=9.6 Hz)	5.87(m)	Not aromatic
11	 **	10	6.25(d,J=7.0 Hz)	5.10(dd,J=7.0,3.2 Hz)	5.92-5.76(m)	Not aromatic
12		10	-----	-----	-----	Unknown
13	 **	10	8.64(m)	6.63(m)		Aromatic

* Spectra determined in $CDCl_3$

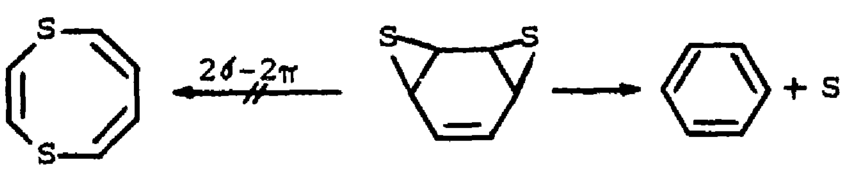
** Spectra determined on acetone-d_6.

Among the 8-membered ring heteroaromatic systems, the 1,4-dithiocin 14 was first synthesized by Vogel[33] and shown to be an olefinic compound by its proton NMR spectrum and its chemical behavior; it undergoes polymerization and hydrogenation easily and equilibrated with syn-benzene dioxide at 60°C.

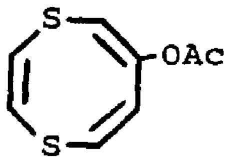


14

Attempted synthesis of 1,4-dithiocin 15 from the syn-benzenebisepisulfide 16 via 2σ-2π isomerization did not give 15, but instead decomposed to give benzene and sulfur. Compound 17 is the only derivative of 15 which has been synthesized. The chemical properties as well as proton NMR indicated 17 is not aromatic[33](see page 18).

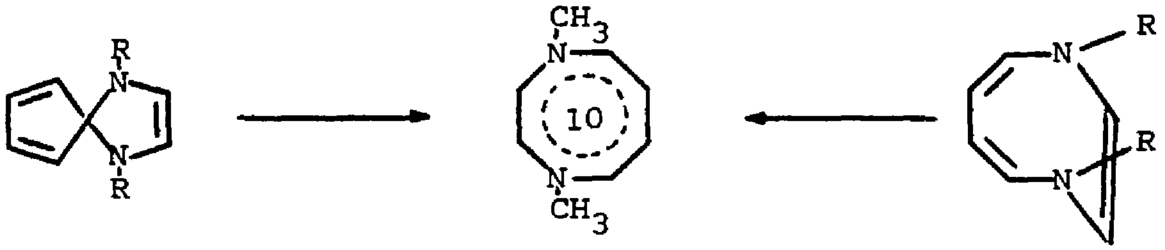


15 16



17

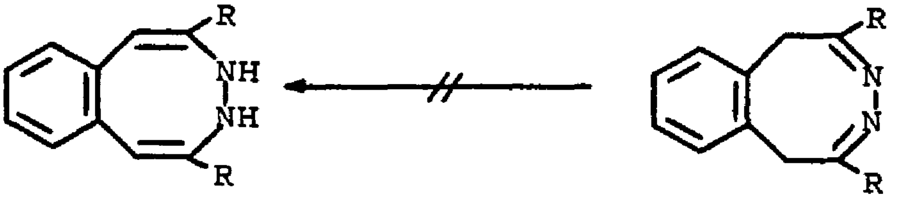
On the basis of a careful investigation of the proton NMR and ^{13}C NMR of compound 18, Prinzbach [32] in 1975 concluded that it maintains a diamagnetic ring current with flattening of the twist conformation.



18

Several benzo-fused derivatives of 14, 15 and 18 have also been synthesized and investigated. Compounds 19,[34] 20,[35] 21,[36] and 22[36] do not display substantial ring current. The UV spectra also imply lack of conjugation and the tub-shape conformation are suggested. Riley and Park synthesized the derivative 23 to which they assign aromatic character on the basis of its ^{19}F NMR spectrum.[37]

HMO calculations by Allinger[38] predicted substantial delocalization energy* for compound 24a and 24, but the failure of 24a to isomerize to 24 illustrates the failure of this prediction. Hence, 24a doesn't have aromatic character or the activation energy for this reaction is too high.



24

24a

The proton NMR data for some heteroatom systems are summarized next page.

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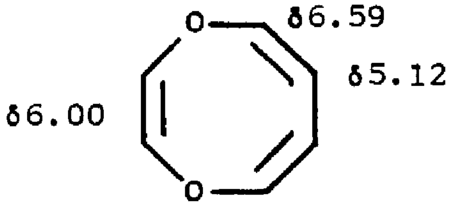
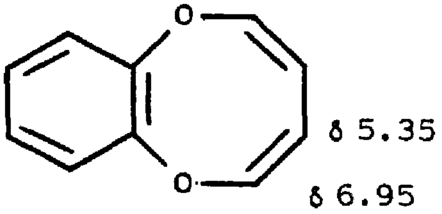
*Delocalization energy: The difference between energy calculated for the delocalized model and that calculated for the localized model.

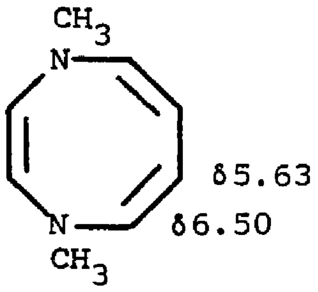
The proton NMR data for parent and benzofused heteroatom systems are summarized below.



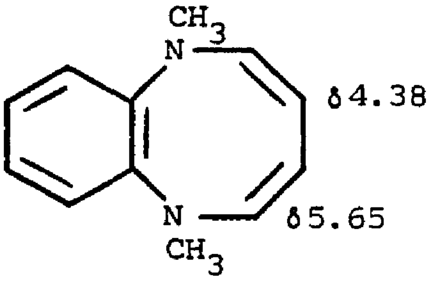
14



19



18



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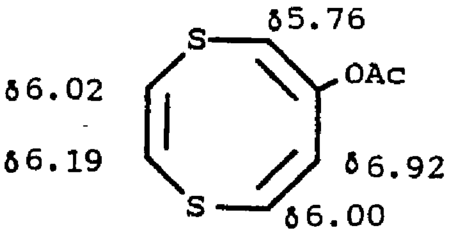
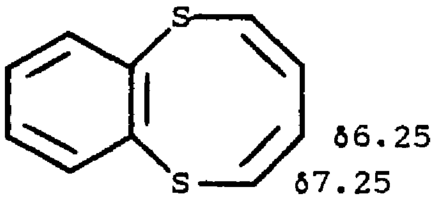
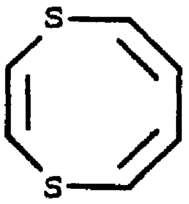


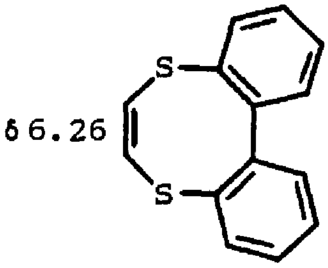
17



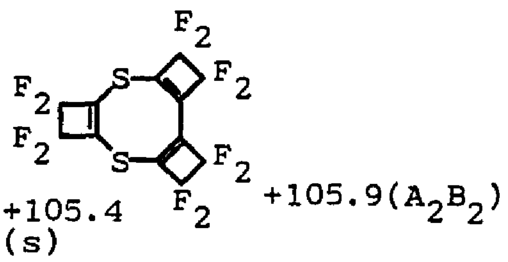
21



15(unknown)

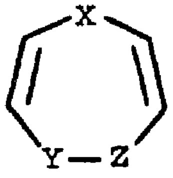


22

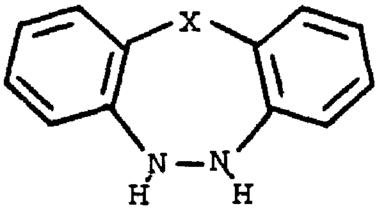


23

Several 7-membered ring heteroaromatic systems are shown below. If three heteroatoms carrying lone pair electrons are introduced into a ring along with two double bonds then it is conceivable that a 7-membered ring can be aromatic by virtue of its being a 10 π-electron system. All of the parent compounds 25 are still unknown. Allinger examined [39] a series of the dibenzo-fused analogues 26a-e and found that their UV spectra were all rather similar, which suggested a lack of delocalization in these 10 π-electron systems.



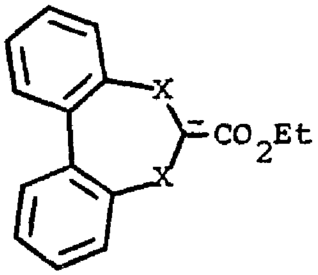
X,Y, or Z
= S,O, or NR
25



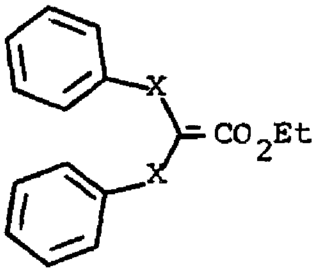
26a X= CH$_2$
b = NH
c = NMe
d = O
e = S

However, the sulfur compound 26e is a slightly weaker base than the carbon analogue 26a(pKa's 2.81 and 3.10), respectively, which Allinger attributes to a small degree of aromaticity in the former, and indeed an proton NMR study showed that the hydrazo protons of 26e were somewhat deshielded with respect to those in 26a. If all the extra acidity of the conjugated acid of 26e compared with that of <u>26a</u> is due to the resonance, the pka difference corresponds to 0.40 Kcal/mole($\Delta G=-RT \ln \frac{10^{-2.81}}{10^{-3.10}}$) of extra resonance stabilization in <u>26e</u>.

Breslow [40] studied the acidities of <u>27a</u>, <u>28a</u> and their open-chain anlogues and found similar acidities for the cyclic compounds and their noncyclic counterparts(rate constants for deuterium exchange in <u>27a</u>, <u>28a</u> are $k=2.86\times10^{-2}$ min^{-1} and $k=3.90\times10^{-2}$ min^{-1},respectively). On this basis, the author suggested that the anions <u>27a</u> and <u>27b</u> are not aromatic.

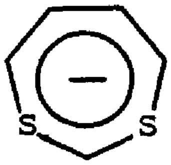


<u>27a</u> X= S
<u>b</u> = O

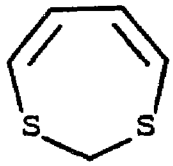


<u>28a</u> X= S
<u>b</u> = O

Recently, Grohmann [41] synthesized the parent 1,3-dithiepin anion <u>29</u>. Based on the greater kinetic and thermodynamic acidities of <u>30</u> than those of the acyclic analogue <u>31</u> and the saturated analogue <u>32</u>, the 1,3-dithiepin anion <u>29</u> was claimed to represent a 10 π-electron heteroaromatic system, although the degree of aromaticity seems to be small. If all the extra acidity of <u>30</u> compared with that of <u>31</u> is due to cyclic conjugation, the pka difference corresponds to 5.60 Kcal/mole($\Delta G=-RT \ln \frac{10^{-26}}{10^{-30}}$) of extra resonance stabilization in <u>30</u>.



29



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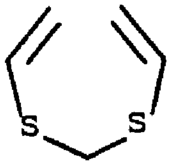

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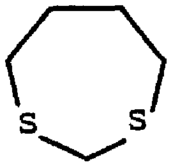
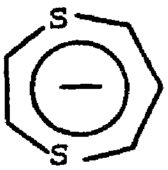


32

pKa 26 30 31

The synthesis of the 1,4-dithiepin anion 33 was attempted by Grohmann[42] and Murata[43] who hoped to metallate compound 34 at the allylic position. Metallation occurred instead at C-2 as shown. However, in constrast, compound 35 was metallated at the allylic position as shown.



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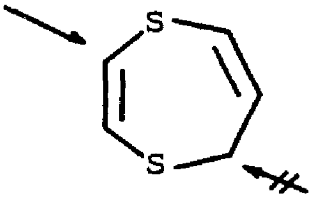

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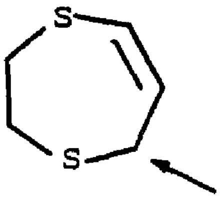
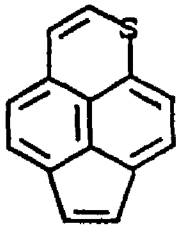


35

Heteroaromatic systems with 14 π-electron were also investigated. Attempts by several groups[44] at syntheses of the parent macrocyclic hetero(14)annulenes of type 36 were unsuccessful. However, the 13-membered ring sulfur heterocyclic compound 37 has been synthesized.[6] Proton NMR spectrum of 37 showed the nonplanar molecule to exhibit no ring current.



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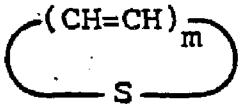

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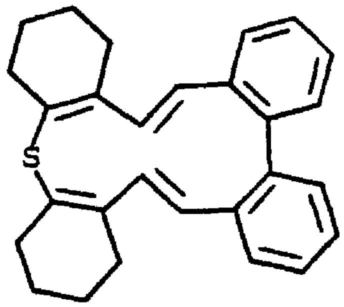
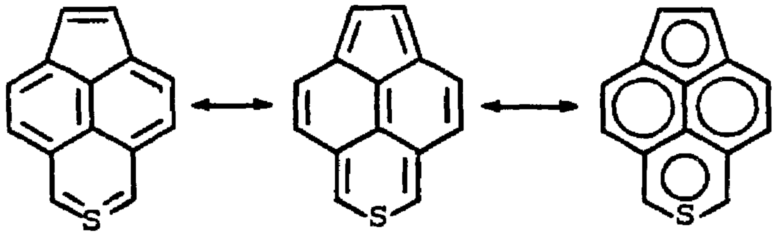


37

By contrast, the tetracyclic compound 38[44] clearly has a substantial ring current associated with the 14 π-electron system because the ring proton resonances lie at δ 6.8 and δ 8.2.



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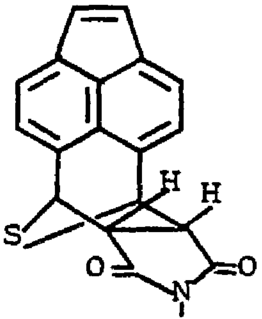
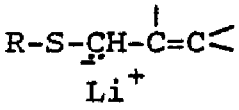


40

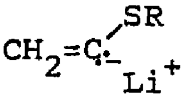
Another compound 39 [46] trapped as its Diels-Alder adduct with N-phenylmaleimide has been considered as a peripheral 14 π-electron aromatic compound. However, failure to isolate 61 casts some doubt on their statement.

In order to elucidate the role of the d orbital of the sulfur atom, thiophene and its derivatives have been subjected to various experimental studies by UV, IR, and ESR, often with conflicting results.[45]

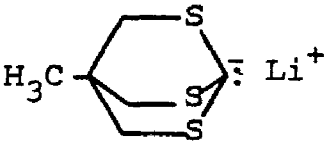
As an electron-acceptor, sulfur atom is expected to stabilize an adjacent carbanion through a pπ-dπ bond. Seebach[46] reported that the d shell of a sulfur atom can stabilize lithium ion pairs 41, 42 and 43 by a conjugative effect.


$R-S-\underset{Li^{+}}{\ddot{C}H}-\overset{|}{C}=C<$

41


$CH_2=\ddot{C}\genfrac{}{}{0pt}{}{SR}{Li^{+}}$

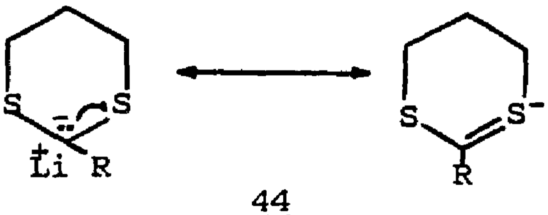
42



43

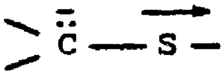
More recently, Bordwell[47] came the same conclusion through a study of the acidifying effects of phenylthio substituents.

However, Stritwieser[48] has studied the acidities of dithianes and pointed out the substituent effects imply a highly localized carbanion with no significant role being assigned to sulfur delocalization as would be implied by the



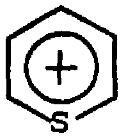
44

R	pKa
H	31.1
CH_3	37.1
C_6H_5	28.2



resonance structure 44; the stabilization of a carbanion by adjacent sulfur is argued to be due to polarizability.

As an electron-donor, the bivalent sulfur atom can stabilize a positive charge on an adjacent carbon atom. It has been shown that electron-donating through-conjugation via sulfur allowed aromatic character for thiapyrylium cation 6,[24] 1,2-dithiolium cation 7,[25] and 1,3-dithiolium cation 8.[26]

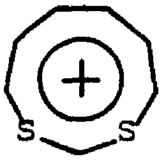

6


8

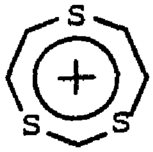

7

As pointed out previously(page 11), in a given aromatic system replacement of double bonds by the bivalent sulfur atoms should result in the formation of an isoelectronically heteroaromatic system. Table 4(page 26) shows the potentially aromatic heterocycles derived from carbocyclic compounds by replacing double bonds successively by one, two or three bivalent sulfur atoms.

With reference to compounds 6, 7 and 8, the monocyclic carbonium ions, such as I, and III containing two or three sulfur atoms, derived from cycloundecapentaene cation 102, should have electron-donating through-conjugation via sulfur allowing the π-electron delocalization in the entire molecule forming an aromatic 10 π cation.

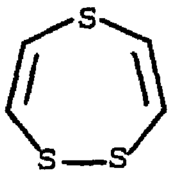


I

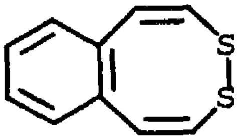


III

Compounds II and V, analogues of cyclodecapentaene 1, are expected to have aromatic character.



II



V

The investigation of compounds I, II, III, and V will provide the experimental evidence for the electron-accepting or electron-donor properties of sulfur in the cyclic sulfur systems and test the validity of the prediction of Hückel(4n+2) rule for heteroaromatic system. Therefore, the aim of the investigation described in this thesis was the syntheses of compounds I, II, III, and V in order to examine their possible aromaticity.

Table 4

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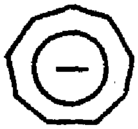
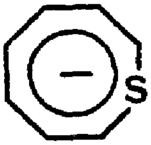
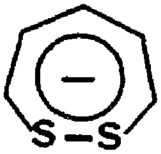
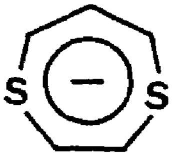
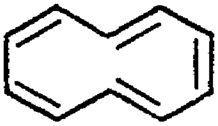
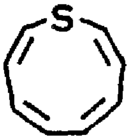
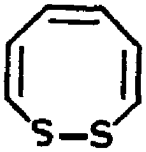
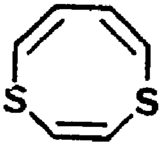
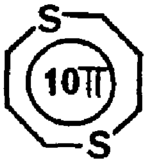
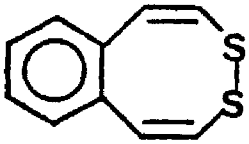
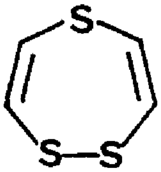
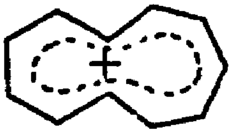
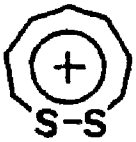
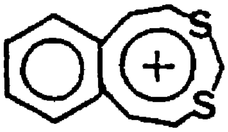
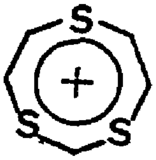
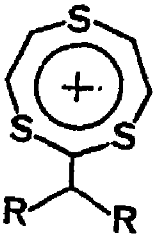
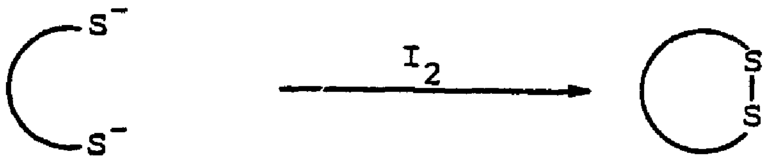
ANION	 69		  29 	
NEUTRAL	 1		  VI   V	 II
CATION	 102		   I 	 III  IV

In syntheses of the monocyclic potentially aromatic sulfur compounds, one should first consider the methods for the construction of the sulfur-containing ring systems. In general, sulfur is approximately 1260 times more nucleophilic than oxygen(For example, the ratio of rate constants for the reactions of n-butyl bromide with sodium salts of thiophenol and phenol was determined at 25°C with 0.1 mole initial concentration in ethanol to be 1260).[49] Therefore, the sulfur linkage within the ring could conceivably be generated by the nucleophilic attack of a thiol or thiolate anion on suitable substrates under various conditions.

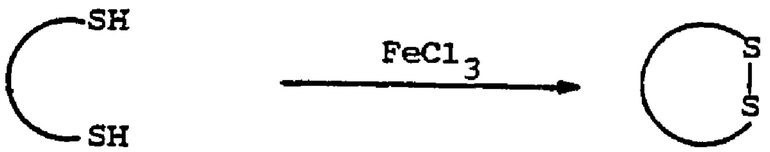
The general routes to construct 1,2-dithia, 1,3-dithia, and 1,4-dithia ring systems are summarized below.

A. <u>1,2-dithia ring system</u>

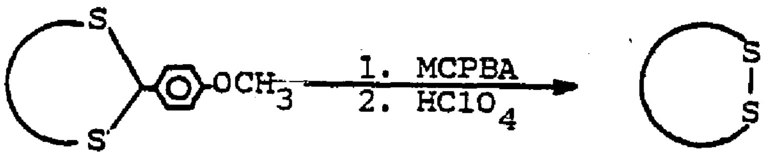
1.



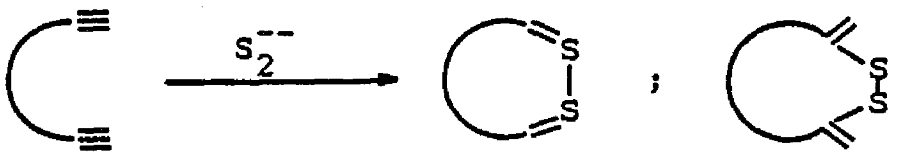
2.



3.



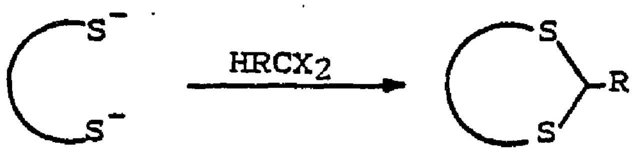
4.



The 1,2-dithia ring systems can be obtained by the oxidation of the bis thiolate anion in the presence of iodine[50] or by the oxidation of the bis thiol itself in the presence of ferric chloride.[51] Kishi[52] reported that the 1,2-dithia ring system could be synthesized by treatment of the 1,3-dithia acetal with m-chloroperbenzoic acid followed by $HClO_4$. The disulfide ring system can also be obtained by the nucleophilic attack of sodium disulfide on diacetylene.[53]

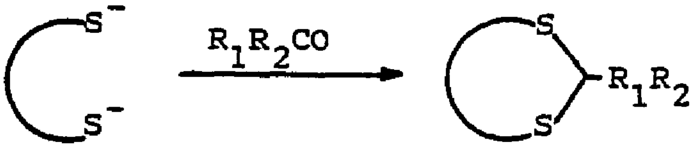
B. 1,3-dithia ring system

1.



R=H, OCH_3, Alkyl, Aryl
X=Halogen

2.

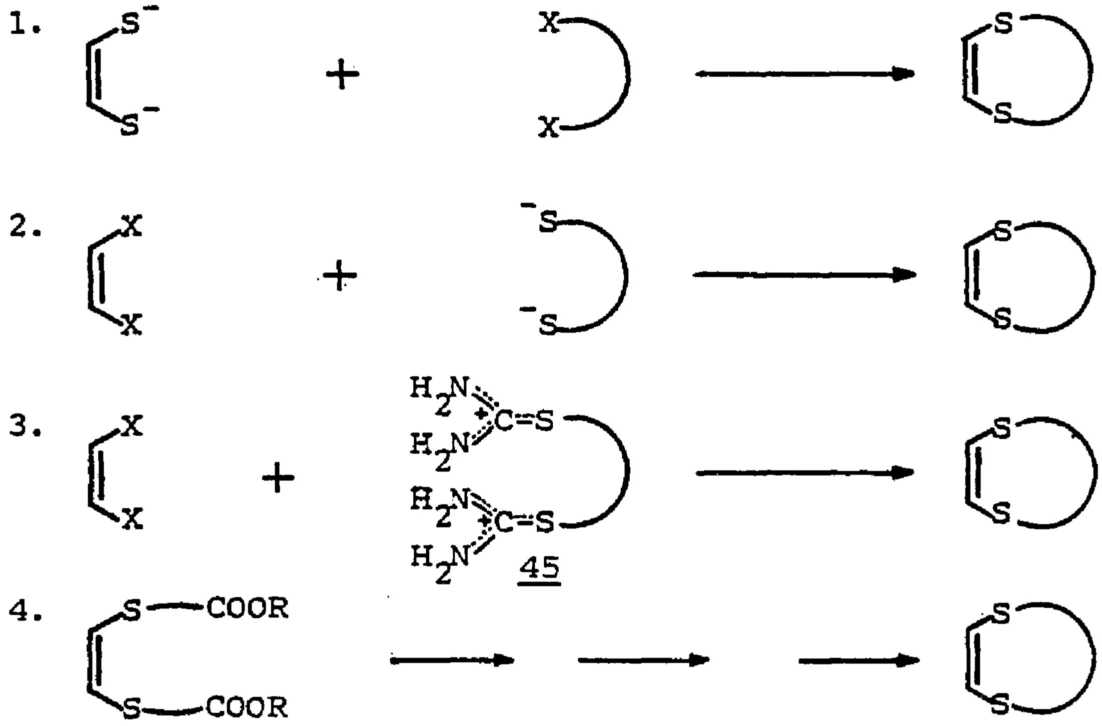


R_1;R_2= H or Alkyl

Stadler[54] utilized the bis nucleophilic attack of bis thiolate anion on dihalo or carbonyl compounds to give the 1,3-dithia ring system.

C. 1,4-dithia ring system

Schroth[55] utilized the bis nucleophilic attack of bis thiolate anion on dihalo compounds to give the 1,4-dithia ring system. The 1,4-dithia system can be obtained also by the reaction of thiolate anion or 45 with dihaloethylene via the "elimination-addition" mechanism,[56] and by a Dieckmann condensation followed by decarboxylation.[57]



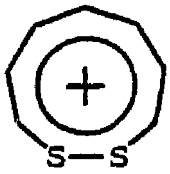
All the cyclization process shown above should be performed under conditions of high dilution, particularly in the synthesis of the medium ring systems, in order to reduce the yield of intermolecular addition and prevent polymer formation.[58] Once the ring systems are constructed, the molecules may then be functionalized and subjected to suitable reactions to generate the potentially aromatic systems.

The following chapters will describe the syntheses and characterization of the target sulfur compounds I-V.

RESULTS AND DISCUSSION

I. 1,3-DITHIACYCLONONATRIENE CATION I

The 10 π-electron homologues of thiapyrilium cation 6, 1,2-dithiolium cation 7 and 1,3-dithiolium cation 8 are 46, I and 47. None of them was known. The synthetic target of this thesis was cation I.



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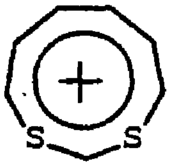
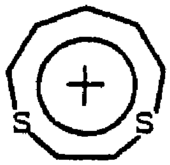


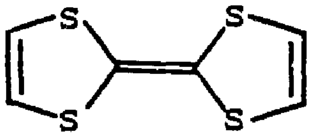
I



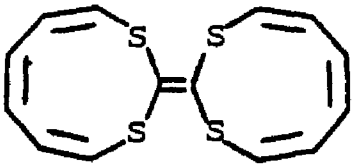
47

Our interest making I was also stimulated by the discovery that the charge-transfer salt of tetrathiafulvalene-tetracyanoquinodimethane(TTF-TCNQ) exhibits high electrical conductivity.[59]

48 TCNQ



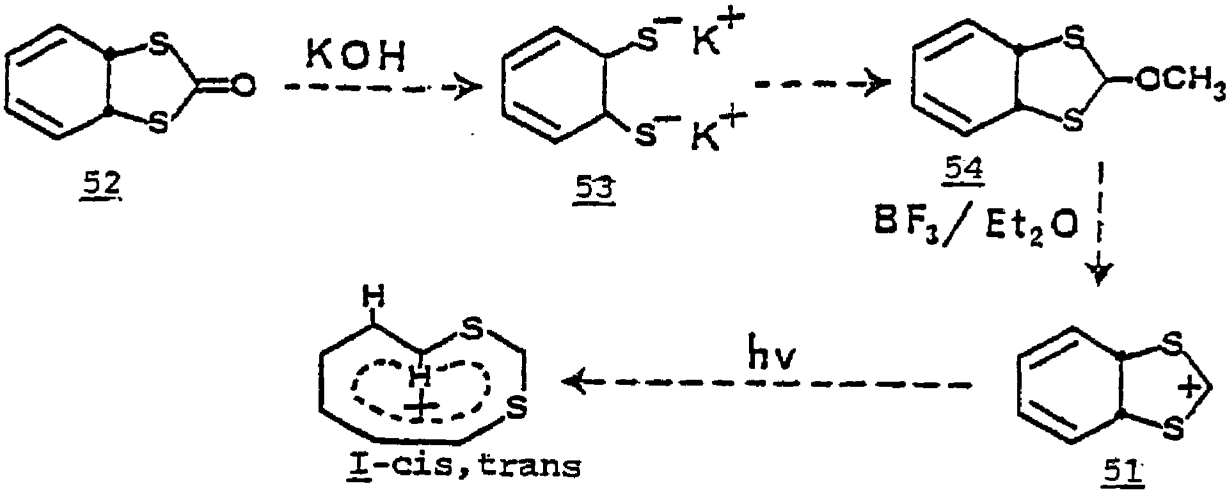
49 TTF



50

Therefore, the tetrathiafulvalene 50, prepared in a similar manner as 49, could be used as the electron donor of an organic metal when complexed with the electron acceptor, TCNQ.

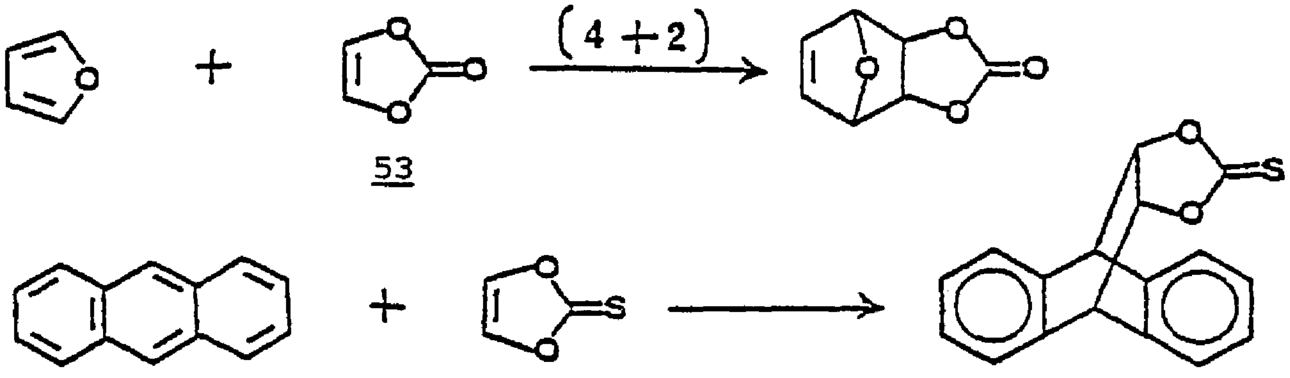
The approach taken below involves the synthesis of bicyclic precursor 51 followed by a photoinduced electrocyclic ring opening to give the cation I.



The aromatic character of I was expected to be detected by proton NMR: the proton inside the ring should exhibit a very highfield chemical shift from those protons outside the ring. The key intermediate, the dithiacarbonate 52, could possibly be obtained by any one of four routes shown on the next few pages. Compound 53 could then be obtained by treatment of 52 with potassium hydroxide. Cycloalkylation of 53 with α,α'-dichloromethylmethyl ether, hydrolysis of 54 with boron trifluoride in ether and finally photolysis of 51 should give mono-trans-1,3-dithiacyclononatriene cation I. The four attempted syntheses of the key intermediate 52 are illustrated below.

A) Via Diels-Alder reaction

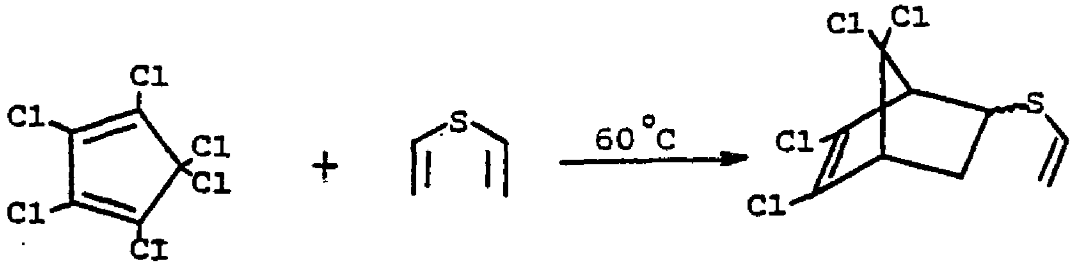
It is known that Diels-Alder reactions of the oxygen analogues 53 and 54 of 55 and 56, respectively, work well to give 1:1 products[60] as shown below.



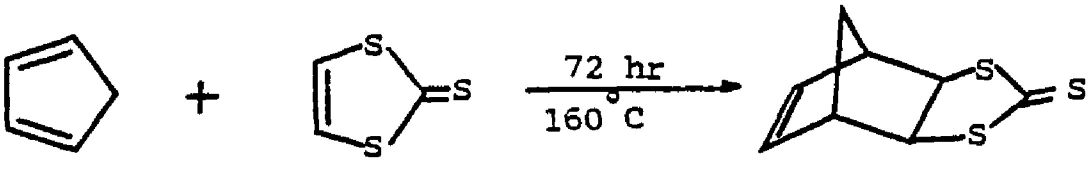
53

54

Also, hexachlorocyclopentadiene and divinyl sulfide in the presence of hydroquinone at 60°C have been reported to give the 1:1 Diels-Alder product.[61]

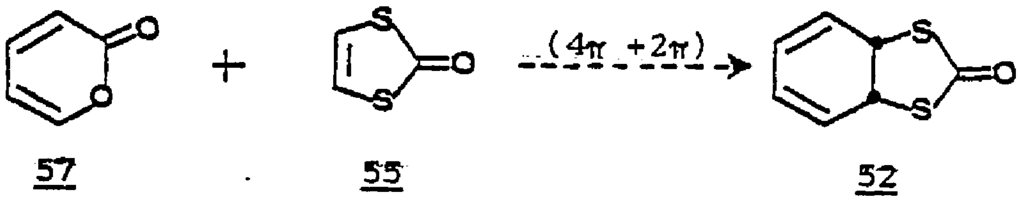


Mayer[62] reported that the Diels-Alder reaction between cyclopentadiene and trithiacarbonate 56 gave only 0.3 % of 1:1 product which was not characterized.

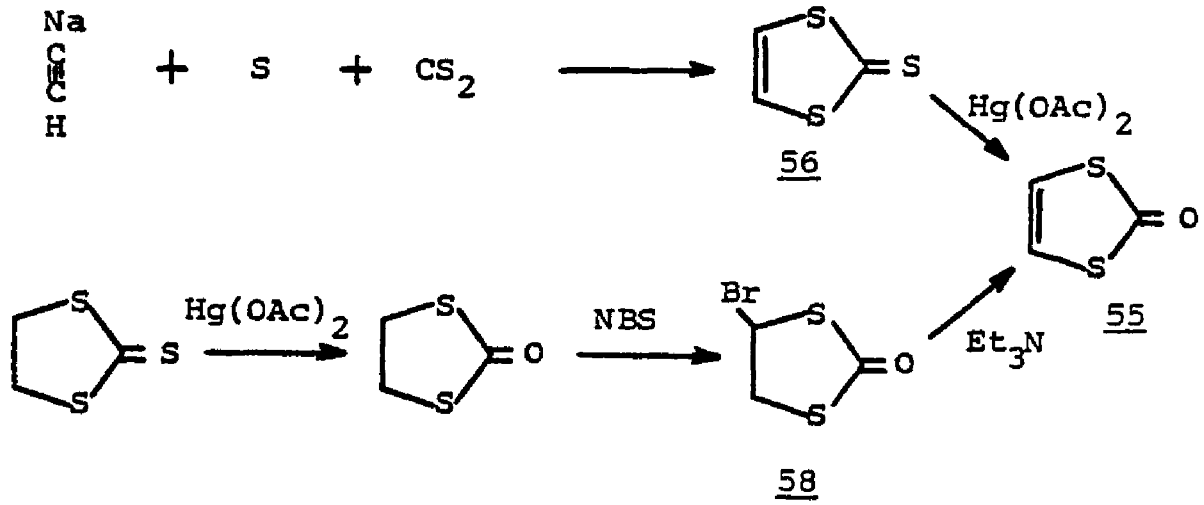


56

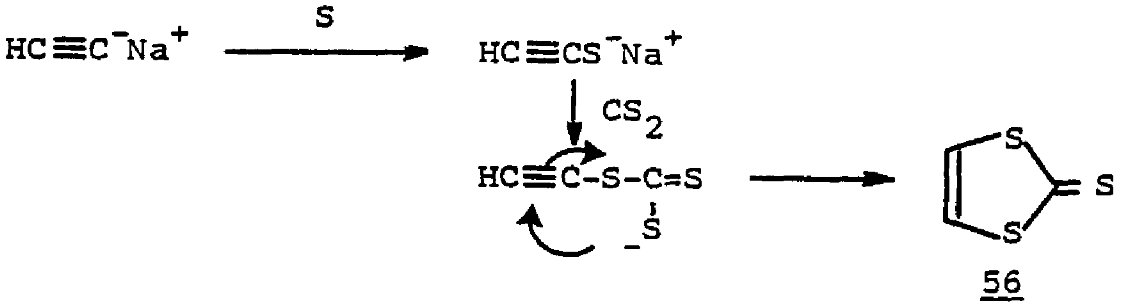
The key intermediate 52 could possibly be obtained by Diels-Alder reaction between α-pyrone 57 and vinylene dithiacarbonate 55. The advantage of using 57 is that the carbon dioxide could be eliminated in the initial Diels-Alder reaction product and yield the diene intermediate 52 in one step.



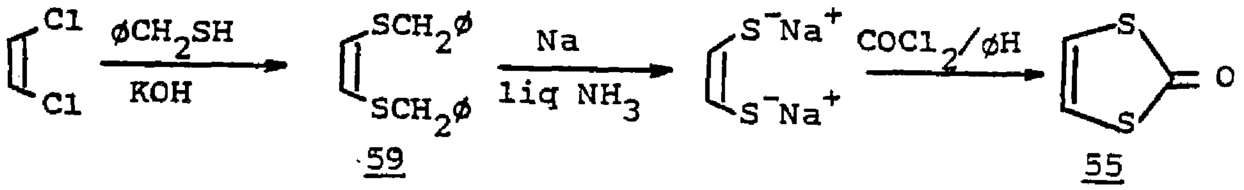
The preparation of the starting vinylene dithiacarbonate 55 is well documented.[63,64,65,66] As reported by Mayer and Gebhardt,[63] 55 results from the reaction between the sodium salt of acetylene, sulfur and carbon disulfide at -30°C followed by $Hg(OAc)_2$ oxidation. Alternatively, 55 may be obtained through dehydrobromination of bromo-S,S'-ethylene dithiacarbonate 58.

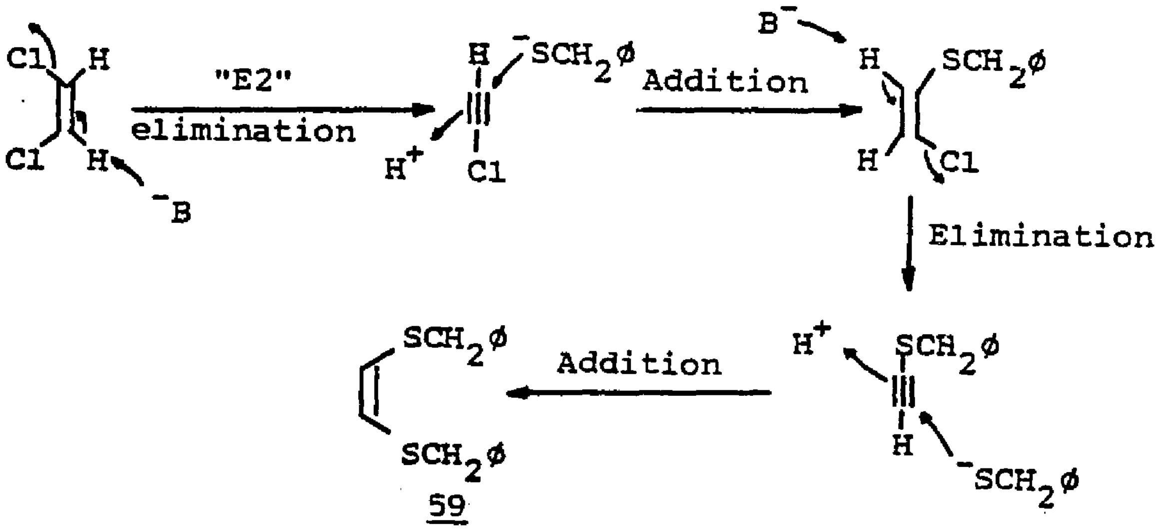


The details of the reaction forming compound 56 are shown below.

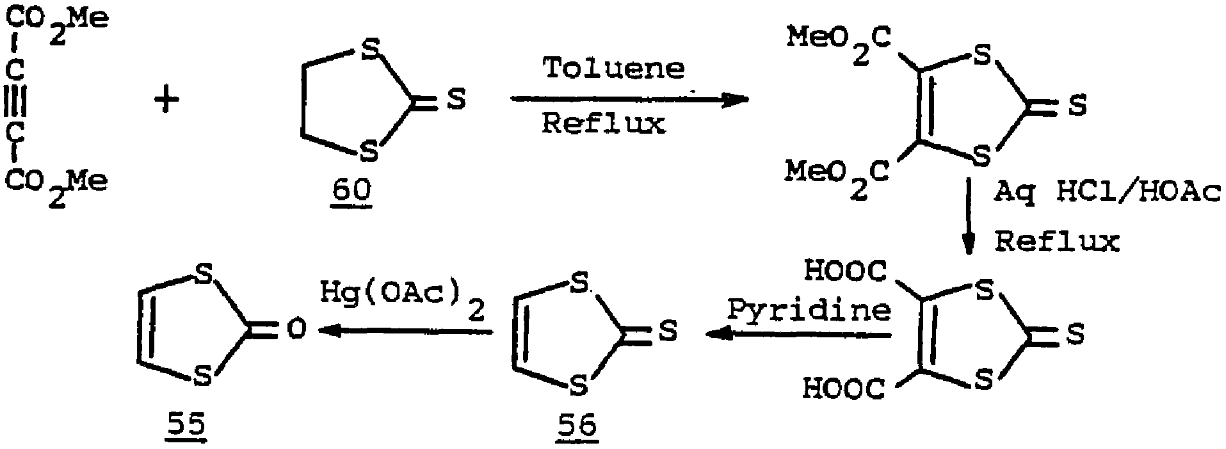


Compound 55 was also prepared [64] by trapping the sodium salt of cis-dibenzylmercaptoethylene 59 with phosgene. The mechanism of the base-catalyzed reaction of cis-dichloroethylene with mercaptans has been shown to proceed via the "elimination-addition" mechanism[65] as shown below.



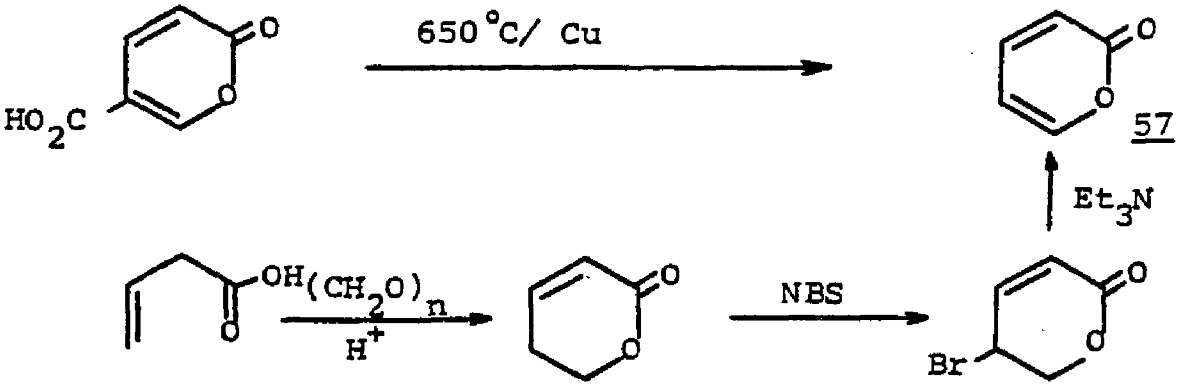


More recently, an improved synthesis of compound 55 has been reported.[66] Reaction of 1,3-dithiolan-2-thione 60 with dimethylacetylenedicarboxylate followed by hydrolysis, decarboxylation and subsequent oxidation by mercuric acetate resulted in vinylene dithiacarbonate 55 in 53 % overall yield.

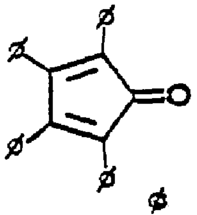


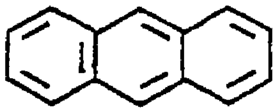
All of the above preparations have been carried out successfully in our laboratory. The best preparation for 55 was utilizing compound 60.

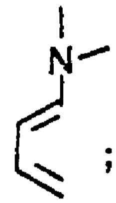
The known preparations[67,68] for α-pyrone 57 are summarized below.



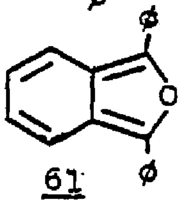
Before the Diels-Alder reaction between 57 and 55 was carried out, several model Diels-Alder reactions on sulfur compounds(used as dienophiles) were tried. The well known excellent dienes tetraphenylcyclopentadienone, furan, cyclopentadiene, anthracene, 1,3-diphenylisobenzofuran 61 and N,N-dimethyl-1,3-butadiene 62 all underwent no Diels-Alder reactions with 55, cis-dibenzyl ethylene dithiaether 59 and dimethyl-2-thioxo-1,3-dithiole-4,5-dicarboxylate 63 in ether, benzene, toluene and even o-dichlorobenzene. In the above cases, the starting materials were recovered.



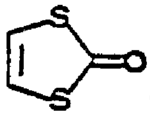




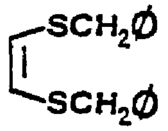
62



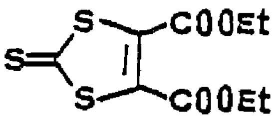
61



55

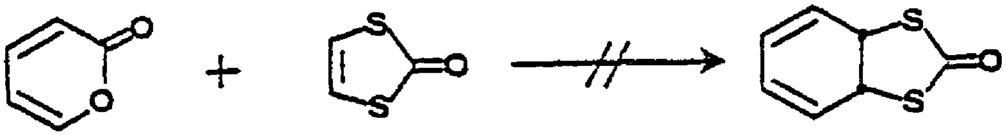


59



63

Finally, the reaction between α-pyrone 57 and vinylene dithiacarbonate 55 was attempted in chlorobenzene for 72 hr, but did not give any of the product 52. When refluxed in o-dichlorobenzene, or even heated up to 220°C without solvent, no Diels-Alder reaction was indicated.

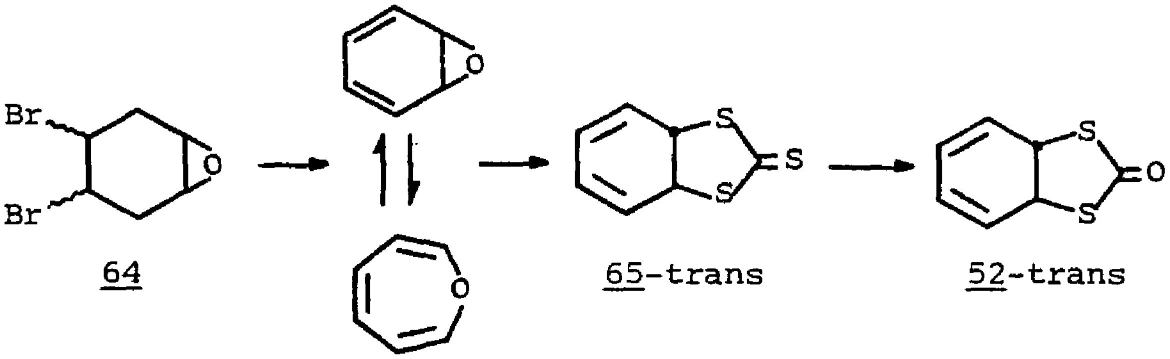


57 55 52

Beacause of the lack of reactivity exhibited above, the synthesis of 1,3-dithiacyclononatriene cation I via the Diels-Alder route was finally abandoned.

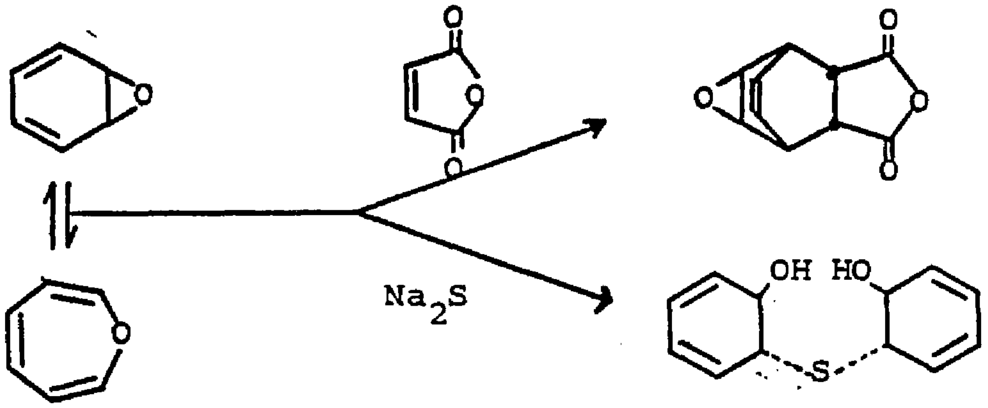
B) Via the oxepin

An alternative route leading to the key intermediate 52-trans is outlined below.

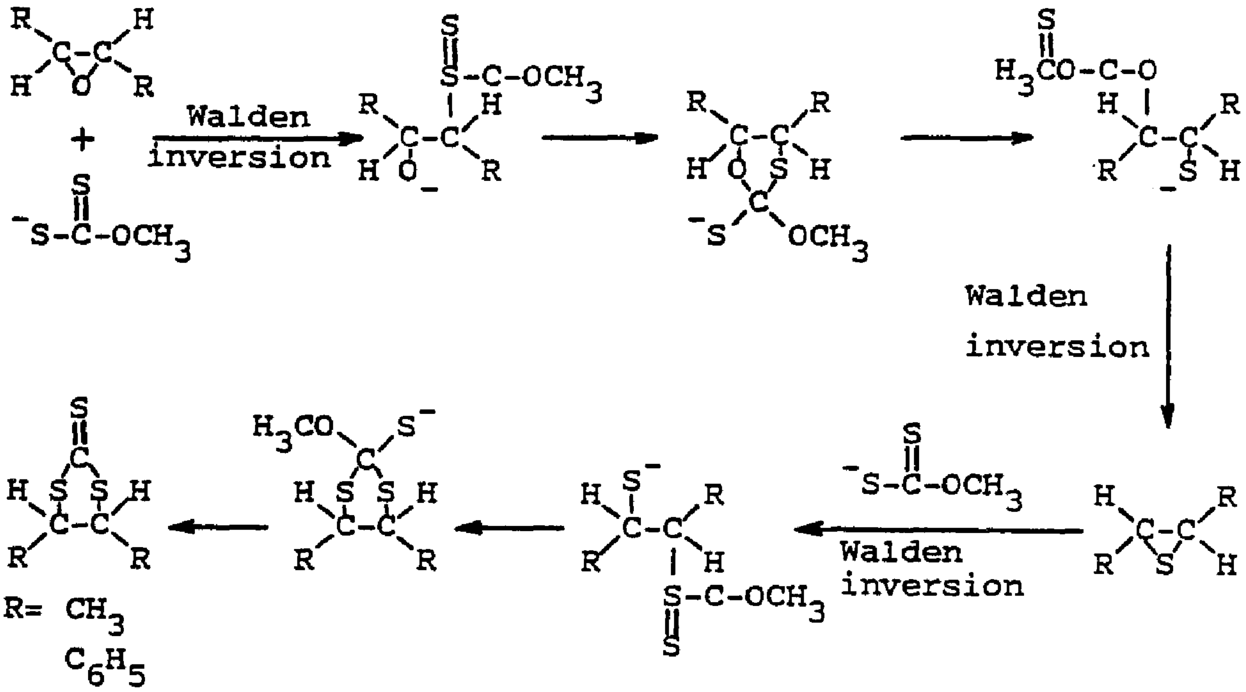


64 65-trans 52-trans

It should be noted that benzene oxide and the potential 8 π-electron system oxepin exist in valence-tautomeric equilibrium. It has been demonstrated that the benzene oxide-oxepin mixture undergoes Diels-Alder reaction at room temperature with maleic anhydride leading to the 1:1 product within a few minutes.[69] Benzene oxide-oxepin also undergoes nucleophilic ring opening[70] with sodium sulfide, although subsequent aromatization occurs in some cases.

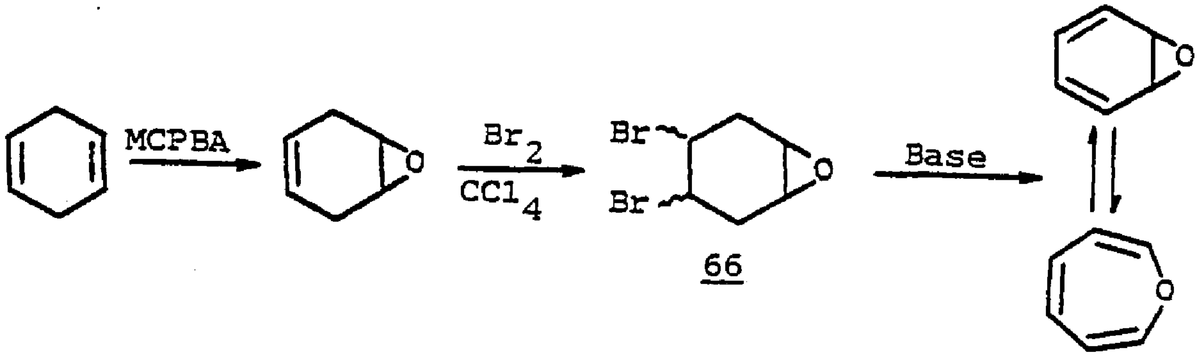


Overberger[71] reported that the reaction of cis- and trans-2,3-epoxybutane or cis and trans-stilbene oxide with potassium xanthate resulted in the formation of the trans and cis cyclic trithiacarbonates, respectively. The conversions are shown below.

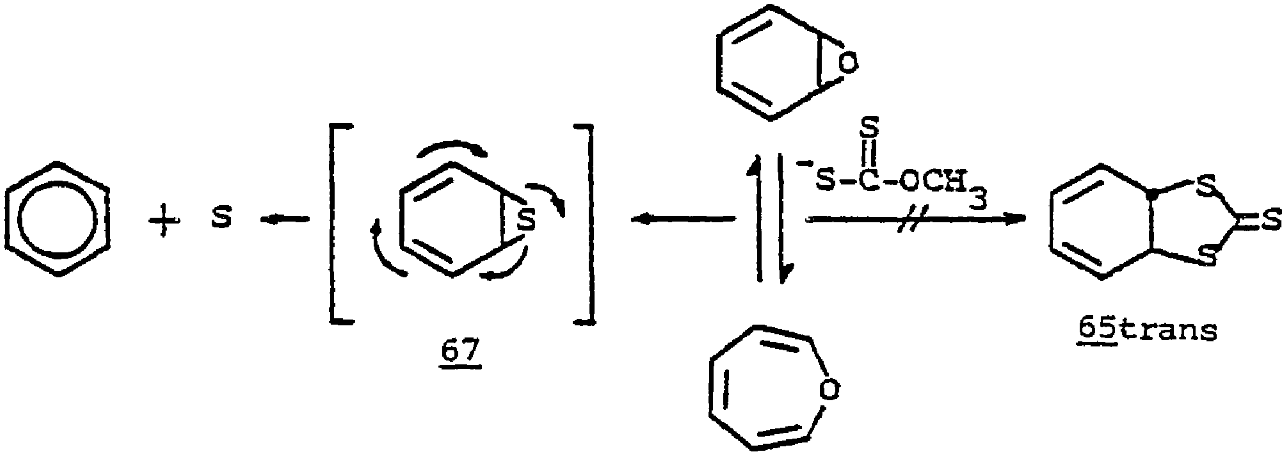


The isomer assignments were based on IR and NMR spectroscopy with the assumption that three Walden inversions occur in going from the cis epoxide to the trans trithiacarbonate, and vice versa. Based on the above evidence, the nucleophilic addition of xanthate to benzene oxide-oxepin mixture should result in the formation of the trithiacarbonate 65-trans.

Vogel[72] reported that the benzene oxide-oxepin mixture can be obtained by the following sequence. Monoepoxidation of 1,4-cyclohexadiene with m-chloroperbenzoic acid followed by reaction with bromine gave 1,2-epoxy-4,5-dibromocyclohexane 66 which was dehydrobrominated by sodium methoxide in boiling ether or by DBN in tetrahydrofuran to give an orange benzene oxide-oxepin mixture.



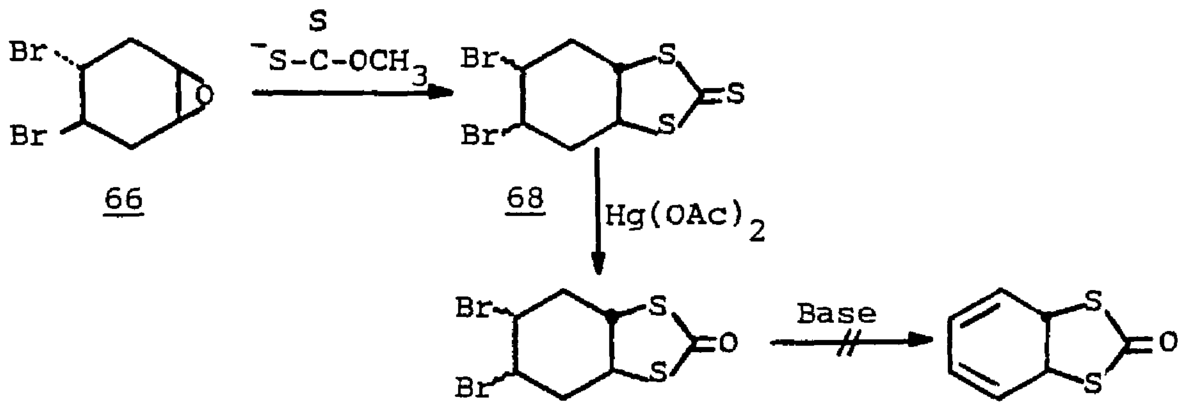
Treatment of the benzene oxide-oxepin mixture with xanthate at room temperature for 2 days did not produce the desired intermediate 65-trans. The failure of this reaction most likely lies in the fact that the extrusion of sulfur from the initial intermediate benzene episulfide 67 is a well known rapid process.[73]



C) Via dehydrobromination

In order to avoid introduction of the benzene episulfide during the construction of the trithiacarbonate skeleton, synthesis of 52-trans by elimination of 2 moles of HBr from the dibromotrithiacarbonate 68 was investigated.

Treatment of 1,2-epoxy-4,5-dibromocyclohexane 66 with xanthate at room temperature for 2 hr affords trithiacarbonate 68 in 80 % yield. This was converted to the corresponding dithiacarbonate 69 by reaction with mercuric acetate. The dibromide 69 was expected to undergo dehydrobromination to give the key intermediate 52. However, treatment of 69 with potassium t-butoxide in tetrahydrofuran, DBN in THF, or with a mixture of lithium chloride and lithium carbonate in HMPA at 85-90°C [74] yielded only monoene rather than diene 52. The complete identification of the monoene was not attempted.



66

68

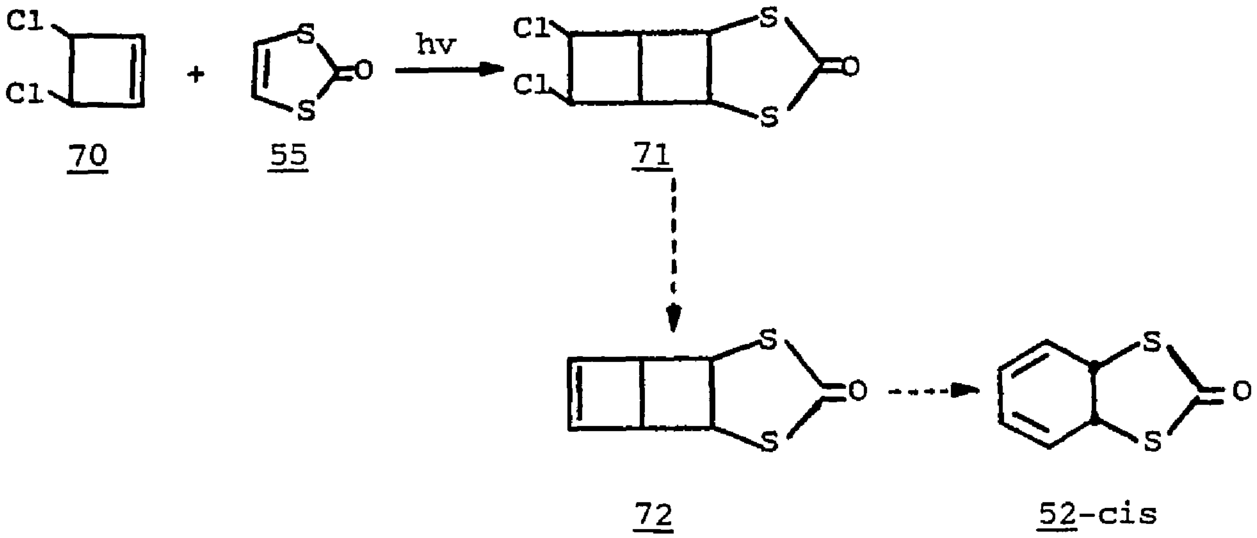
69-trans

52-trans

The failure of this reaction could be attributed to the absence of hydrogens trans-coplanar to bromine since the two C-S bonds in the five-membered ring are constrained to be equatorial.

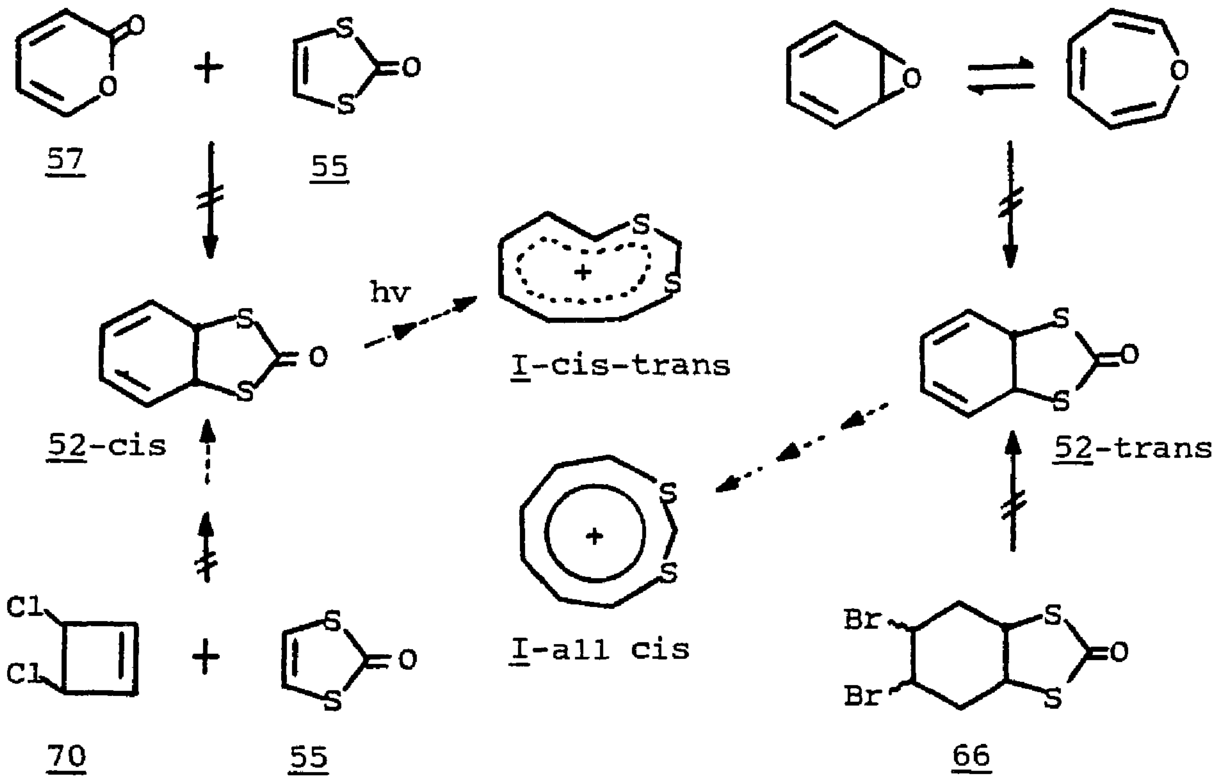
D) Via [2π+2π] photolysis product

The preceeding three routes failed to generate the key intermediate 52. Considering the structure of 52, the formation of the 6-membered ring diene function could result from ring opening of a cyclobutane in compound 72. The dichloro compound 71, the precursor of 72, could be obtained by the (2π+2π)photolysis of cis-3,4-dichlorocyclobutene 70[75] with vinylene dithiacarbonate 55.



Unexpectedly, when photolysis was carried out at 0 °C for 10 hr with a Hanovia-W mercury lamp none of the desired adduct 71 was obtained. Most of 70 and 55 were recovered.

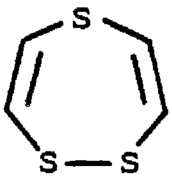
The attempted synthesis of the precursor cis and trans-52 via four routes are summarized on next page.



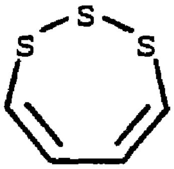
beacuse of our inability to obtain key intermediate 55 further pursuit to I had to be abandoned.

II. 1,2,5-TRITHIEPIN(1,2,5-TRITHIA-3,6-CYCLOHEPTADIENE) II

The second target during this thesis was 1,2,5-trithiepin II. Two possible thiepins 1,2,5-trithiepin II and 1,2,3-trithiepin II' derived from cyclodecapentaene are potentially aromatic.

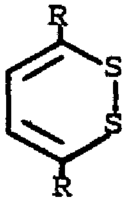


II



II'

Zahradnik[76] predicted on the basis of extended HMO calculation that compound II might be prepared, but probably not compound II'. Except for the 8 π-electron system 1,2-dithiins 73,[77] the deep red, highly reactive molecule considered as 1,2-dithia analogue of cyclooctatetraene, no cyclic conjugated α,β-unsaturated disulfides have been reported.

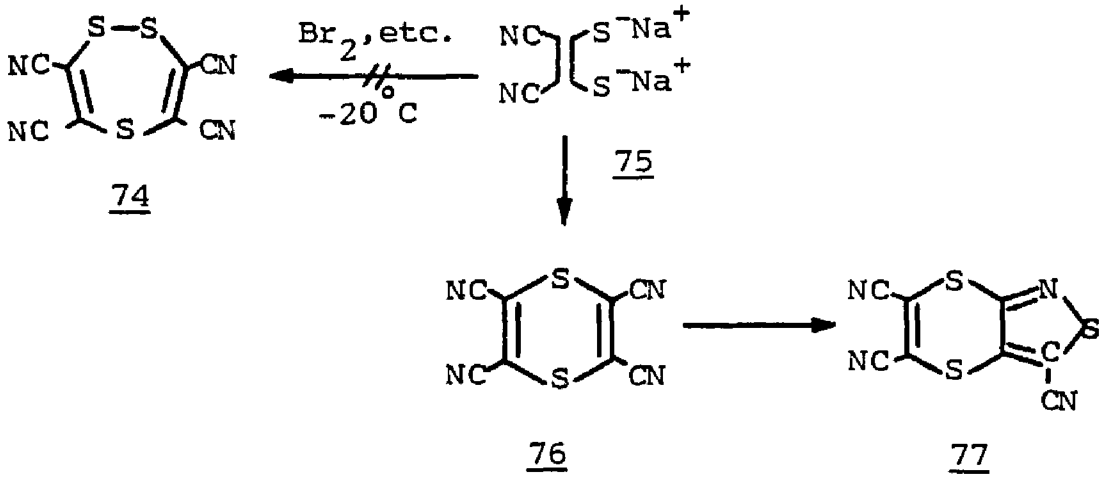


R: H, C_6H_5, p-CH_3-C_6H_4, p-CH_3O-C_6H_4, 2-Thienyl

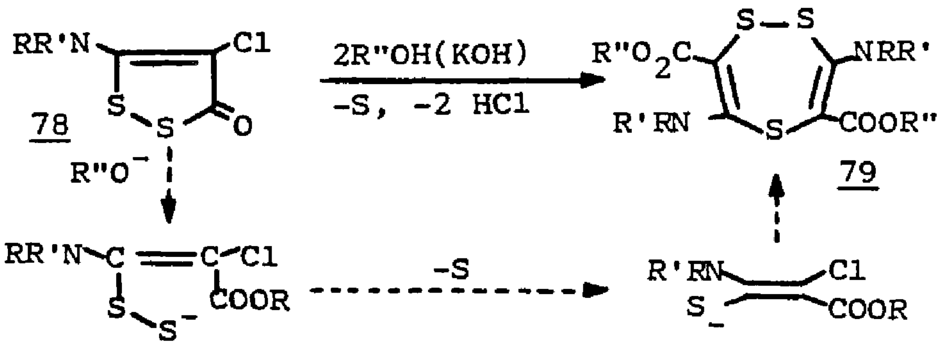
73

Because of the known reactivity of the S-S bond towards nucleophilic attack the synthetic scheme chosen for compound II must be as mild as possible and not involve nucleophilic conditions.

A monocyclic trithiepin, 1,2,5-trithiepin-3,4,6,7-tetracarbonitrile 74, was claimed as a product from the oxidation of disodium dimercaptomaleonitrile 75.[78] Simmons and coworkers,[79] after a thorough study of the oxidation product by IR, UV and ^{13}C-NMR spectroscopy concluded that it was really the isothiazole 77 formed through intermediate 76. The compound was also identical to authentic isothiazole 77 prepared via an independent route.

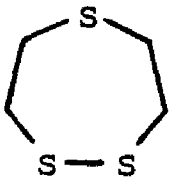


Boberg[80] reported that alkaline cleavage of the dithia compound 78 at 55°C gave 1,2,5-trithiepin 79. He explained the conversion of 78 to 79 in terms of the three-step mechanism shown below.

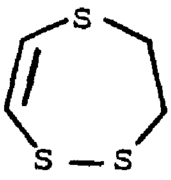


R= Aryl; R'= Alkyl; R"= CH_3 or C_2H_5

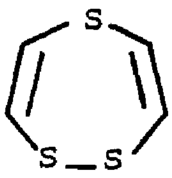
No synthesis of the parent compound, 1,2,5-trithiepin II, has yet been described. The key feature of the synthesis projected involves the construction of the saturated 7-membered ring, 1,2,5-trithiepane 81, followed by successive introduction of the two double bonds. The route also has the important advantage that one intermediate in this sequence is 6,7-dihydro-1,2,5-trithiepin 83, a molecule closely related to the 1,2,5-trithiepin II, but lacking the expected 10 π-electron conjugation. This provides an ideal reference model for spectral comparison.



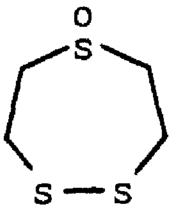
81



83



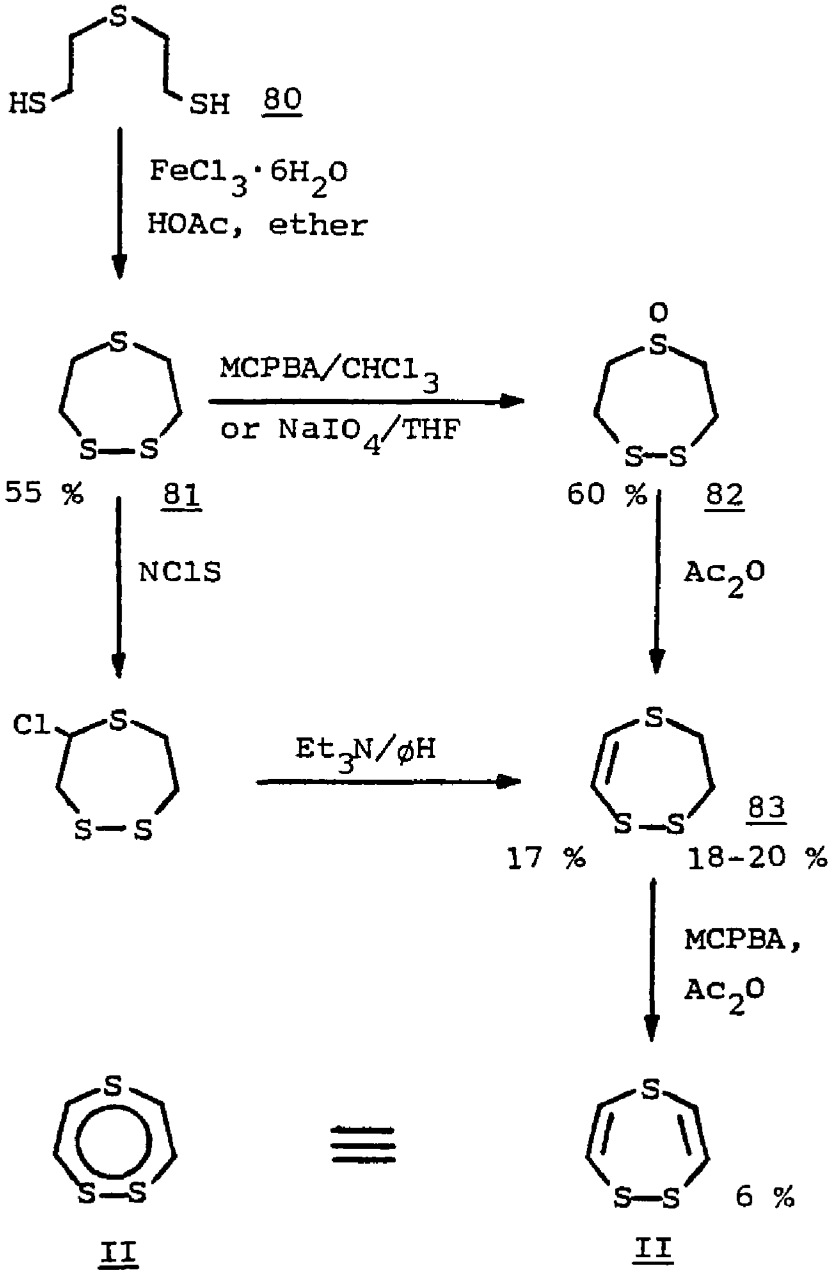
II



82

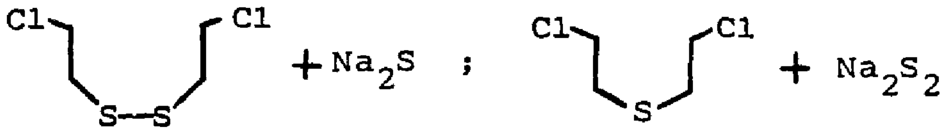
The introduction of the double bonds in 1,2,5-trithiepane 81 was carried out either by a Pummerer reaction[81] on 1,2,5-trithiepane-5-oxide 82 or by chlorination [82] of 81 with N-chlorosuccinimide followed by dehydrochlorination.

The sequence for the synthesizing compound II is shown next page.

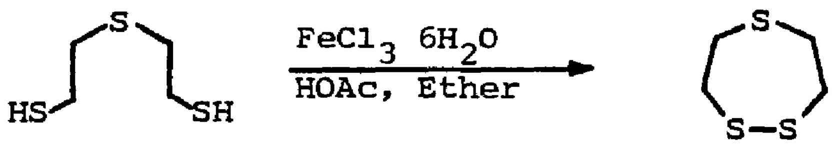

HS
SH
80
FeCl3·6H2O
HOAc, ether
55 %
81
MCPBA/CHCl3
or NaIO4/THF
O
60 %
82
NClS
Ac2O
Cl
Et3N/øH
17 %
83
18-20 %
MCPBA,
Ac2O
6 %
II
II

A) Preparation of 1,2,5-trithiepin 81

The starting material for synthesizing 1,2,5-trithiepin II is the known 1,2,5-trithiepane 81 which has been the subject of much controversy. In the first report, Ray[83] claimed that a solid byproduct(mp 96°C) of the reaction of dithioethylene glycol with benzylidene chloride was 81. Later, Fromm[84] obtained a solid product(mp 74-75°C) from either the reaction of bis(2-chloroethyl)disulfide with Na_2S or bis(2-chloroethyl)sulfide with sodium disulfide, which was considered to be 1,2,5-trithiepane 81.



Later, Westlake[85] suggested that a colored liquid, n^{20}D 1.5746, a product from ethylene and sulfur, might be 81. Finally, Field,[51] in 1970, claimed that the colorless liquid obtained from the oxidation of bis(2-mercaptoethyl)sulfide 80 with ferric chloride in acetic acid, was 81, based on IR, UV and mass spectrum. Field's method afforded 81 in

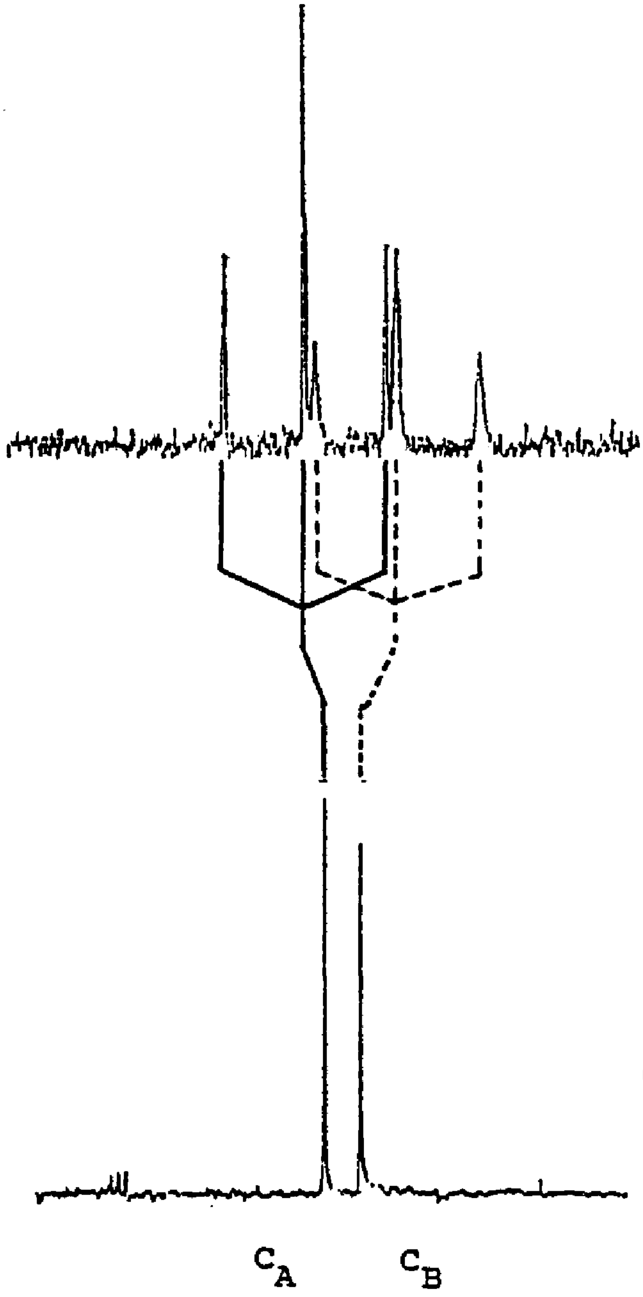


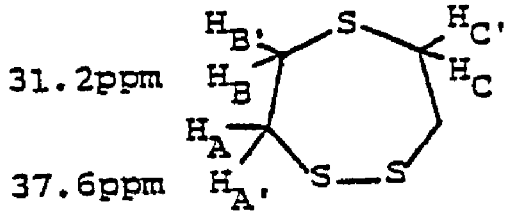
80

81

55 % yield, and consequently constituted our route of choice for the synthesis of 81, providing the structure was correct.

Since the proton NMR spectrum of 81 at room temperature surprisingly showed only a sharp singlet in carbon tetrachloride at δ3.1, in benzene at δ2.7, and in deuteriochloroform at δ3.05, further identification of compound 104 by ^{13}C NMR spectroscopy was necessary. The proton decoupled ^{13}C NMR spectrum of 81 shows two peaks at 37.6 and 31.2 ppm downfield from TMS as expected for the number of peaks and the chemical shifts. The gated decoupled ^{13}C NMR spectrum of 81 was also determined in order to assign the carbons. The lowfield carbon is split into a triplet of triplets with coupling constants of 140 and 2.6 Hz. The highfield carbon is split into a triplet of broad multiplets. The assignments are based upon the assumption [86] that long range coupling decreases with increasing distance. Since carbon A, α to the disulfide linkage, displays no long-range coupling through the S-S bond, the resonance at 37.6 ppm is split into triplets with $J_{C_A-H_A} = J_{C_A-H_{A'}} = 140$ Hz, $J_{C_A-H_B} = J_{C_A-H_{B'}} = 2.6$ Hz. This resonance is thus assigned to be carbon A. The other signal at 31.2 ppm is split into triplets of multiplets because of the three-bond $^{13}C-^{1}H$ long range coupling with H_C and $H_{C'}$ and assigned to carbon B.

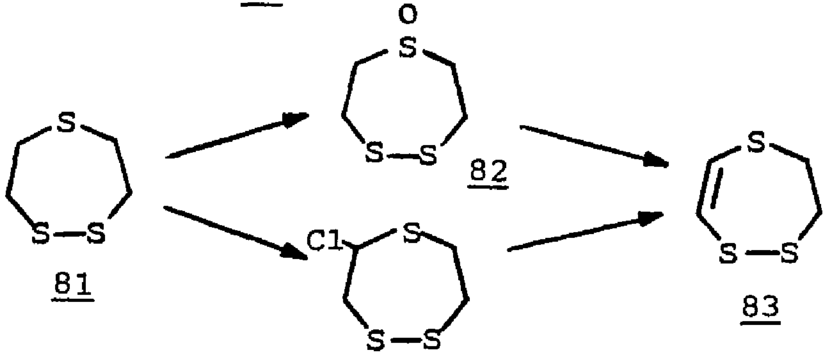




81

B) Preparation of 6,7-dihydro-1,2,5-trithiepin 83

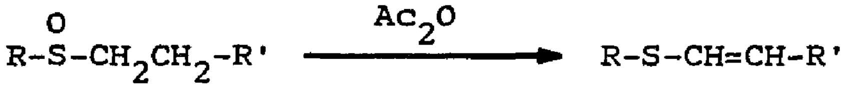
With the saturated 1,2,5-trithiepane 81 in hand the next task involved the introduction of the double bond. This was carried out by two independent routes. First, selective oxidation of the 1,2,5-trithiepane 81 gave the corresponding sulfoxide 82 which was heated in acetic anhydride(Pummerer reaction) to afford compound 83. Alternatively, chlorination of 1,2,5-trithiepane 81 with N-chlorosuccinimide followed by elimination with triethylamine afforded 83.



The details will be discussed below.

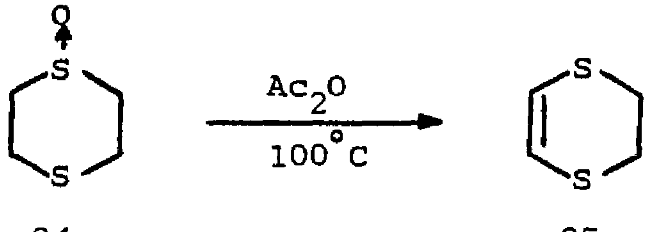
a) Via Pummerer reaction on 82

The decomposition of sulfoxides in hot acetic anhydride, a reaction analogous to that originally reported by Pummerer[87], has been shown to be an attractive route to α,β-unsaturated sulfides.



$$R\text{-}\overset{O}{S}\text{-}CH_2CH_2\text{-}R' \xrightarrow{Ac_2O} R\text{-}S\text{-}CH{=}CH\text{-}R'$$

This reaction has been extended successfully to heterocyclic compounds containing more than one sulfur atom. Parham[88] reported that 1,4-dithiane-1-oxide 84 in acetic anhydride at 100°C was converted to 1,4-dithiene 85 in 53 % yield.

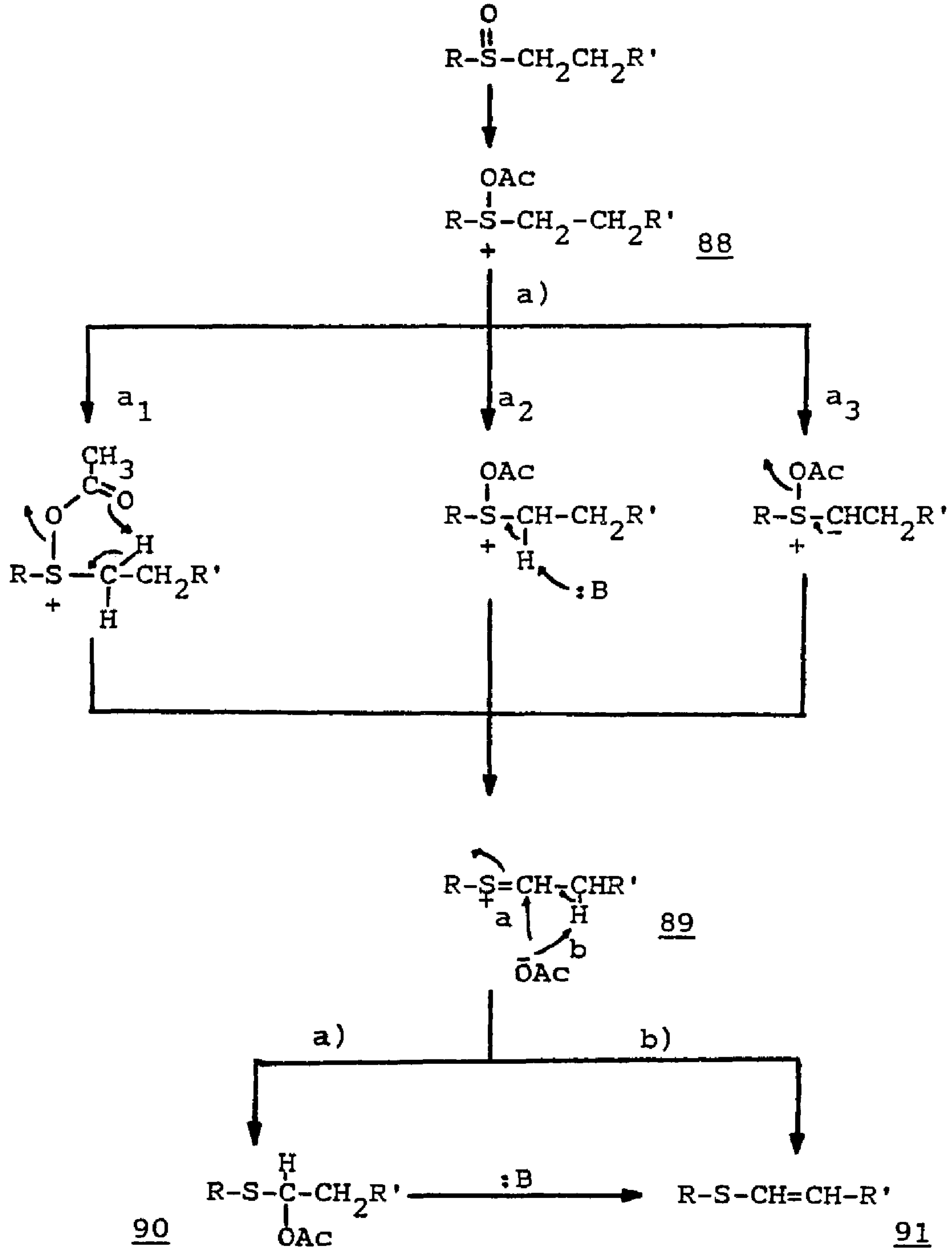


84 85

Later, Schlessinger[89] utilized this method to synthesize thieno-3-thiepin 87 by treatment of the corresponding vinyl monosulfoxide 86 with freshly distilled acetic anhydride at 150°C in the absence of oxygen.

86 87

The Pummerer reaction has been the subject of much mechanistic speculation. Although the detailed mechanism of this reaction is still unknown, it is generally accepted that the first step involves the formation of a sulfonium salt 88. The following mechanism has been postulated:[90,91]



a_1: through cyclic elimination of HOAc

a_2: through elimination of HOAc with external base

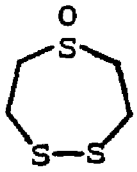
a_3: through ylid intermediate

The formation of the α,β-unsaturated sulfide could take place via either of the following pathways:

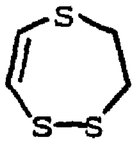
i) a-a pathway; either through the cyclic elimination of HOAc (a_1), or through the elimination of HOAc with external base (a_2), or through the ylid intermediate (a_3), the sulfonium salt 88 would give 89. Nucleophilic attack by acetate would then give the α-acetate 90 which finally upon elimination would give the α,β-unsaturated sulfide 91.

ii) a-b pathway; the intermediate 89 would yield the α,β-unsaturated sulfide 91 by the direct attack of an external base.

One should, therefore, be able to utilize the Pummerer reaction to prepare 6,7-dihydro-1,2,5-trithiepin 83 from the corresponding trithiepane oxide 82.

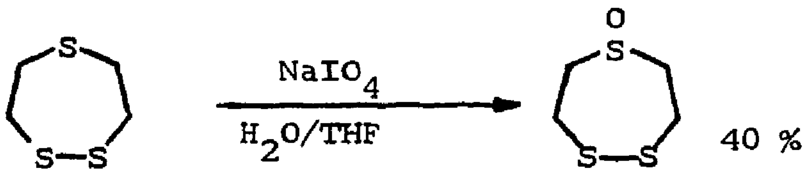


82



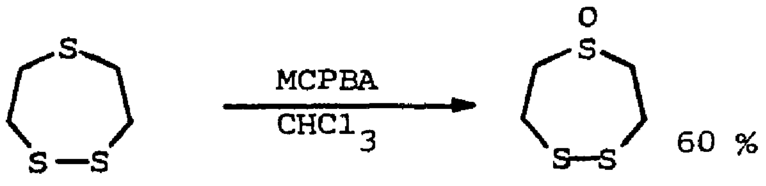
83

Field[51] reported that 81 could be selectively oxidized with sodium metaperiodate at 10°C to give 82 in 40 % yield.



81 82

An efficient way to prepare the same sulfoxide 82 was developed in this work using meta-chloroperbenzoic acid in $CHCl_3$. This process had the additional advantage that the Pummerer reaction may be carried out without isolation of the sulfoxide 82.

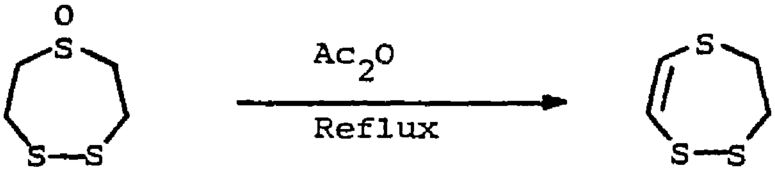


81 82

The infrared spectrum of 82 shows characteristic strong SO absorption at 1025 and 1005 $cm.^{-1}$ The proton NMR($CDCl_3$, TMS) shows two signals at δ2.5-3.4(m,4H, methylene protons α to sulfur) and δ3.4-4.3(m, 4H, methylene protons α to disulfide). The compound is stable for more than 10 months at 5°C.

The sulfoxide 82 was heated to 140°C in freshly distilled acetic anhydride for 35 minutes in the absence of oxygen. The crude product was purified either by column chromatography or distillation to give the dihydrotrithiepin 83 in 18-20 % yield as a pale yellow oil. The preparation of 83 can be simplified if the isolation of sulfoxide 82 is omitted. Both of the above procedures gave almost the same yield(10 %) from the 1,2,5-trithiepane 81.

The reaction conditions were varied in order to optimized the yield. When the reaction was run at a low temperature(110°) for a longer time, a considerable amount of 1,2,5-trithiepane 81 and only 2-3 % of deisred product 83 were obtained. The reaction was also conducted at reflux temperature in the presence of excess sodium acetate, but the yield was no better.



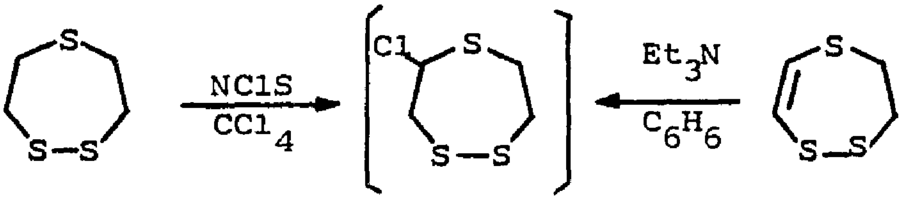
82 83

b) Via Chlorination-Dehydrochlorination

Another approach to the preparation of compound 83 is by construction of a properly substituted trithia 7-membered ring. The substituent could then be eliminated to form the double bond in the ring system.

Wilson[92] reported that treatment of tetrahydrothiophene with N-chlorosuccinimide in carbon tetrachloride afforded α-chlorothiophane in high yield. The nature of the transformation of the intermediate halosulfonium salt to the α-halosulfide is not yet resolved completely. Recent evidence suggests that the reactive species in the N-chlorosuccinimide reaction may be a succinimyl sulfonium salt[93] rather than a chlorosulfonium salt. Although it has been accepted for some time that a sulfonium salt may exist as a reaction intermediate, no firm proof for this species has been reported.

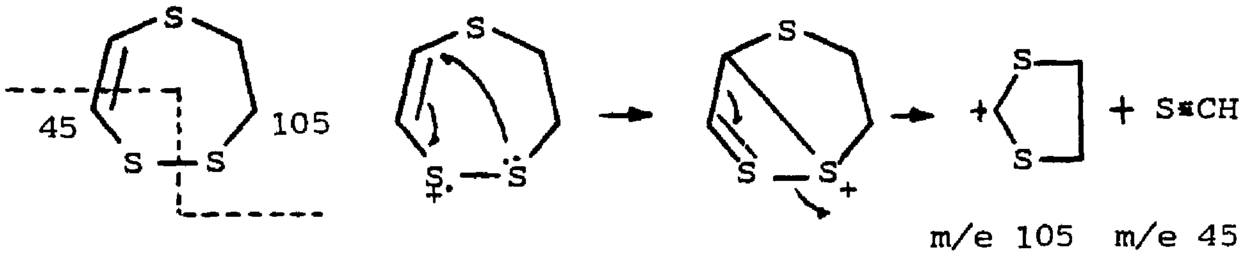
Chlorination of 1,2,5-trithiepane 81 with N-chlorosuccinimide in carbon tetrachloride followed by dehydrochlorination with triethylamine afforded 6,7-dihydro-1,2,5-trithiepin 83 in 17 % yield. The α-chloro compound was not isolated owing to its known sensitivity to moisture.



81 83

The 6,7-dihydro-1,2,5-trithiepin 83 isolated after distillation is a stable pale yellow liquid. The proton NMR($CDCl_3$, TMS) exhibits an AB quartet for the olefinic protons at δ6.17(H_B of AB quartet, 1H, J=9 Hz, cis) and δ5.99(H_A of AB quartet, 1H, J=9 Hz, cis) and two sets of triplets for the methylene protons at δ3.83(t, 2H, $-S-CH_2-$, J=6 Hz), δ3.11(t, 2H, $-S-S-CH_2-$, J=6 Hz). The proton decoupled ^{13}C NMR shows four singlets at 126.6 ppm(carbon α to sulfide linkage), 119.4 ppm(carbon α to the disulfide linkage), 33.0 and 35.7 ppm(methylene carbons) downfield from TMS. The gated decoupled ^{13}C NMR displays a doublet of doublets for C_A and two sets of quartets for C_B. The assignment of H_A, H_B, C_A and C_B is discussed on page 64. The ultraviolet spectrum also shows absorptions at λ_{max} 277 nm(ϵ 2.5×10^3) and 321 nm(ϵ 2.7×10^3). The mass spectrum exhibits an moleculat ion at m/e 150(69.1 %) and a peak at

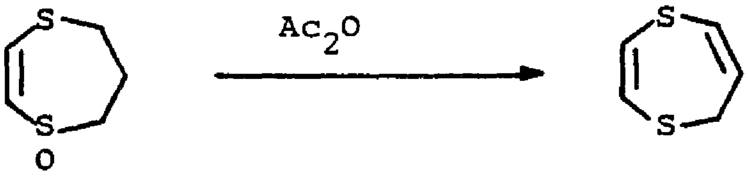
105(100 %). The peak at m/e 105 presumably arises from loss of S≡CH. The overall fragmentation pattern is outlined below.



Compound 83 from both sources was to prepare 1,2,5-trithiepin II.

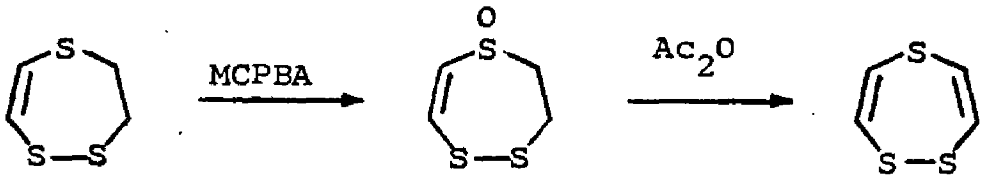
C) Preparation of 1,2,5-trithiepin II

In a manner analogous to the synthesis of dihydrotrithiepin 83, the synthesis of 1,2,5-trithiepin II could be carried out either through the chlorination of dihydrothiepin 83 with N-chlorosuccinimide followed by elimination with base, or through the Pummerer reaction of 94, the monoxide of 83. However, based on model reaction systems, alkylvinyl sulfides are usually chlorinated at the alkene carbon[93] when treated with N-chlorosuccinimide, so the route via N-chlorosuccinimide chlorination followed by base elimination was not seen as favorable. On the other hand, the Pummerer reaction of 92, a monoxide of 1,4-dithiacyclohepta-2-ene, has been used in the preparation of 1,4-dithiin 93.



92 93

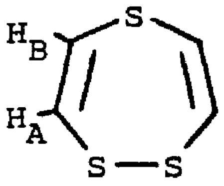
Therefore, the Pummerer reaction of monoxide of dihydrotrithiepin 83 was chosen for the synthesis of 1,2,5-trithiepin II.



83 94 II

The dihydrotrithiepin 83 was first converted into the corresponding sulfoxide 94 by treatment with m-chloroperbenzoic acid. The single sulfoxide oxidation product was shown to be 94 from its proton NMR spectrum and by analogy to the previous oxidation of 81 and the subsequent Pummerer reaction of 82. The sulfoxide 94 in freshly distilled acetic anhydride was then refluxed in the absence of oxygen to afford 1,2,5-trithiepin II. The product was isolated and purified either by column chromatography over silica gel or by preparative thin layer chromatography(silica gel) at 0°C under carbon dioxide. The yield from 83 is only 6 %.

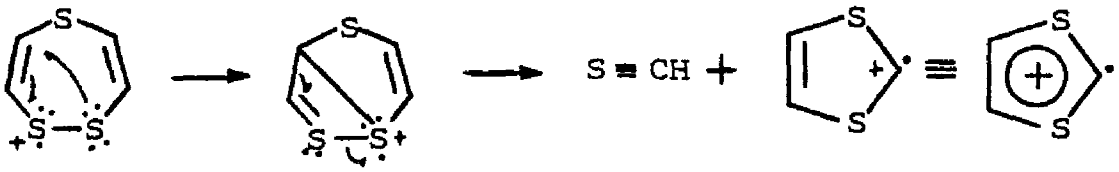
The compound II is stable at 0°C for more than 5 months in solution; at room temperature without solvent it polymerizes easily. Gas chromatography gave no indication of the formation of 1,4-dithiin or thiophene which could have arisen from the decomposition of 1,2,5-trithiepin II.



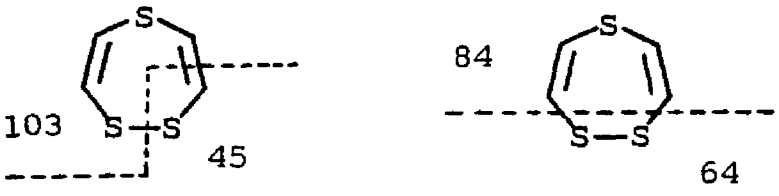
II

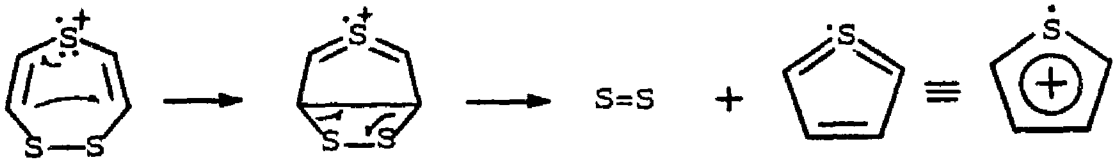
The proton NMR($CDCl_3$,TMS) exhibits an AB quartet for the olefinic protons at δ7.24(2H, H_B, J=9 Hz, cis), and δ6.57(2H, H_A, J=9 Hz). The proton decoupled ^{13}C NMR shows two singlets at 131.4 and 128.6 ppm for C_A and C_B, respectively, relative to TMS. The gated decoupled ^{13}C NMR shows two sets of quartets for the highfield carbon(C_B) and a doublet for the lowfield carbon(C_A). The assignment of H_A, H_B, C_A and C_B is discussed on page 68. The infrared spectrum exhibits no absorptions for saturated C-H stretching and trans [94] double bonds at 925 cm^{-1}. The UV spectrum shows absorption maxima at 263 nm(ϵ2.25x10^3), 296 nm(ϵ1.72 x10^3) and 353 nm(ϵ1.40x10^3). The mass spectrum shows the molecular ion at m/e 148(29.9 %). Fragments arising from loss of S≡CH and two sulfur atoms give rise to peaks at m/e 103 and 84, respectively. The fragmentation patterns are outlined below.

m/e		m/e	
148	29.9 %	84	46 % ( , M^+-2S)
116	51.8 % ( , M^+-S)	64	14.9 % (2S , M^+- )
103	100 % ( , M^+-CHS)	45	86 % (CHS, M^+- )



m/e 45 m/e 103





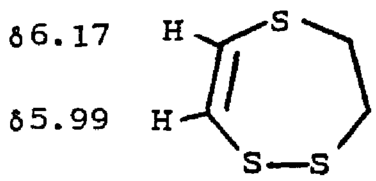
m/e 64 m/e 84

The overall yield from bis-(2-mercaptoethyl)sulfide 80 is only 0.3 %. In order to prepare 1 gram of 1,2,5-trithiepin II, 350 g of bis-(2-mercaptoethyl)sulfide 80, 10 gallons of ether, 2 gallons of glacial acetic acid and 500 g of m-chloroperbenzoic acid were used for the reactions.

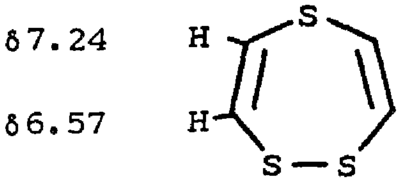
1,2,5-TRITHIEPIN II AS AN AROMATIC MOLECULE

The concept of an aromatic π-electron ring current was first stated by Pople[95] to explain the chemical shifts of the benzene ring protons compared to those in ethylene. Elvidge and Jackman[96] extended this concept to other aromatic systems, and suggested that the magnitude of the ring current could be used as a measure of the aromaticity of the molecules, with general result that protons outside the ring would be deshielded, while those inside would be shielded.

In order to obtain evidence for the ring current in II and hence ascertain the aromaticity of II, one should compare the chemical shifts of II with those of a suitable closely related model compound, the corresponding dihydrothiepin 83.



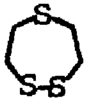
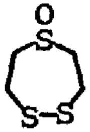
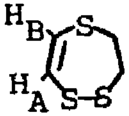
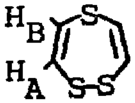
83



II

As pointed out above, the olefinic protons of 83 give rise to an AB quartet at δ6.17 and δ5.99. The corresponding signals of II lie at δ7.24 and δ6.57. But in order to compare the observed chemical shifts accurately, it becomes necessary to assign the signals to specific protons in each compound. This could not be based on the proton NMR spectra alone. Rather, it was necessary to use the ^{13}C NMR spectra and ^{13}C-^{1}H coupling constants of 83 and II. The proton and ^{13}C NMR data are summarized in table 5.

Table 5   Proton and ^{13}C NMR spectra for 1,2,5-trithiepin II and related compounds

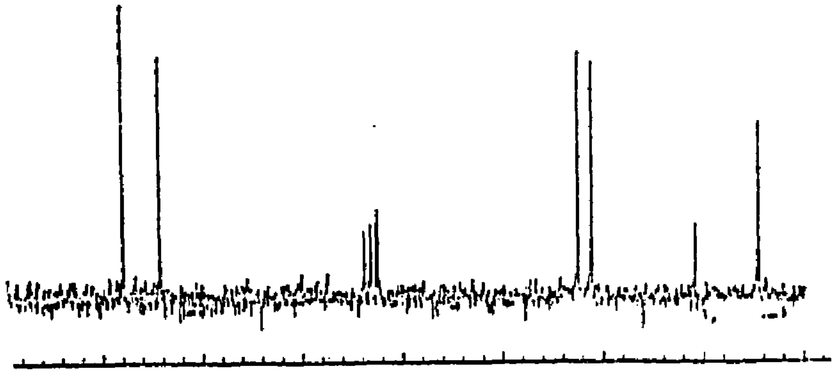
	^{1}H NMR (δ,CDCl$_3$,TMS)	^{13}C NMR (ppm,CDCl$_3$,TMS)	Coupling constants from gated decoupled ^{13}C NMR spectra	
 81	δ3.05(s)	C_B:31.2	C_B:t of m	140.0 and 2.6 Hz
		C_A:37.6	C_A:t of m	
 82	δ2.5-3.4(m)			
	δ3.4-4.3(m)			
 83	H_B δ6.17(AB q)	C_B: 126.6	C_B:2 sets of q	171.0 and 5.8 Hz
	H_A δ5.99(AB q)	C_A: 119.4	C_A: d of d	176.3 and 3.65 Hz
	Methylene δ3.83(t)	35.7		
	protons δ3.11(t)	33.0		
 II	H_B δ7.24(AB q)	C_B: 128.6	C_B:2 sets of q	170.4,10.3& 6.9Hz
	H_A δ6.57(AB q)	C_A: 131.4	C_A:d	179.7 Hz
 96	Olefinic δ5.95	114.3(Olefinic)		
	proton	26.3(Methylene)		
 96'	δ5.99	120.6		

A) Signal assignment for 6,7-dihydro-1,2,5-trithiepin 83

Assignment of carbon signals

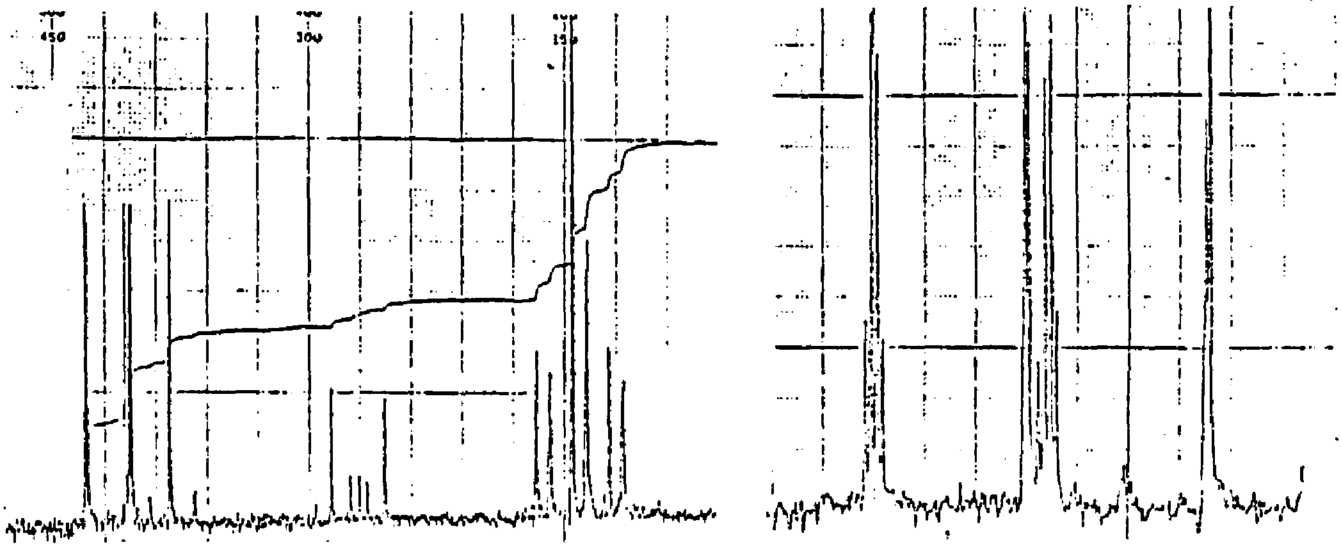
One-bond and long-range $^{13}C-^{1}H$ coupling constants can be obtained from "high-resolution" ^{13}C NMR spectra, and $^{13}C-^{1}H$ coupling constants can be obtained as well from ^{13}C satellites in the proton NMR spectrum. Once the ^{13}C chemical shift and $^{13}C-^{1}H$ coupling constants of dihydrotrithiepin 83 are obtained from the ^{13}C NMR spectra, one should be able to assign the proton chemical shifts of 83 by comparison of the $^{13}C-^{1}H$ coupling constant obtained from the ^{13}C spectrum to those obtained from ^{13}C satellites in the proton NMR spectra.

The proton decoupled ^{13}C NMR spectra of dihydrotrithiepin 83 show resonances at 126.6 and 119.1 ppm for the olefinic carbons and 33.0 and 35.8 ppm for the methylene carbons(TMS as reference).



^{1}H decoupled ^{13}C NMR spectrum of 83

Fig. 1

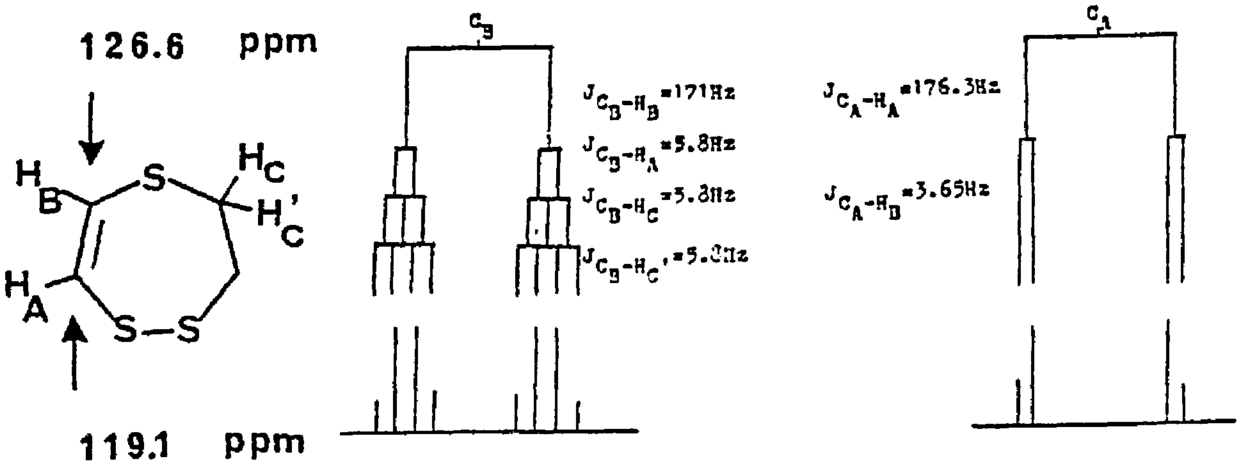


Gated decoupling ^{13}C NMR spectrum Dihydrothiepin <u>83</u>

Expanded spectrum of olefinic region

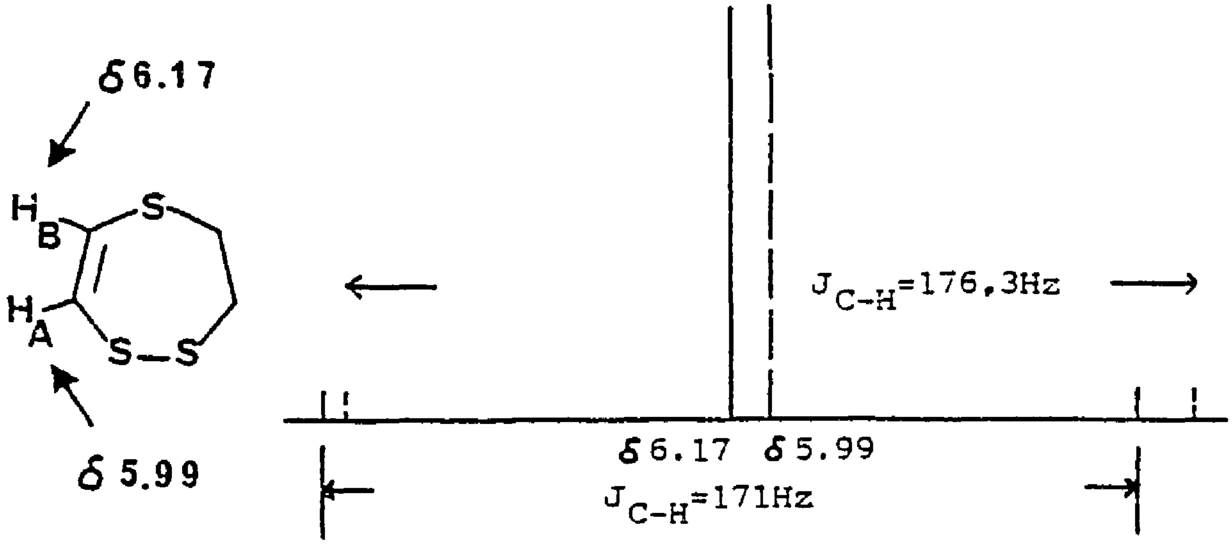
The gated decoupled ^{13}C NMR spectrum shows doublets of doublets for the highfield carbon and two sets of quartets for the low field carbon(Fig. 1). From Fig. 2, it is seen that the carbon α to the disulfide linkage(C_A) should couple only with protons A and B, while the carbon α to the sulfide linkage(C_B) may couple not only with H_B and H_A but also with H_C and $H_{C'}$ through three-bond $^{13}C-^{1}H$ long-range coupling. From the gated decoupled ^{13}C NMR spectrum, the resonance at 119.1 ppm is split into a doublets of doublets with $J_{C_A-H_A} =$ 176.3 Hz, $J_{C_A-H_B} =$ 3.65 Hz. This carbon is thus assigned to C_A(α to disulfide linkage). The other carbon at 126.6 ppm, split into two sets of quartets with $J_{C_B-H_B} =$ 171 Hz, $J_{C_B-H_A} = J_{C_B-H_C} = J_{C_B-H_{C'}} =$ 5.8 Hz is assigned to be C_B(α to sulfide linkage).

Fig. 2



Assignment of proton signals

The gated decoupled ^{13}C NMR was used to determine that $J_{C_A-H_A}$ = 176.3 Hz and $J_{C_B-H_B}$ = 171 Hz. These data, used in conjunction with $^{13}C-^{1}H$ coupling constants obtained from ^{13}C satellites in the proton NMR should be sufficient to assign the chemical shifts of H_A and H_B. The 220 MHz proton NMR spectrum shows for the downfield proton at δ6.17 a set of ^{13}C satellite peaks with J_{C-H}= 171 Hz which is the same $^{13}C-^{1}H$ coupling constant found from ^{13}C NMR. Therefore, the downfield proton at δ6.17 is assigned to be H_B(α to sulfide linkage).



^{13}C-^{1}H satellites in ^{1}H-NMR spectrum of dihydrothiepin <u>83</u>

The high field proton at δ5.99 has ^{13}C satellite peaks with J= 176.3 Hz which is the same ^{13}C-^{1}H coupling constant found from ^{13}C NMR spectrum. Therefore, the high field proton at δ5.99 is assigned to be H_A(α to the disulfide linkage).

B) Signal assignment for 1,2,5-trithiepin II

In a similar manner to 6,7-dihydrotrithiepin 83, the signals for 1,2,5-trithiepin II may be assigned by examining the proton decoupled ^{13}C NMR spectrum, the gated decoupled ^{13}C NMR spectrum and the ^{13}C satellite ^{1}H NMR.

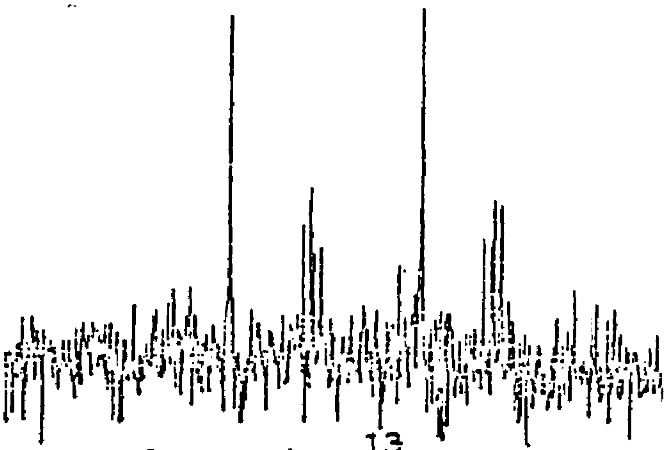
However, the ^{1}H chemical shifts of H_A and H_B in II are about 40 Hz apart at 60 MHz, so partial proton decoupling of the ^{13}C NMR spectrum might be expected to give the required chemical shifts. In a partially proton decoupled ^{13}C NMR spectrum, the coupling pattern and residual ^{13}C-^{1}H coupling constants should change depending upon the value of the decoupling frequency. Irradiation of the protons at higher field will decouple the upfield protons more extensively than the downfield protons, and vice versa. By inspection of the changes in the ^{13}C-^{1}H coupling constants, one should be able to distinguish both sets of protons. The convenience of this method led us to choose it for the proton assignment of 1,2,5-trithiepin II.

Assignment of carbon signals

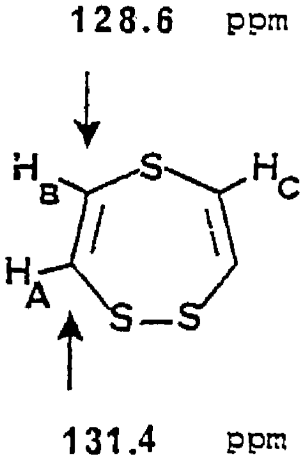
The proton decoupled ^{13}C NMR spectrum of II shows resonances at 128.6 and 131.5 ppm(TMS as reference). The gated decoupled ^{13}C NMR spectra show two sets of quartets for the high field carbon at 128.6 ppm and a doublet for the low field carbon at 131.4 ppm. The experimental spectrum may be compared with the expectations based on structure II

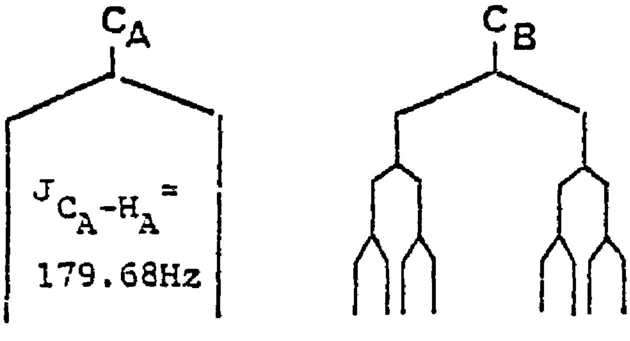
(Fig. 3). If $J_{C_A\text{-}H_B}$ is very small,* then carbon A couples only with H_A, while carbon B(α to the sulfide linkage) not only couples with H_B and H_A but also with H_C through the three-bond $^{13}C\text{-}^{1}H$ long-range coupling. Therefore, in the gated decoupled ^{13}C NMR spectrum, the resonance at 131.4 ppm($J_{C_A\text{-}H_A}$ = 179.7 Hz) is assigned to be C_A(α to the disulfide linkage), and the resonance at 128.6 ppm Hz, $J_{C_B\text{-}H_B}$ = 170.4 Hz, $J_{C_B\text{-}H_A}$ = 10.3 Hz and $J_{C_B\text{-}H_C}$ = 6.9 Hz, is assigned to be C_B(α to the sulfide linkage).

Fig. 3



Gated decoupling ^{13}C NMR spectrum of trithiepin II





$J_{C_B\text{-}H_B}$ = 170.41 Hz

$J_{C_B\text{-}H_A}$ = 10.254 Hz

$J_{C_B\text{-}H_C}$ = 6.846 Hz

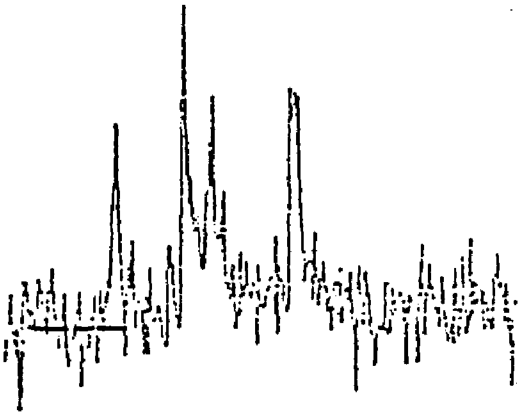
---

*Apparently the two-bond coupling $J_{C_A\text{-}H_B}$ is very small.

Assignment of proton resonances

As discussed above, inspection of $^{13}C-^{1}H$ coupling constant changes as a function of the proton decoupling frequency should allow distinction between both sets of protons in II. Figure 4 shows the gated decoupled ^{13}C NMR spectrum with proton irradiation at $\delta 3.75$ on the proton scale.

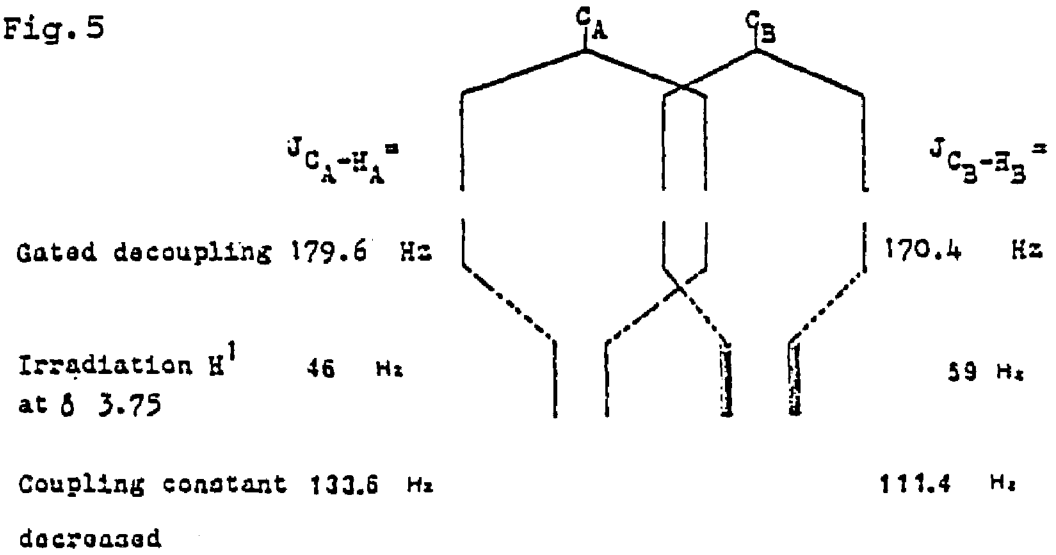
Fig. 4



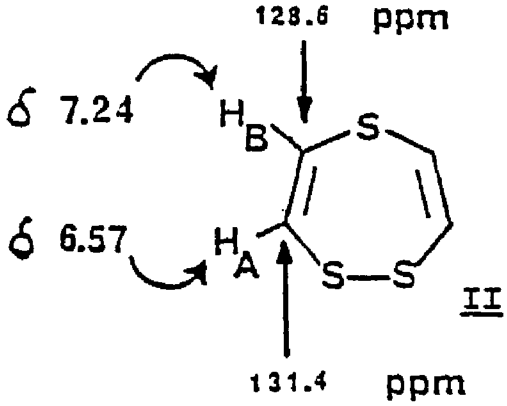
Gated decoupled ^{13}C NMR Spectrum with proton irradiation at δ 3.75 on proton scale

From Figure 4 it is evident that both the doublets and the quartets collape due to the irradiation of higher field proton. As summarized in Figure 5, the coupling constant decrease for C_A-H_A upon irradiation in the higher field proton region is 133 Hz, whereas the decrease for C_B-H_B is only 111.4 Hz. Hence, the C_A splitting is affected more than C_B by the higher field proton irradiation. Therefore, the upfield proton at $\delta 6.57$ may be assigned to C_A and the downfield proton at $\delta 7.24$ assigned to C_B.

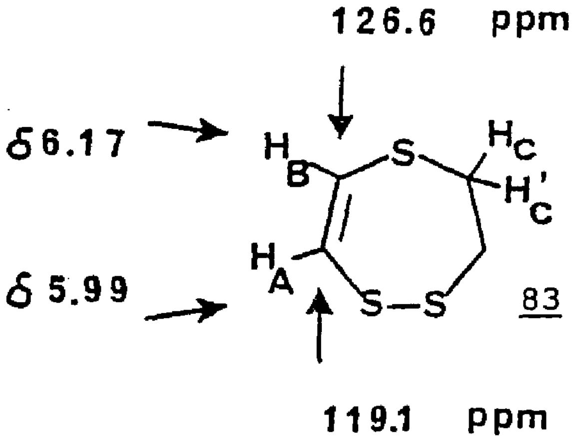
Fig. 5



With the ^{13}C and ^{1}H resonances now unambiguously assigned, a comparison of the ^{1}H and ^{13}C shifts of trithiepin II and dihydrotrithiepin 83 shows several interesting features.



II



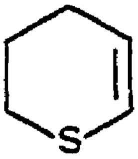
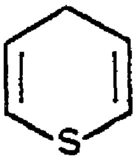
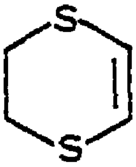
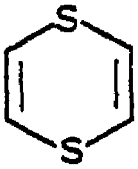
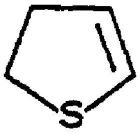
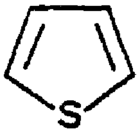
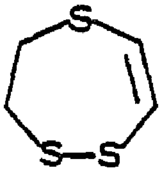
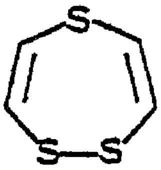
83

The structural assignment of the proton and carbon chemical shifts in 1,2,5-trithiepin II and its dihydrocompound 83 allows now a comparison of the NMR data between theses two compounds. As pointed out before, II is formally a conjugated heterocyclic system containing 10 π-electrons. The aromaticity of this molecule should be documented by the presence of a diamagnetic ring current, which should result in downfield proton chemical shifts in the 1,2,5-trithiepin II as compared to its dihydroderivative 83.

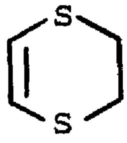
In general, introducing a second double bond into cyclic vinylsulfides changes the olefinic proton chemical shifts only slightly. As seen in Table 6, introduction of a second double bond in dihydrothiapyrane 95 results in upfield shifts of 0.11 and 0.13 ppm for H_α and H_β, respectively. Introduction of the second double bond in dihydrodithiin 96 results in downfield shifts of only 0.04 ppm. However, introduction of the second double bond in dihydrothiophene 97 causes a downfield shifts of 1.01 and 1.41 ppm for H_α and H_β, respectively. The observed changes in chemical shifts when going from dihydrothiophene 97 to thiophene can be used as a guide in determining the aromaticity of other sulfur heterocycles.

Comparing the 6,7-dihydrotrithiepin 83 with 1,2,5-trithiepin II, one notes that the second double bond shifts H_A and H_B downfield by 0.58 and 1.07 ppm, respectively. This is highly consistent with the presence of a diamagnetic ring current in the 1,2,5-trithiepin II, which therefore may be considered to be aromatic.

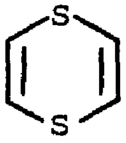
Table 6

	Chemical shifts of olefinic protons			Chemicals shifts of olefinic protons		Δδ
95		δ 5.68 δ 6.01			δ 5.55 δ 5.90	-0.13 ppm -0.11 ppm
96		δ 5.95	96'		δ 5.99	0.04 ppm
97		δ 5.61 δ 6.18	97'		δ 7.04 δ 7.17	1.41 ppm 1.01 ppm
83		δ 6.17 δ 5.99	II		δ 7.24 δ 6.57	1.07 ppm 0.58 ppm

Very interesting are the changes in the carbon chemical shifts in II and 83. The carbon α to the S-S linkage in 83 is upfield(119.1 ppm) relative to the carbon α to the sulfide linkage(126.6 ppm). Upon introducing the second double bond in 83 yielding II both carbons experience a downfield shift, however to a different degree. Carbon 3 or 7, α to the disulfide linkage in II shift by 12.3 ppm downfield($C_{3;7}$=131.4 ppm) and carbon 4 or 6, α to the sulfide linkage shifts by 2 ppm downfield($C_{4;6}$=128.6 ppm). Very similar shifts are observed if one compares 1,4-dithiacyclohexadiene 96' and 1,4-dithiacyclohexene 96.

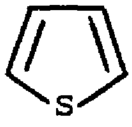


96

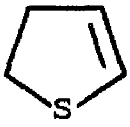


96'

The carbon chemical shifts for thiophene[141,142] and for the corresponding 4,5-dihydrothiophene[142] are as follows.

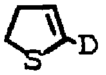


97'



97

(The positions have been assigned using



)[142]

In order to evaluate the effect of the changing geometry at the -S-S- bond(cf p 76 ff) on the ^{13}C chemical shifts at the adjacent carbon it would be desirable to compare the

^{13}C NMR spectra of the following compounds. Unfortunately,

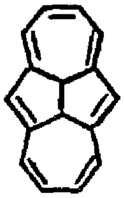
 and  ;  and 

 and  and 

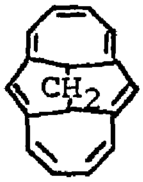
those compounds are either unknown or their ^{13}C NMR spectra have not been measured.

In the studies on bridged Annulenes and (12)paracyclophane, Boekelheide[138] and Vogel[139] came to the general conclusion that the ring current effect on carbon-13 chemical shifts is small compared to other factors such as changing geometry, changing hybridization, and changing charge.

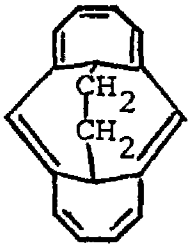
A Dreiding model of II shows that the molecule is nearly planar. Generally, planarity is a necessary for efficient π overlap in the molecule. However, the benzene nucleus in (8)paracyclophane [98] tolerates a distortion calculated to be 20° from a planar configuration and yet retains its aromaticity, i.e., a ring current is detected by proton NMR. Vogel[99] studied the series of systematically bent syn-bridged(14)Annulene 98, 99, 100, and 101 and found that even the most highly bent member of this series, i.e., 101, exhibiting an orbital torsional angle as high as 40°, still exhibited aromaticity.



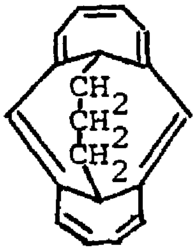
98



99



100

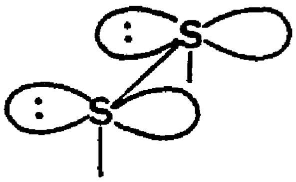


101

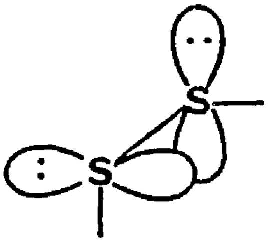
Moreover, the bridged(10)Annulene, bent 41° out of planarity, still sustains a diamagnetic ring current. Therefore, one sees that the steric requirements for aromaticity are rather flexible. The actual magnitude of the distortion which an aromatic molecule can accommodate is not known yet.

By comparison of resonance energies, thermal stabilities, and ring currents of (18)Annulene, benzene, and thiophene the aromatic ring current appears not to be related in any direct way to the resonance energies or reactivities of the systems.[100] Several thermally unstable compounds such as the tropylium ion, the air-sensitive(18)Annulene,[101] the mono-trans cyclononatetraene anion 3,[16] and the readily polymerizing arsenbenzene are all considered to be aromatic on the basis of the presence of a diamagnetic ring current. Although 1,2,5-trithiepin II can be considered aromatic on the basis of its proton NMR, its lability may be related to the geometry of the S-S unit as shown below.

In studying the interaction of the neighboring lone pairs of the S-S linkage Yamabe[102] reported that the splitting of the 3p lone-pair levels decrease as the dihedral angle between the S-S linkage increases from 0° to 90°. As a



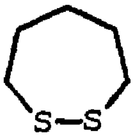
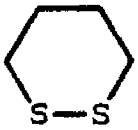
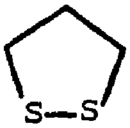
0°



90°

result, the gap between LUMO and HOMO becomes larger with the dihedral abgles increasing from 0° to 90°.

Therefore, disulfides having a dihedral angle close to 90° should be less reactive and more stable, which is well documented.[122]

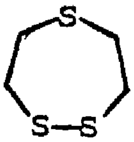




Dihedral angle	90°	40°	0°
Stability	most stable	intermediate	least stable

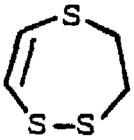
The 7-membered ring compound with a dihedral angle of 90° is the most stable while the 5-membered ring compound with a dihedral angle of 0° is the least stable.

The dihedral angles of compounds 81, 83, and II, estimated from Dreiding model are 90°, 80°, and 20°, respectively.

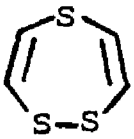
81



83



II



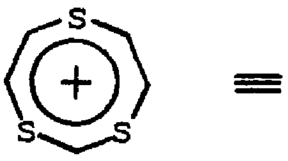
	81	83	II
Dihedral angle	90°	80°	20°

The high reactivity of the 1,2,5-trithiepin II therefore could be due to the small dihedral angle(C_7-S_1-S_2-C_3).

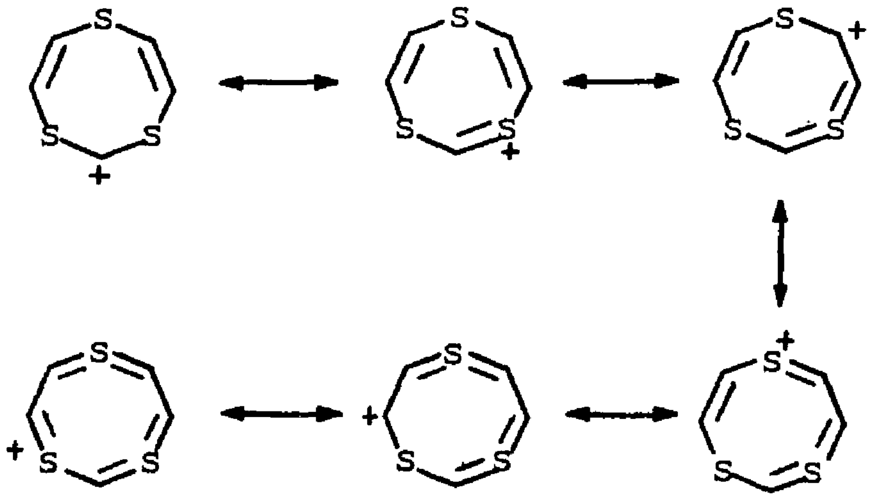
III. 1,3,6-TRITHIACYCLOOCTA-4,7-DIENE CATION III

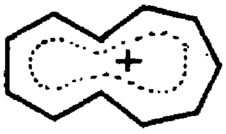
On the basis of the introductory discussion, replacement of three double bonds of cycloundecapentaene cation 102 by three sulfur atoms, should give the potentially aromatic 1,3,6-trithiacycloocta-4,7-diene III.

It is well known that sulfur stabilizes the π-electron system in thiapyrilium cation 6, 1,2-dithiolium cation 7 and 1,3-dithiolium cation 8 [24,25,26] through electron donation. In cation III, containing three sulfur atoms, one might expect a similar π-electron delocalization as in 6, 7, and 8 leading to a 10 π heteroaromatic system.

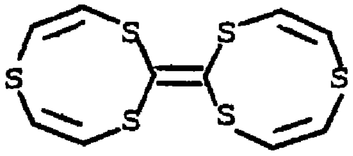


III





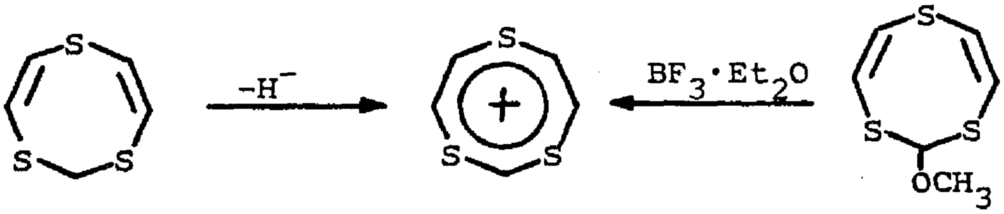
102



103

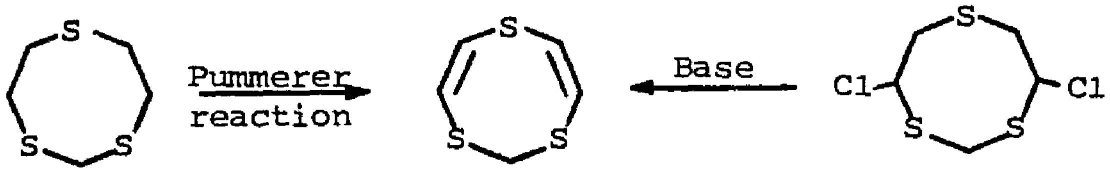
The hexathiafulvalene 103, prepared in a similar manner as 49, should be able to complex with TCNQ 48.

The 8-membered ring skeleton conceivably could be prepared by cyclization of the readily available bis-(2-mercaptoethyl)sulfide 80 with dibromoethane, or by nucleophilic addition of sulfur dichloride to divinylmercaptomethane at high dilution. The use of equimolar amounts of reagents at high dilution [58] is required to reduce the yield of intermolecular addition and polymer formation. The double bonds were expected to be introduced by a Pummerer reaction or by elimination with base. Removing the hydride or methoxy group in the 1,3-dithioacetal would be used as a last step to obtain the trithia cation III. Hence, the approach to III involves the construction of its precursors 104 or 105.



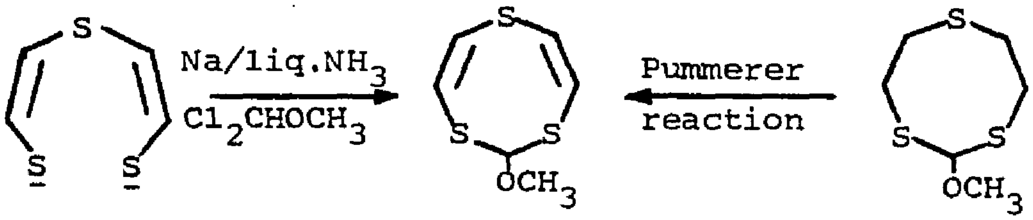
104 III 105

A precursor of 104 could be either the saturated analogue 106 or the chlorosubstituted analogue 107. Both the 1,3-dithioacetals are known to be stable to acidic condition.[103] Compound 106 would undergo the Pummerer reaction under acidic condition to give the corresponding α,β-unsaturated 104. The introduction of two double bonds in 107 could be achieved by dehydrochlorination of 107 with base.



106 104 107

Another intermediate 105 could be obtained by the successive Pummerer reaction from 108 or the cyclization of 109 with α,α'-dichloromethylmethyl ether based on the known reductive cleavage [104] of S-S bond in disulfide compounds.

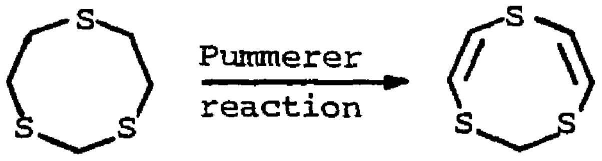


109 105 108

The attempted synthesis of 1,3,6-trithia cation III via both the intermediate 104 and 105 will be discussed below.

A) Approaches toward 1,3,6-trithiacycloocta-4,7-diene 104

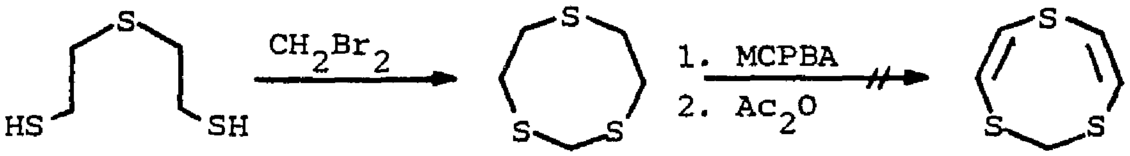
a) Via compound 106



106 104

Under high dilution, treatment of the sodium salt of bis-(2-mercaptoethyl)sulfide 80 with dibromomethane afforded the 8-membered ring compound 1,3,6-trithiacyclooctane 106 in

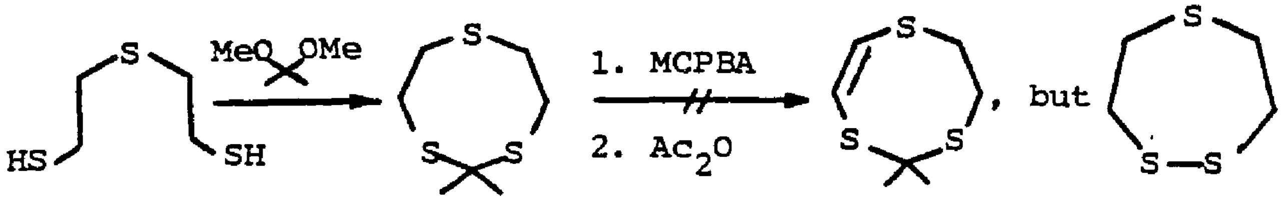
21 % yield. The proton NMR spectrum showed two singlets at δ4.30(S-CH_2-S,2H) and δ2.93(-SCH_2CH_2S-,4H). The proton decoupled ^{13}C NMR spectrum showed three singlets at 38.8, 35.5 and 31.2 ppm as expected for the number of peaks and the chemical shifts. The GC-MS spectrum exhibited fragment ions at m/e 106(100 %), 60(64 %) and 45(94 %). The acid-stable acetal 106 was then oxidized to give the corresponding sulfoxide which, without isolation, was refluxed with acetic anhydride. However, the reaction did not give any of the expected product 104. Only decomposed and polymerized materials were obtained.



80 106 104

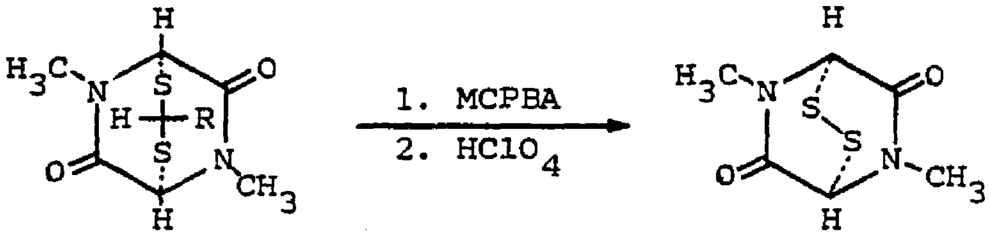
The failure of the above Pummerer reaction led the attempt to prepare 2,2-dimethyl-1,3,6-trithiacyclooctane 110 in which the carbon 2 was blocked to avoid any unnecessary oxidation on carbon 2 during the Pummerer reaction.

Compound 110, prepared from bis-(2-mercaptoethyl)sulfide 80 and 2,2-dimethoxypropane, was oxidized and then refluxed with acetic anhydride. A small amount of 1,2,5-trithiepane 81 was isolated along with much decomposed and polymerized material. However, none of the desired product 111 was observed.



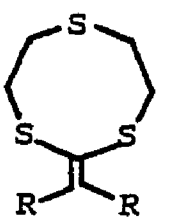
80 110 111 81

The formation of 1,2,5-trithiepane 81, containing an S-S bond, during the Pummerer reaction is similar to the finding of Kishi[52] shown below.

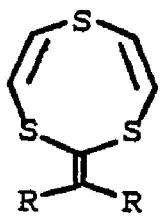


112 R= p-$CH_3OC_6H_5$ 113

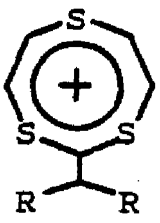
The failure of 110 to yield 111 turned our attention to prepare the ketene thioacetal 115 which could be prepared from the corresponding saturated ketene thioacetal 114, already blocked at carbon 2, which would prevent the unnessary oxidation on carbon 2 during the introduction of the two double bonds by the Pummerer reaction. The ketene thio-



114



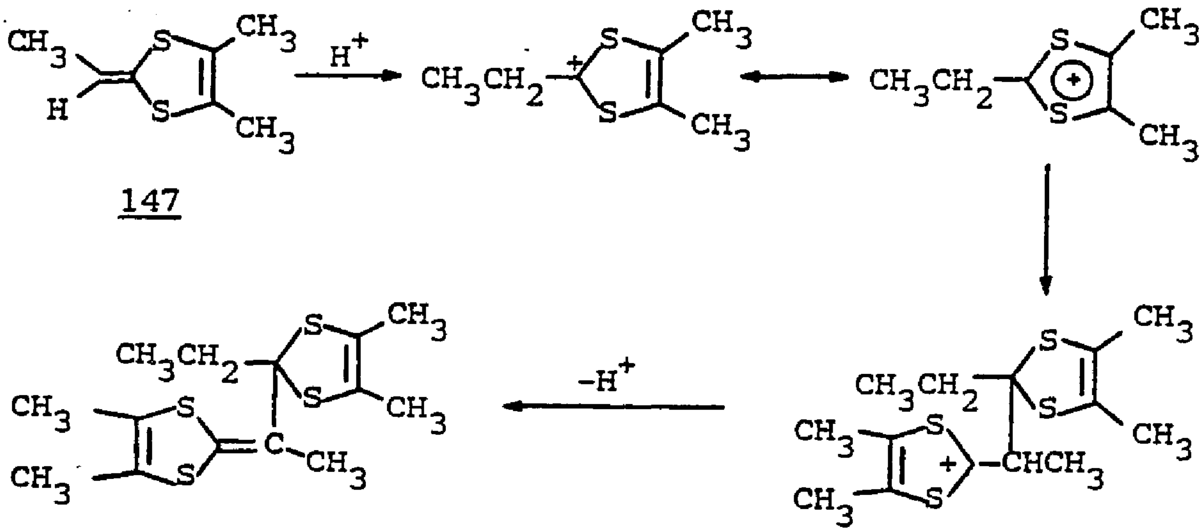
115



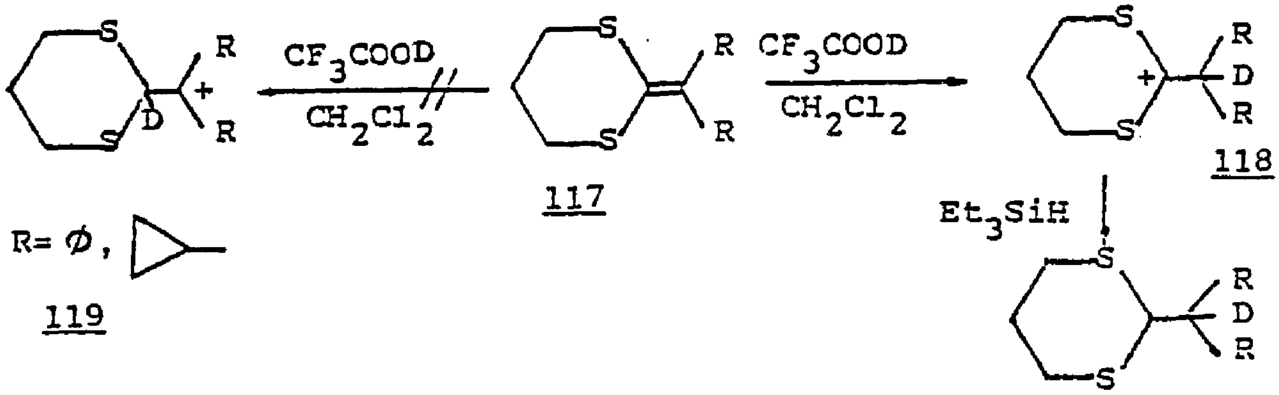
IV

acetal 115, upon protonation should afford the sulfur stabilized potentially aromatic 10 π-electron cation IV.

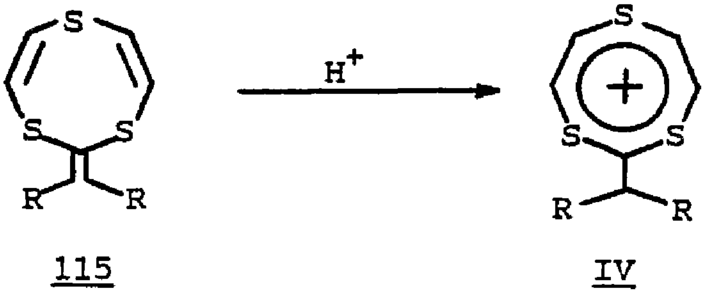
The protonation of ketene thioacetal has been reported. Meijer[105] reported that ketene thioacetal 116 dimerized in the presence of a trace of acid. Traces of base inhibited this dimerization. The dimerization can be rationalized by the following scheme which involves the formation of a sulfur stabilized carbocation.



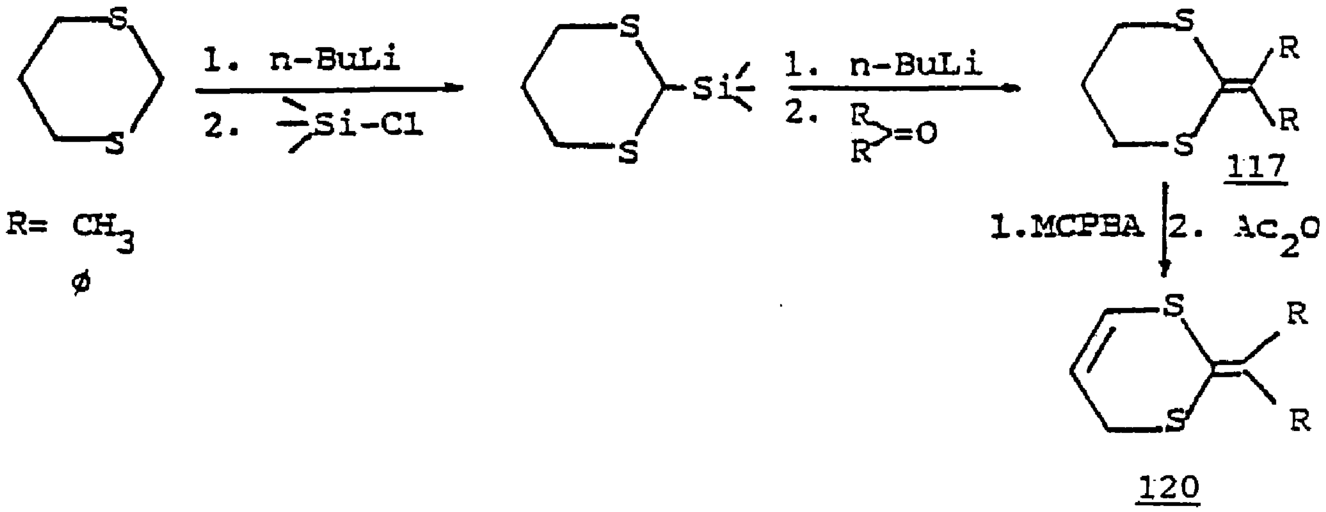
Carey [106] reported that protonation of ketene thioacetal 117 with trifluoroacetic acid gave the sulfur stabilized cation 118 rather than the cation 119 without sulfur stabilization.



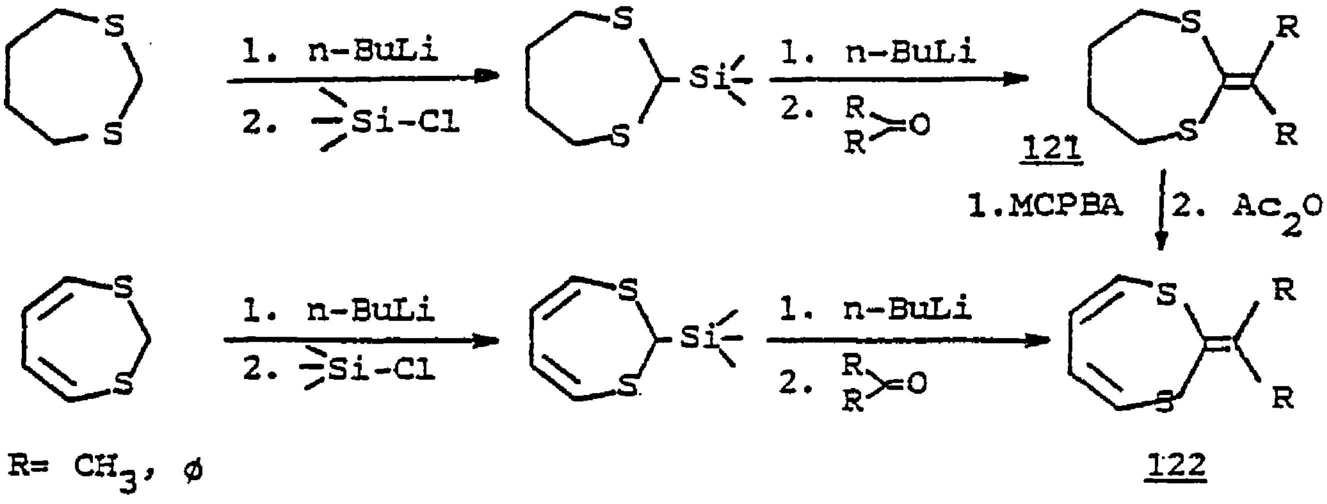
Hence, protonation of 115 should result in the formation of the sulfur stabilized carbocation IV.



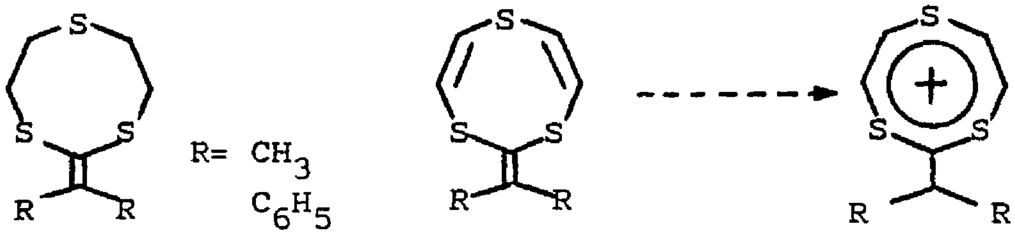
In view of the Pummerer reaction on 106, 108, and 110 carbon 2 should be blocked in another way before the Pummerer reaction is performed. For model studies of the Pummerer reaction on ketene thioacetal, compound 117 was chosen.[106] Metallation of 2-trimethylsilyl-1,3-dithiane followed by reaction with a benzophenone gave the ketene thioacetal 117. Treatment of 117 with m-chloroperbenzoic acid followed by refluxing with acetic anhydride gave the expected product 120.



The seven-membered ring ketene thioacetal 121 was also used for the model study of the Pummerer reaction. Compound 121 was prepared from 1,3-dithiapane via metallation with n-butyllithium, silylation with trimethylsilyl chloride, followed by a second metallation and nucleophilic attack on a ketone or aldehyde. The ketene thioacetal 121 was treated with 2 equivalents of m-chloroperbenzoic acid acid and then refluxed with acetic anhydride to afford the desired diene 122, which was identical to that obtained by Grohmann[41] using the alternative synthetic route shown below.

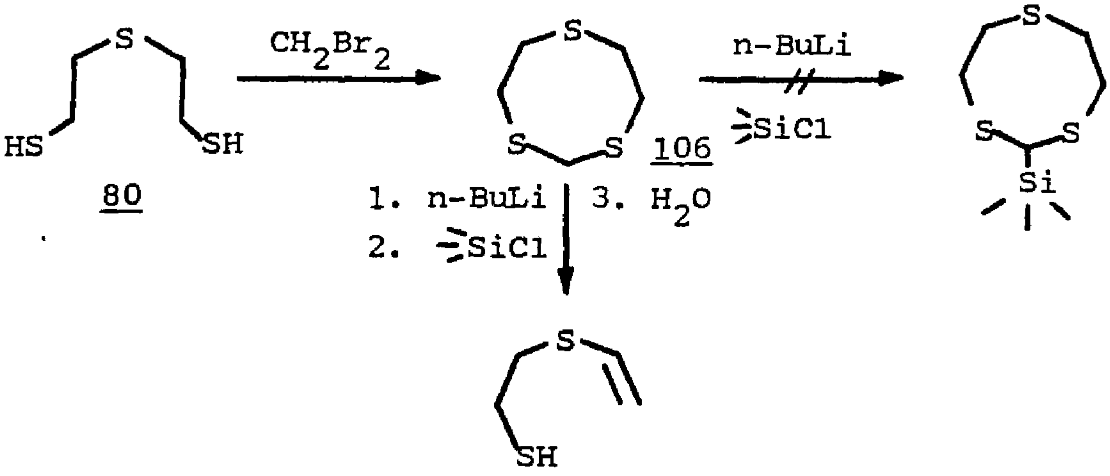


The above successful reactions encouraged us to prepare compound 114. Once the dimethyl or diphenyl ketene thioacetal 114 is made, the Pummerer reaction was expected to proceed easily. Finally, protonation of 115 should then give IV.



114 115 IV

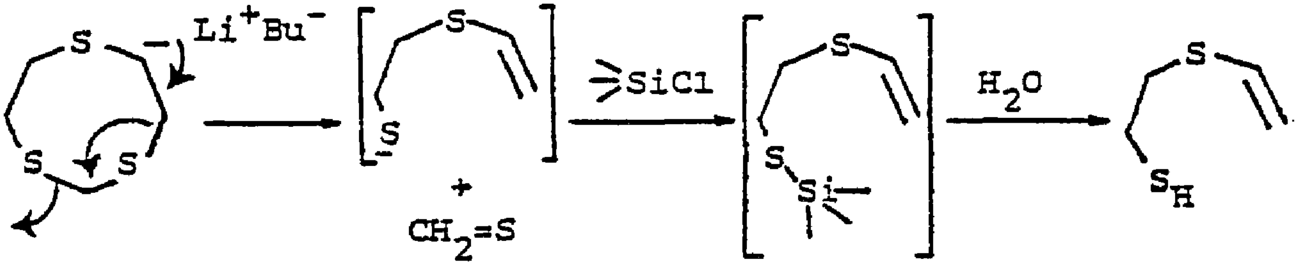
Compound 106 was metallated with n-butyllithium in THF at -70°C under nitrogen, then trapped with trimethylsilyl chloride. However, instead of the expected compound 123 a completely Si free compound was obtained, which was identified as 2-mercaptoethylvinyl sulfide 124(50 %).



80 106 123 124

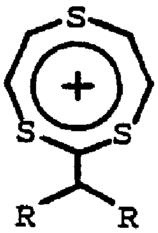
The assignment of structure 124 is based mainly on the proton NMR spectrum. The vinylic protons of a vinyl sulfide in general give rise to an ABX pattern at δ5.6-6.5 [107]; the methylene protons appear as multiplets centered at δ3.5 and 2.9; the thiol proton signal is a triplet at δ1.3.

The formation of the ring-cleaved compound 124 can be rationalized as follows: anti-β-elimination fragmentation competes with the metallation on carbon 2 and dominates the reaction to give the sulfur silylated compound, which, upon hydrolysis, would afford the thiol compound 124.

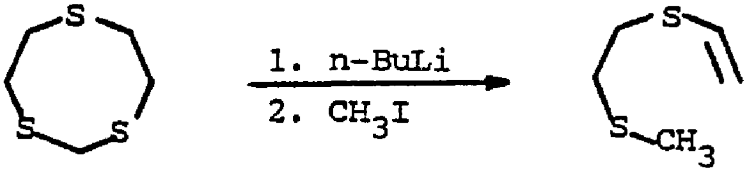


106 124

For further confirmation, 106 was allowed to react with n-butyllithium and the mixture was quenched with excess methyl iodide to give the cleaved 125. The proton NMR spectrum shows an ABX pattern at δ5.0-6.50, a multiplet at δ2.85 for the methylene protons and a singlet at δ2.12 for the methyl protons.



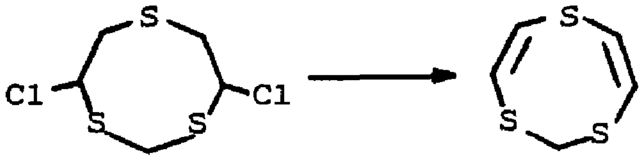
IV



106 125

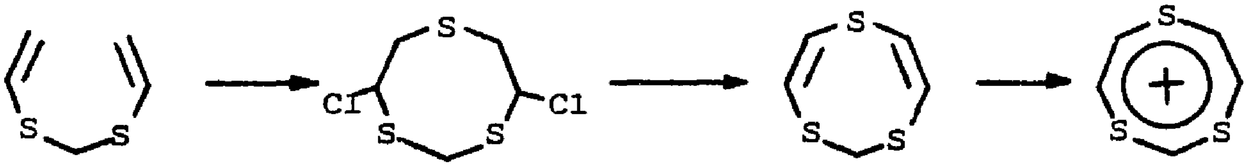
Because of the unexpected elimination-fragmentation reaction, this approach to cation IV was abandoned.

b) Via compound 107



107 104

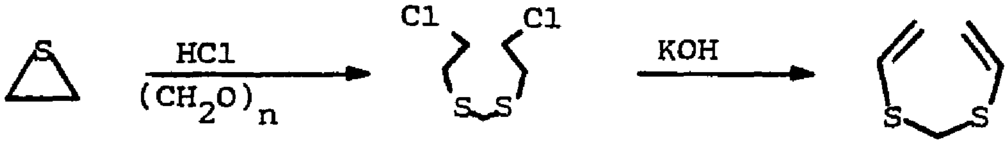
The approach using 107 exploits the Markovnikov addition of sulfur dichloride to linear diolefins.[108] Therefore, the addition of sulfur dichloride to bis-divinylmercaptomethane 126 should give 1,3,6-trithia-4,8-dichlorocyclooctane 107 which upon dehydrochlorination should give 104.



126 107 104 III

A number of preparations[109-112] of compound 126, the starting material for this approach, have been reported, as summarized below.

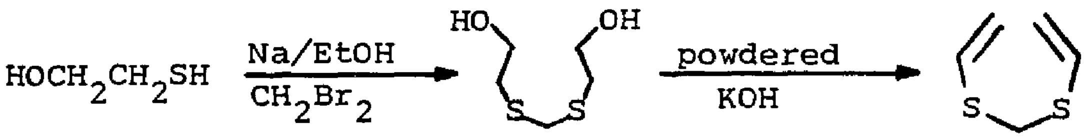
1\.



[109]

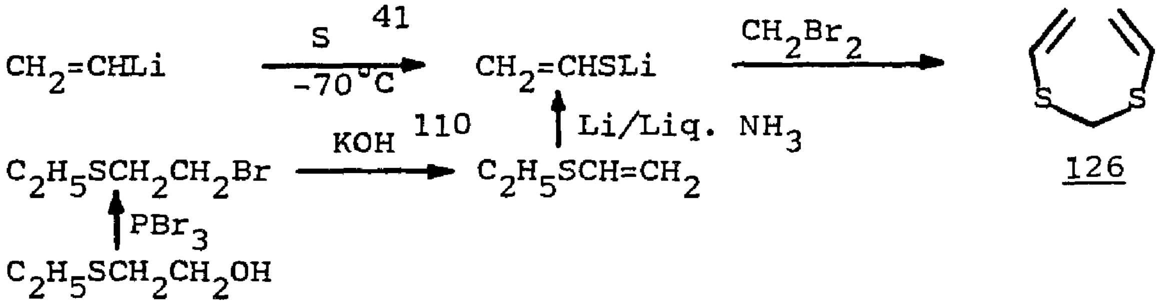
127 126

2. 111,112

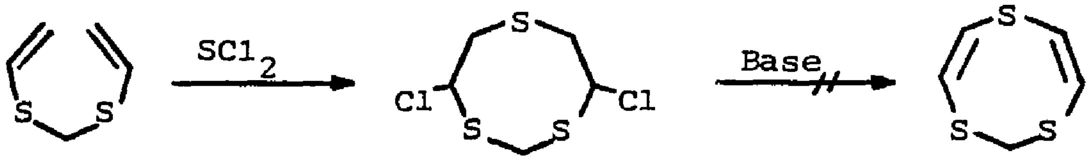


128 126

3.



Bis-divinylmercaptomethane 126, obtained from all of the above preparations, was allowed to react with sulfur dichloride at 0°C in ether or THF at room temperature for 10 hr. The clear solution was decanted from polymeric material and evaporated to give a deep yellow very unstable material 107. The assignment of the structure is based on the proton NMR spectrum ($CDCl_3$,TMS): δ5.49(t,2H,J=7 Hz), δ4.18(s,2H,S-CH_2-S), δ3.35(d,4H,J=7 Hz). Treatment of the yellow crude product in THF with potassium t-butoxide, DBN, triethylamine, diisopropylethylamine or powdered KOH gave none of the desired trithiadiene 104; rather, decomposed and polymerized material were obtained which were not identified further.



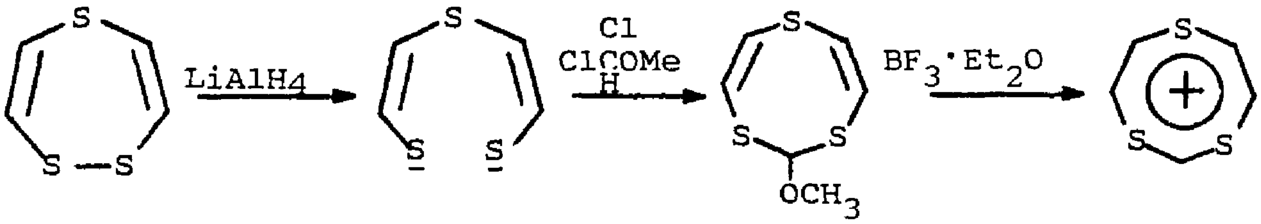
126 107 104

Another attractive route to compound III via 105 is shown below.

B) Approaches toward 2-methoxy-1,3,6-trithiacycloocta-4,7-diene 105

a) Via the cyclization of 109

The known reductive scission of the S-S bond in disulfide compounds by lithium aluminum hydride [104] suggested the use of 1,2,5-trithiepin II as the starting material leading to the trithia cation III. The synthetic route was based on the strategy summarized below.

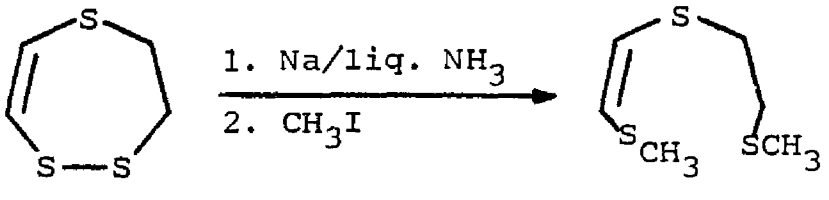


II 109 105 III

The reductive cleavage of 1,2,5-trithiepin II should give the sodium dithiolate 109 which then, trapped with α,α'-dichloromethylmethyl ether, should give 105. After removal of methoxy group, 105 should be convertable to III.

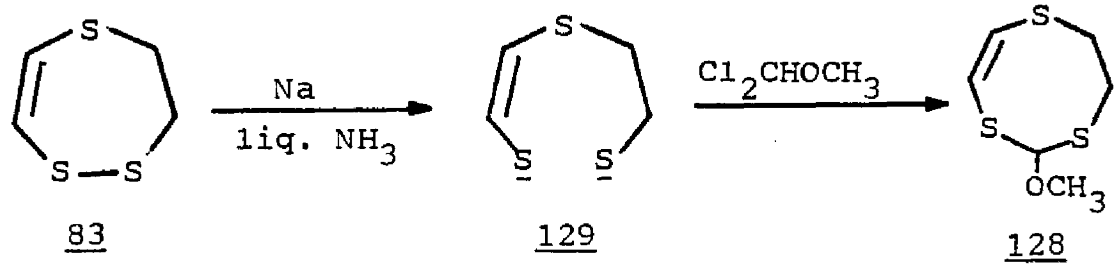
Before the reductive cleavage of the S-S bond in 1,2,5-trithiepin II was carried out, the reductive cleavage of the S-S bond and the construction of the 8-membered ring system from dihydro-1,2,5-trithiepin 83 were performed successfully as illustrated below.

Compound 83 was treated with sodium in liquid NH_3 at -70°C, and then trapped with excess methyl iodide to give the expected 127. The spectral features of 127 were fully compatible with the structural assignment. The proton NMR($CDCl_3$,TMS) shows a singlet at δ6.30 for the olefinic protons, a multiplet at δ2.80-3.15 for the methylene protons, a singlet at δ2.41 for the methyl protons of the vinylic S-CH_3 and a singlet δ2.20 for the methyl protons of the other S-CH_3. The GC-MS exhibits a molecular ion at m/e 180(14 %) and other fragment ions at m/e 75(100 %), 61(54.4 %), 45 (39.8 %), and 47(37.5 %).



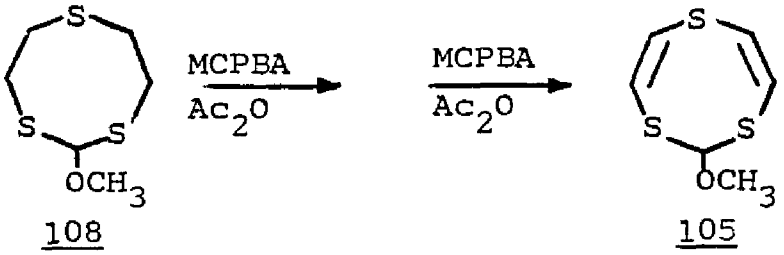
83 127

Further, 83 was treated with sodium in liquid NH_3 at -70°C then trapped with α,α'-dichloromethylmethyl ether to give the expected 8-membered ring compound 128. The proton NMR($CDCl_3$,TMS) shows an AB quartet at δ6.73 and δ6.23 for the olefinic protons with J=9 Hz(cis), a singlet at δ6.10 for the methine proton, a singlet at δ3.50 for the methyl protons, and a multiplet at δ2.76-3.30 for the methylene protons.



The starting material for 109 was available in only small quantities. So reductive cleavage to 109 has not been performed yet.

b) Via Pummerer reaction from 108

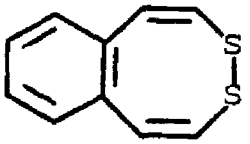


Treatment of 108 with m-chloroperbenzoic acid followed by refluxing with acetic anhydride gave none of the desired product 105 but decomposed materials which were not identified further.

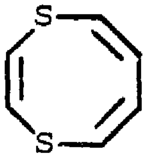
The failure to synthesize 1,3,6-trithia cation III shifted our interests to the preparation of another potentiallt aromatic 10 π-electron system, as shown below.

IV. 5,6-BENZO-1,2-DITHIOCIN V

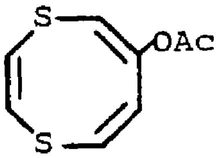
In dealing with the parent or benzo-fused 8-membered bis sulfur heterocycles, several attempts have been made to synthesize the 1,4-dithiocin VI.[109-112] So far only 17,[33] 22,[109] and 131 [109] have been synthesized, none of them exhibits aromaticity based on their proton NMR spectrum (see page 16). The most prominent chemical feature of these compounds is their propensity to lose sulfur to give benzenoid aromatics. Upon heating up to 200°C, 131 was converted to naphthalene. This reaction pathway is formulated as follows:



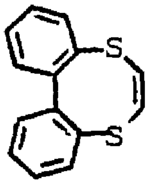
V



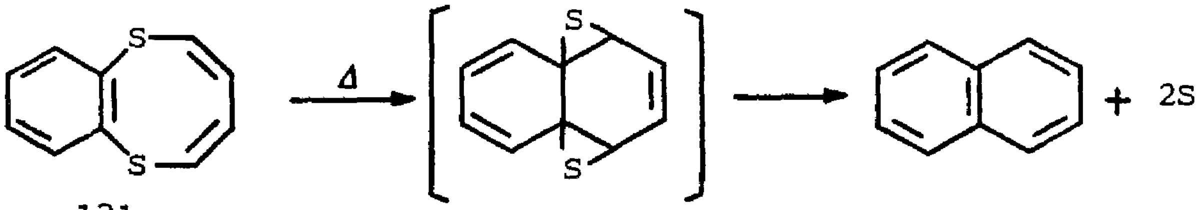
VI



17



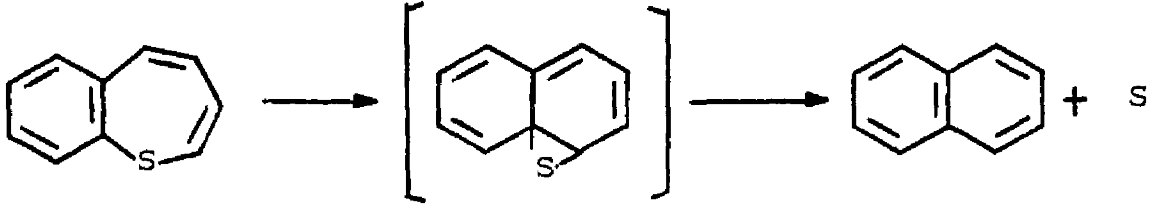
22



131

The sulfur extrusion has been proposed to involve valence isomerization to a bisepisulfide, which can lose sulfur.[113] The formation of naphthalene therefore suggests that there is no significant aromatic stabilization in the 2,3-benzo-1,4-dithiocin 131.

The 2,3-benzo-1,4-dithiocin 131 is considerably more stable than 1-benzothiepin 132,[127] which decomposes at room temperature.



132

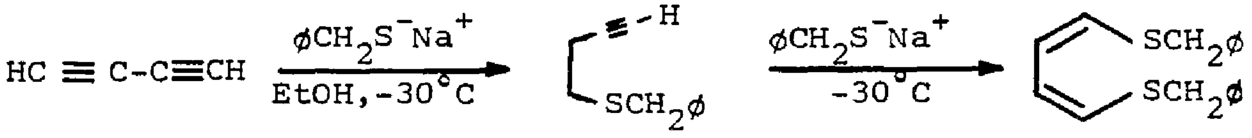
The 5,6-benzo-1,2-dithiocin V is isoelectronic with the aromatic dianion of cyclooctatetraene, and according to the Hückel's 4n+2 rule, is a potentially aromatic compound. However, facile desulfurization leading to benzenoid aromatics takes place in dithiocin and thiepin systems.[109,115] It would be of interest to synthesize and investigate 133 and V which is a potentially 8 π antiaromatic and a potential 10 π aromatic compound, respectively. The comparison of the spectral properties and chemical behavior of these two structurally related molecules is expected to provide some information concerning 10 π aromaticity predicted for V.

The nucleophilic additions of mercaptans to various monosubtituted acetylenes in the presence of base proceed via "trans-addition" and result in the formation of cis-1,2-disubstituted alkenes.[141]

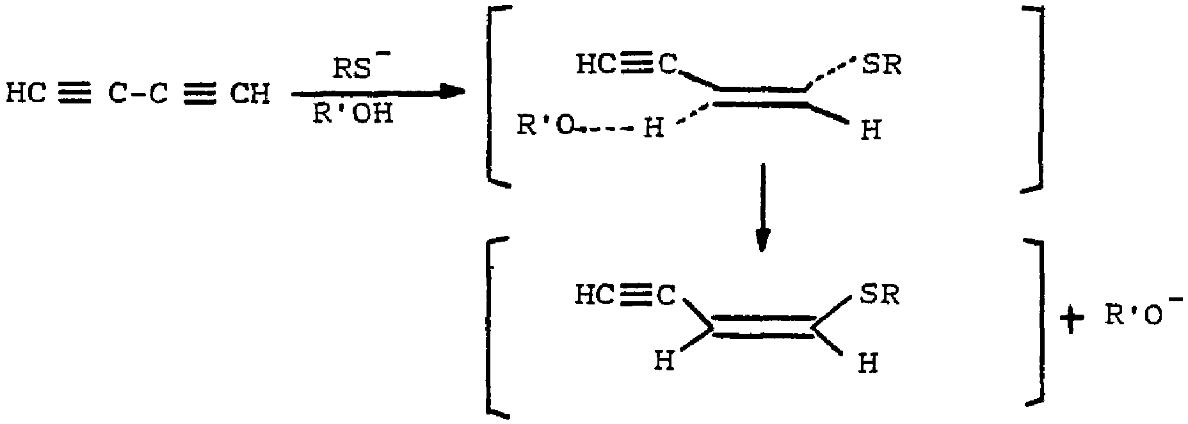
X= C_6H_5, ArS

The activation of the triple bond increases with the electron-accepting properties of the substituent[142] in the order $ArS < Cl < C_6H_5 < COO < COOR < COAr$.

Nucleophilic attack of mercaptans on diacetylene under polar conditions also results in the formation of cis-isomers exclusively,[77] while under free radical conditions this reaction proceeds nonstereospecifically and leads to mixtures of trans and cis isomers.[116]

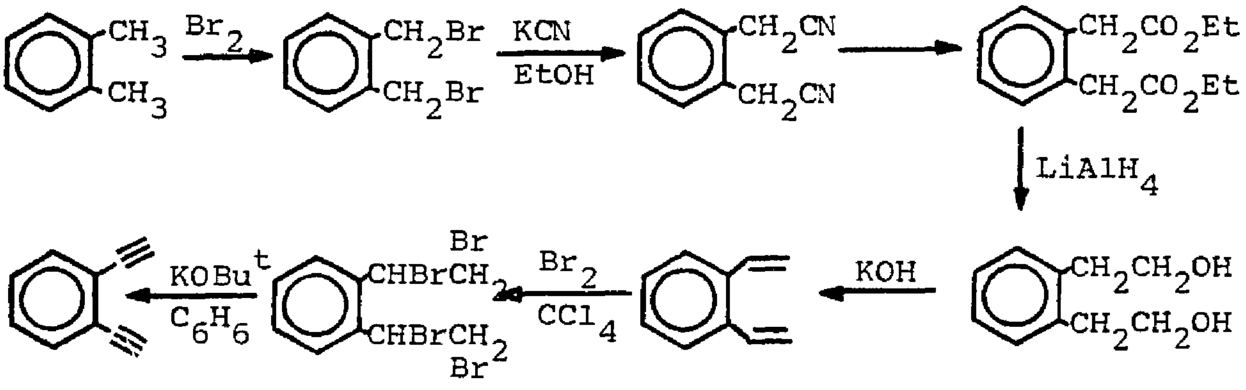


The nature of the solvent plays an important role in the course of this reaction. The high stereospecificity of the nucleophilic addition of mercaptans to diacetylene in an alcoholic medium has been proposed to result from formation of an intermediate complex involving the attacking reagent and the solvent.[117]



On the basis of the cis configuration of the double bond in 5,6-benzo-1,2-dithiocin V we may consider a possible route which utilizes o-diethynylbenzene 134 as the key intermediate. Compound 134 could then be allowed to react with a suitable mercaptan and the resulting product could be transformed into the desired product V.

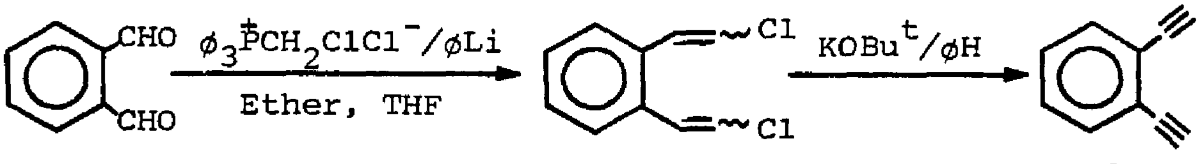
o-Diethynylbenzene 134 has been prepared by Eglinton and Galbraith[118] using the following sequence.



134

The overall yield from o-xylene is 13 %.

A more efficient way to prepare the o-diethynylbenzene 134 was developed by utilizing the Wittig reaction as shown.



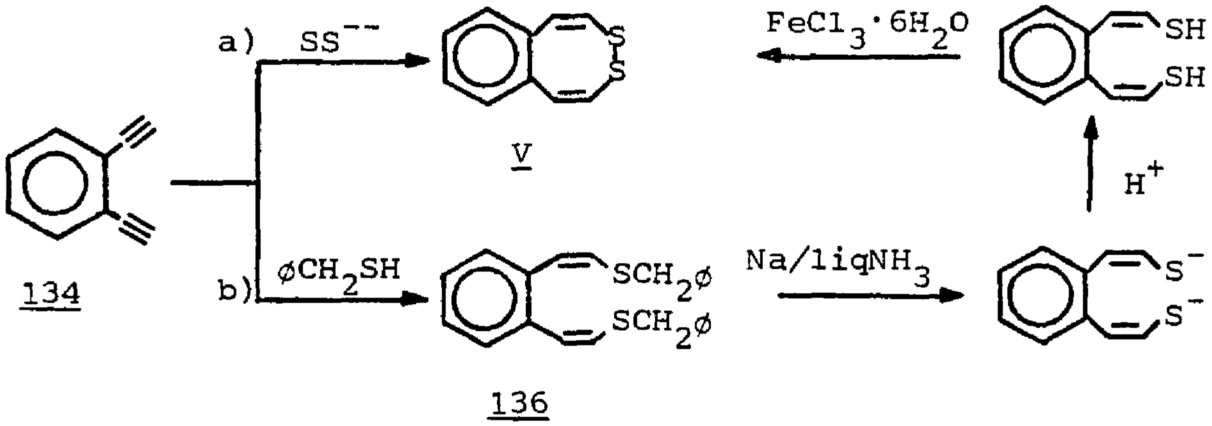
EE,ZE,ZZ

135

134

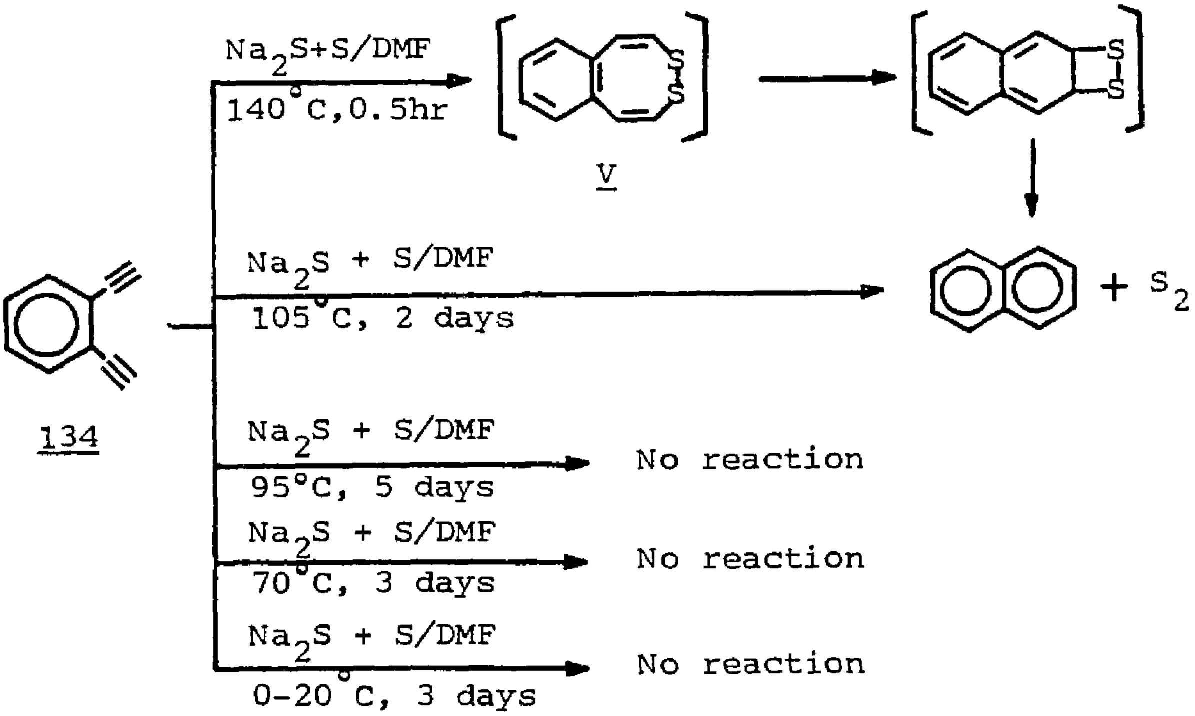
Chloromethyltriphenylphosphonium chloride in dry ether was treated with phenyl lithium, then with o-phthaldehyde at -30°C to give o-bis-(β-chlorovinyl)benzene 135 in 50 % yield. The product consisted of three isomers, a 1:1:1 mixture of EE, ZE and ZZ stereoisomers, whose presence and molecular weight were confirmed by GC-MS. The proton NMR spectrum shows both cis and trans vicinal coupling. No attempt was made to separate the isomers. Compound 135 rapidly eliminated hydrogen chloride when refluxed with potassium t-butoxide in benzene forming o-diethynylbenzene 134 in 60 % yield.

Two synthetic routes to compound V starting with o-diethynylbenzene 134 have been attempted.



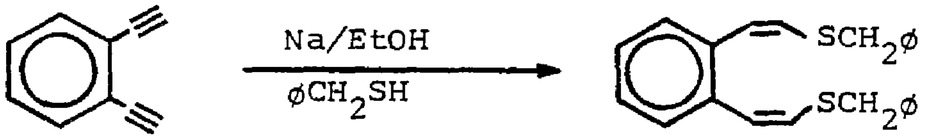
Approach a) involved the bis addition of sodium disulfide to o-diethynylbenzene 134 expecting to prepare V in one step. In approach b) benzylmercaptan was added to V, and the product was debenzylated, acidified and oxidized. The results are as follows:

a) Several sets of reaction conditions have been used for this approach.



When sodium disulfide,[146] prepared from sodium sulfide and sulfur, was added to o-diethynylbenzene 134 in DMF at 140°C for 0.5 hr, naphthalene and sulfur resulted instead of the expected 5,6-benzo-1,2-dithiocin V. Apparently, the initially formed product V immediately underwent Cope rearrangement followed by extrusion of sulfur.[109] The reaction was also attempted unsuccessfully at 20°C for 3 days, 70°C for 3 days and 95°C for 5 days. However, when the temperature was increased to 105°C for 2 days, the starting material completely disappeared and naphthalene and sulfur were detected exclusively with no indication of V. The above reactions were monitored by gas chromatography, thin layer chromatography and proton NMR.

b) The apparent thermal instability of V suggested focussing on low temperature methods for its preparation. Debenzylation of o-bis-(β-benzylmercaptovinyl)benzene 136 at -70°C followed by oxidation at low temperature would be one low temperature route.



134 136

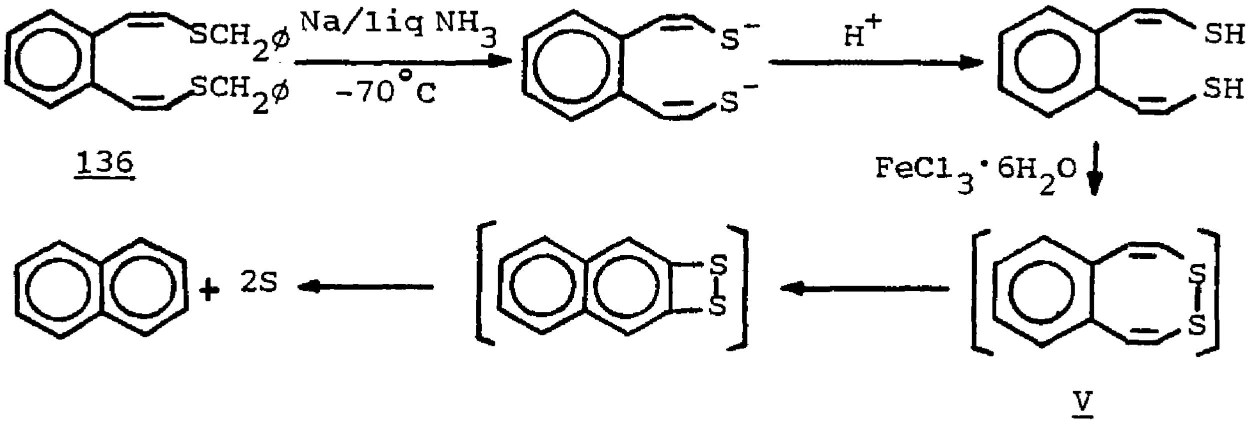
Nucleophilic addition of benzyl mercaptan to o-diethynylbenzene 134 in sodium ethoxide-ethanol solution at reflux temperature afforded exclusively cis-o-bis(β-benzylmercaptovinyl)benzene 136 in 70 % yield. The cis stereochemistry was established by proton NMR and IR. The proton NMR showed the olefinic protons as an AB quartet at δ6.5 and δ6.2 with a coupling constant J=10 Hz. The IR spectrum showed the characteristic cis double bond absorption at 745 cm^{-1} and no absorption at 925 cm^{-1}, which is characteristic of the trans double bond;[120] ^{13}C-NMR and mass spectra are consistent with the assigned structure.

Sodium in liquid ammonia is commonly employed for the cleavage of vinylic sulfides. α,β-Unsaturated thiols

(-C=C-SH) can be obtained [121] by cleavage of the corresponding alkyl sulfides -C=C-SR with sodium or lithium in liquid ammonia followed by acid hydrolysis after evaporation of the ammonia. The many studies by Schroth,[122] Truce [123] and Bransma[110] imply that the order of the tendency of thiolates to cleavage with alkali metals is

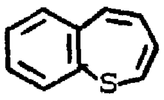
$$\text{Aryl } S^- > -C{=}C{-}S^- > -C{\equiv}C{-}S^- > \text{Alkyl } S^-$$

Hence, the reaction leading to 5,6-benzo-1,2-dithiocin V was expected to succeed. In the event, sodium was added to 136 in liquid ammonia until a permanent blue color persisted. After the disappearance of all starting material(TLC), the ammonia was evaporated, the solid residue dissolved in methanol, and oxidized with ferric chloride at 10°C. Naphthalene and sulfur were the only products obtained. There was no indication of the desired compound V.

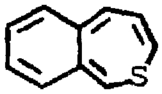


Hence, compound V appeared to be unstable even at 10°C and might only be stable at subzero temperature. From these results, it is reasonable to infer that 5,6-benzo-1,2-dithiocin V is not aromatic in the classical sense.

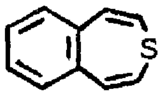
The tendency to lose sulfur giving benzenoid aromatics in 1,2-and 1,4-dithiocins suggests that no aromatic stabilization appeared in that systems. This behavior may be compared with the facile desulfurization leading to benzenoid aromatics which is displayed by thiepines.[124] In order to do this comparison it is necessary to prepare 3-benzothiepin 133. There are three possible benzo-fused derivatives of thiepin, 1-, 2-, and 3-benzothiepin(132, 137, 133, respectively). The 8 π-electron systems are predicted to be antiaromatic. Their resonance energies have been calculated by Hess.[125]



132



137

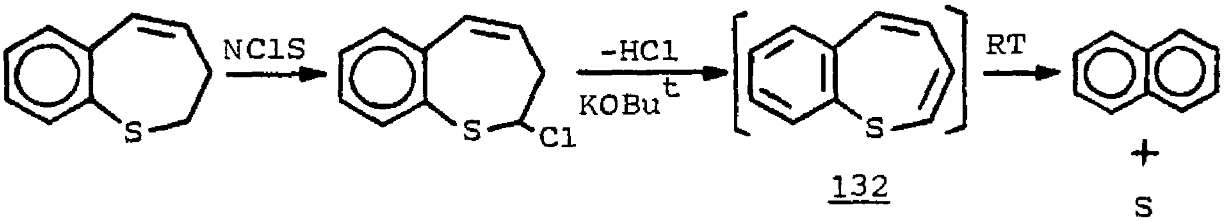


133

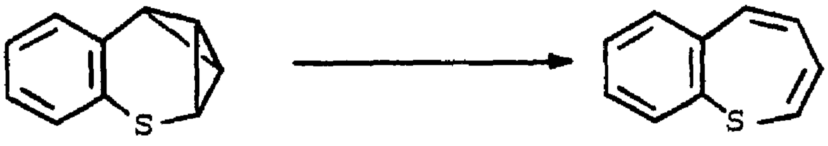
Resonance energy(β)	0.196	-0.233	0.209
REPE(β)	0.016	-0.019	0.017

* REPE represents the resonance energy per π electron

Traynelis [126] has reported the synthesis and characterization of 1-benzothiepin 132 which decomposes slowly at room temperature with extrusion of sulfur and formation of naphthalene.



Recently, Murata[127] reported the novel synthesis of 1-benzothiepin 132 by Rh'-catalyzed isomerization of 132'. All manipulations during work-up had to be carried out below -10°C in order to avoid the extrusion of sulfur.

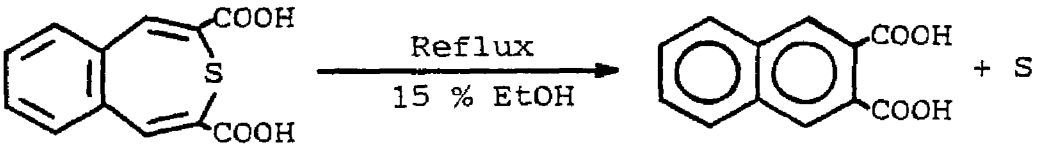


132'

132

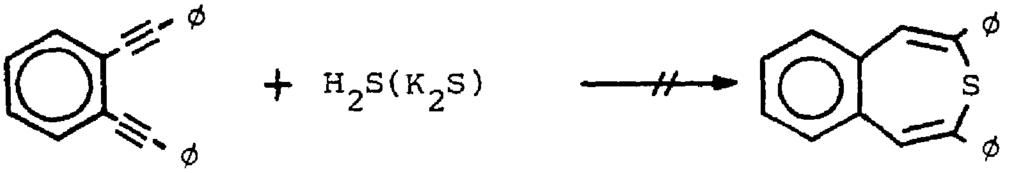
As indicated previously, 2,3-benzo-1,4-dithiocin 131 is more stable than that of 1-benzothiepin 132. Neither 2-benzothiepin 137 nor any of its derivatives are known.

Although 3-benzothiepin 133 has not been reported,[128] 3-benzothiepin-2,4-dicarboxylic acid 138 has been prepared and upon refluxing in 15 % ethanol underwent sulfur extrusion to afford 2,3-naphthalenedicarboxylic acid.[129]

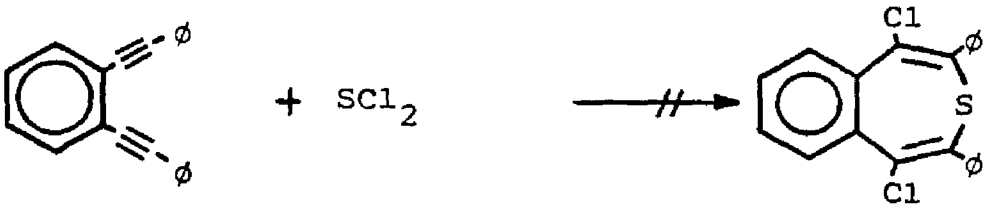


138

The preparation of compounds 139 and 140 have been attempted by Barton.[140] o-Bis(phenylethynyl)benzene 141 was treated with hydrogen sulfide or potassium sulfide in the hope of preparing compound 139, but, only the starting material was recovered. Attempted addition of sulfur dichloride, an electrophilic reagent, to o-bis(phenylethynyl)benzene 141 also failed to give compound 140.

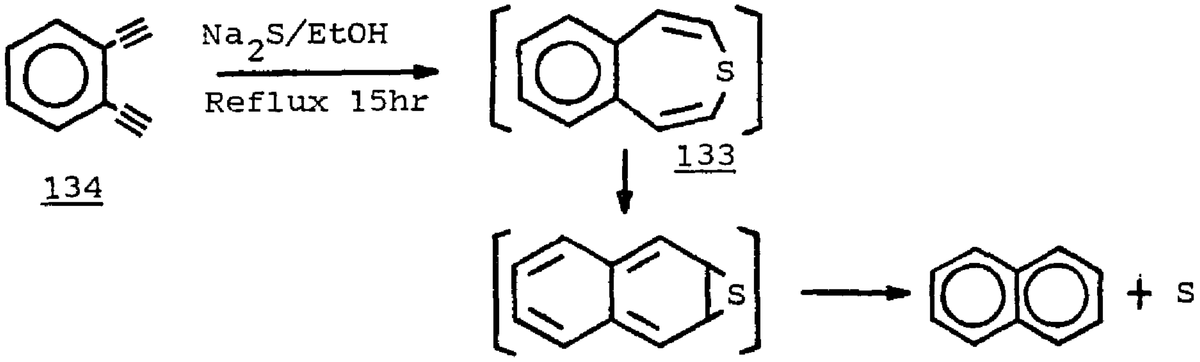


141 139

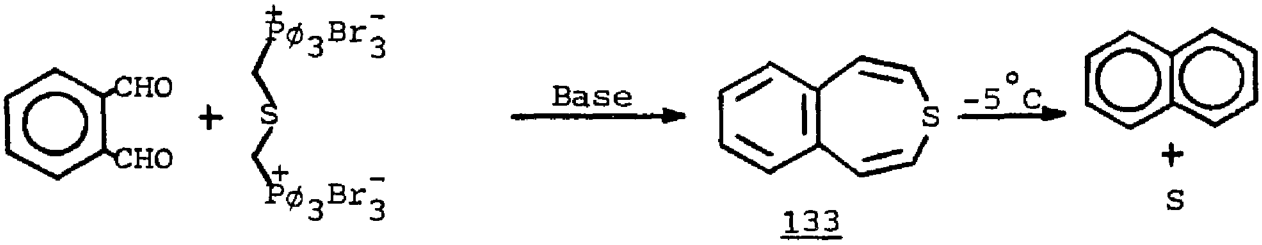


141 140

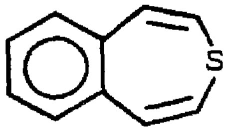
The attempted synthesis of 133 followed our successful approach to 5,6-benzo-1,2-dithiocin V. When a mixture of o-diethynylbenzene 134 and sodium sulfide in absolute ethanol was refluxed for 15 hr, only naphthalene and sulfur were obtained. Apparently unstable, the initial product 133, probably underwent a Cope rearrangement to give naphthalene episulfide, which extruded sulfur and gave naphthalene.



The above result is consistent with that of Buschken[128] who described the synthesis of 133 involving the Wittig reaction at subzero temperature as shown below. The 3-benzothiepin decomposed above -5°C to give nephthalene and sulfur.



While 3-benzothiepin 133(8 π) is as stable as 5,6-benzo-1,2-dithiocin V(10 π), 2,3-benzo-1,4-dithiocin 131 (10 π) is more stable than 1-benzo-thiepin 132(8 π).



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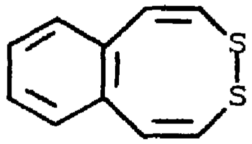
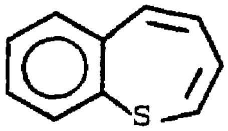
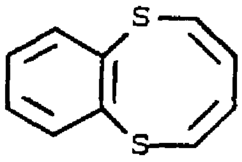


V



132

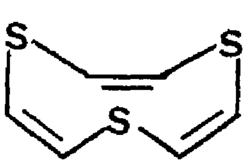


131

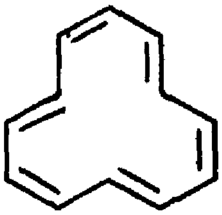
The high reactivity of V compared to 131 indicated the lack of aromaticity in V. A reason for the rather unexpected high reactivity of V might be the previously discussed reactivity of S-S unit in V. Further investigation have to be carried out to provide more information concerning reactivity of V. However because of the unavailability of V we were unable to measure its proton NMR spectrum in order to detect the presence or absence of a diamagnetic ring current.

V. 1,4,7-TRITHIANIN 142

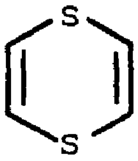
As the final part of this thesis we considered the synthesis and investigation of 1,4,7-trithianin 142, the symmetric trithia analogue of (12)Annulene.



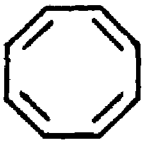
142



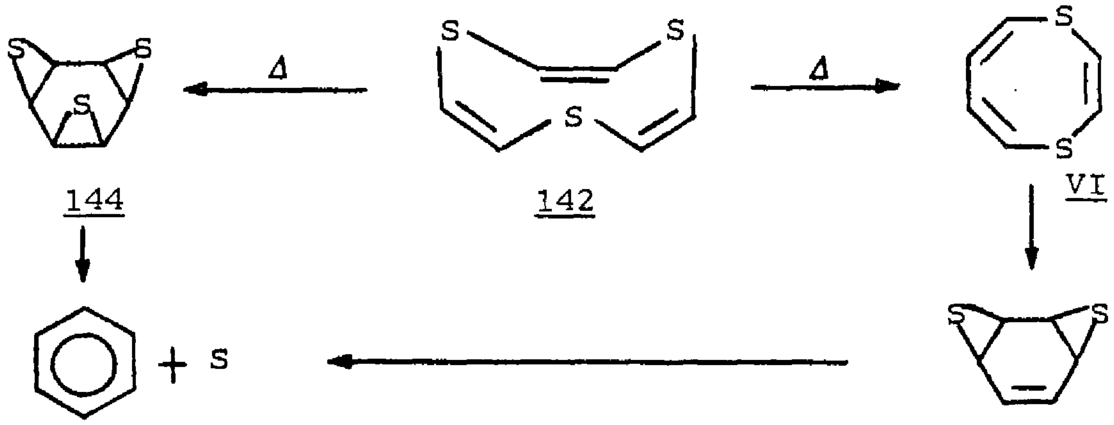
(12)Annulene



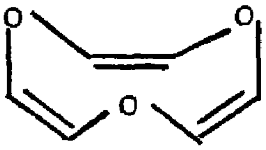
143



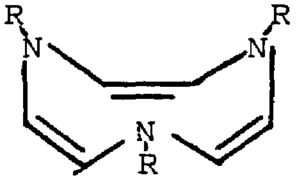
This molecule 142 is in a similar relationship to (12)Annulene as 1,4-dithiin 143 to cyclooctatetraene. 1,4-Dithiin 143 was converted to thiophene on heating with extrusion of sulfur. Therefore, 142 could be regarded as a precursor of 1,4-dithiocin VI, the potentially aromatic 10 π-electron system. Conceivably, 142 could be converted to 1,4-dithiocin VI by heating or by treatment with trimethylphosphite,[130] although benzene could be released with extrusion of sulfur as shown below.



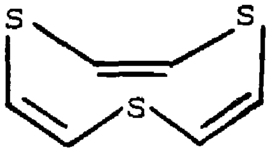
The syntheses of the corresponding oxygen and nitrogen analogues, 1,4,7-trioxanin 145 and 1,4,7-triazanin 146 have been reported by Vogel [130] and Prinzbach,[131] respectively.



145

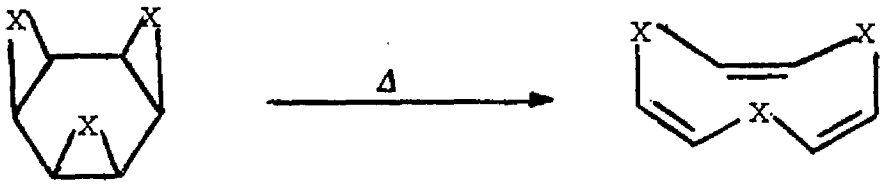


146



142

These compounds have been synthesized[130,131] by heating the corresponding cis-benzene-trioxide 147 and cis-benzene-triimine 148, respectively as shown below.

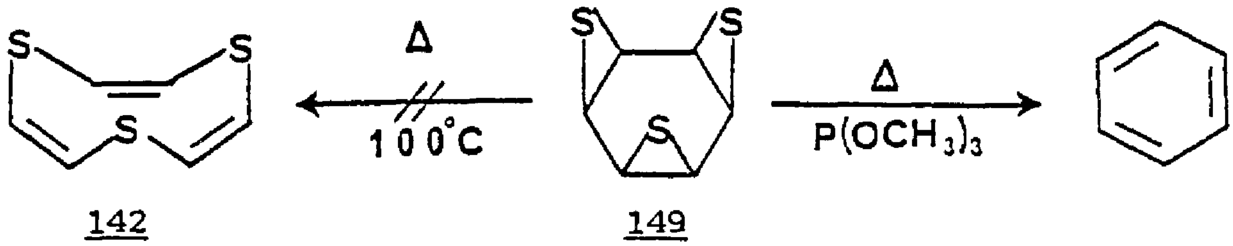


147 X= O 145

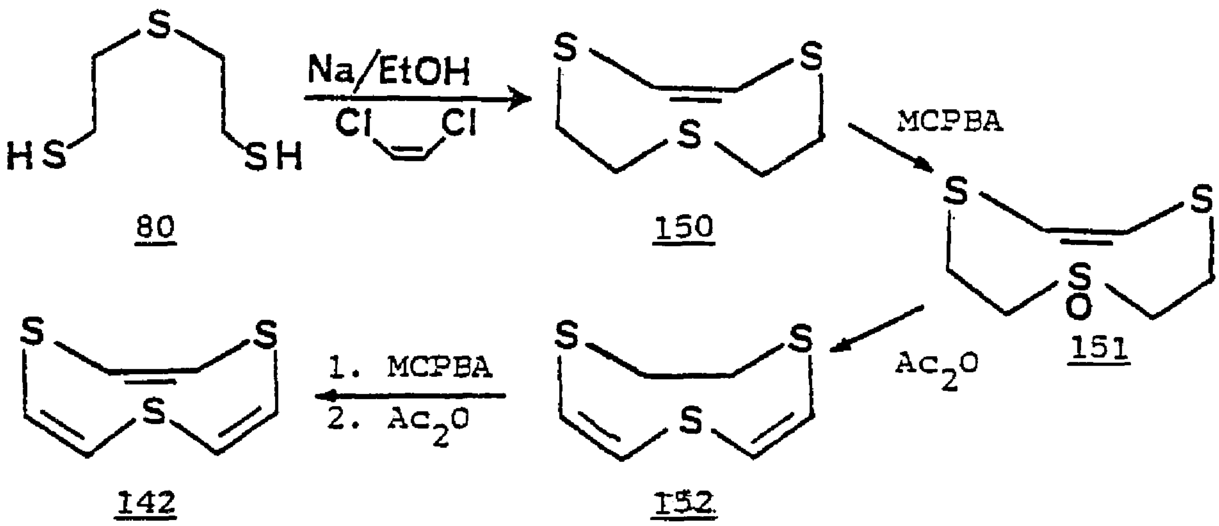
148 X= NR 146

The above thermal 3σ-3π[132] isomerization reactions are interesting preparatively useful entries to 9-membered ring.

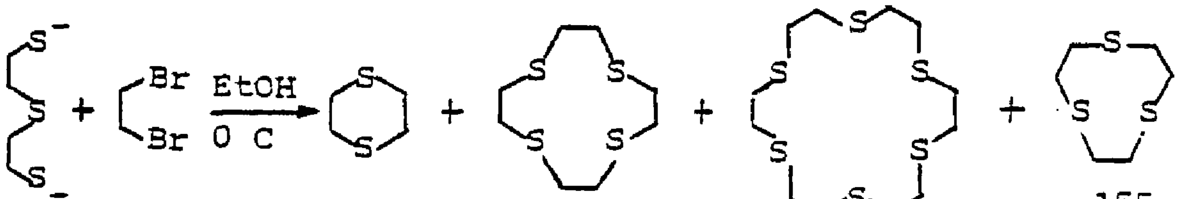
However, Prinzbach reported[133] that heating the cis-benzenetrisulfide 149 to 100°C did not afford the expected 1,4,7-trithianin 142, but decomposed with liberation of benzene. The sulfur elimination with trimethyl phosphite is even faster at 20°C.



The above unsuccessful attempt prompted us to prepare 1,4,7-trithianin 142 by a different route. The strategy of the synthetic route was summarized below.



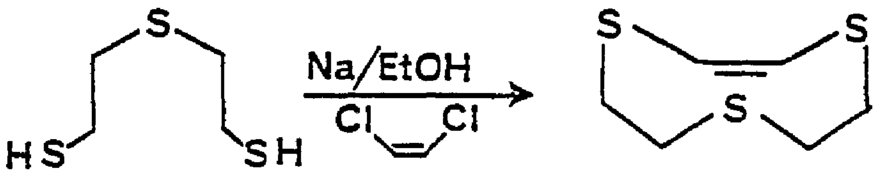
The key feature of the synthesis involves the initial construction of the nine-membered ring followed by the successive introduction of the double bonds. The tetrahydrotrithianin 150 could be obtained by the reaction of 80 with cis-1,2-dichloroethylene under high-dilution conditions. The double bonds could be introduced by successive Pummerer reaction via 151 and 152. Assess to this system conceivably could be limited by the success of the ring forming reaction. Indeed, Ochrymowycz[134] reported that the saturated 9-membered ring trithia compound 155 can be prepared under high-dilution condition from the reaction of 153 with 154 in only 0.04 % yield.



155

153 154 7.9% 0.9% 4.3% 0.04%

In fact, however, compound 150 was prepared from the reaction of bis(2-mercaptoethyl)sulfide 80 and cis-1,2-dichloroethylene in 4 % yield. The high-dilution conditions were achieved by simultaneously dripping each reactant into a large amount of rapidly stirred ethanol. The 9-membered ring compound 150 is formed via the elimination-addition mechanism shown on page 34.

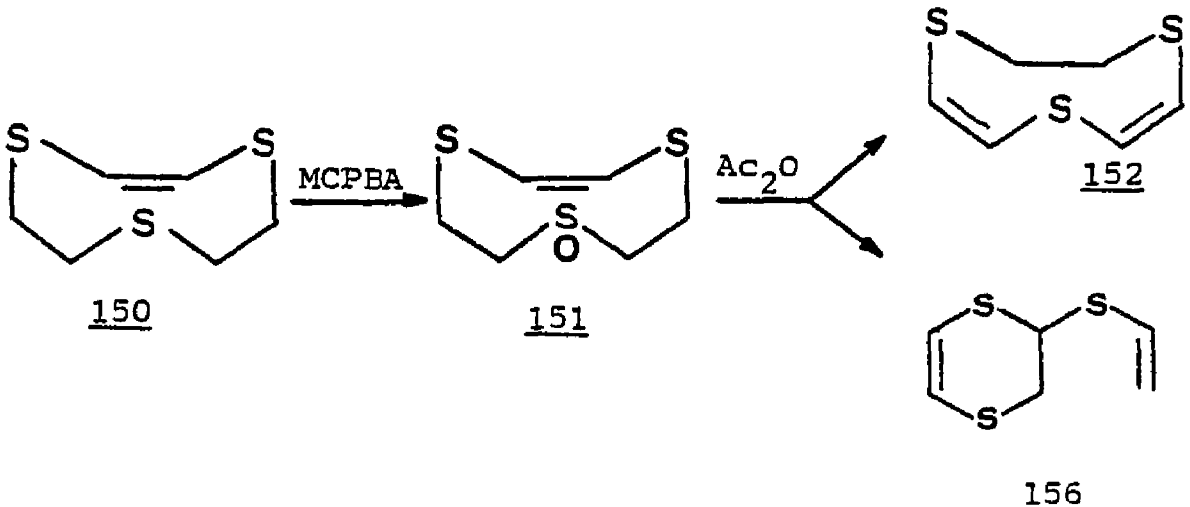


80 150

The product was assigned structure 150 on the basis of the following spectral data. The proton NMR spectrum($CDCl_3$, TMS) exhibited a singlet at δ6.30 for the olefinic protons, a triplet at δ3.4 for the methylene protons($-SHC=CH-SCH_2-$) and a triplet at δ2.90 for the methylene protons($-CH_2SCH_2-$). The three singlets at 124.7, 37.9 and 33.3 ppm in the proton-decoupled ^{13}C NMR spectrum provided additional support for the assigned structure.

Compound <u>150</u> was then oxidized with one equivalent of m-chloroperbenzoic acid to give the corresponding sulfoxide <u>151</u>. The structural assignment for <u>151</u> is based on its proton NMR, which exhibited a singlet at δ6.40 for the olefinic protons, a triplet at δ3.4 for the methylene proton α to the sulfoxide group, and a multiplet at δ3.2-3.7 for the methylene protons β to the sulfoxide group.

The sulfoxide <u>151</u> was then refluxed with acetic anhydride in the hope of preparing dihydrotrithianin <u>152</u>. However, both the diene compound <u>152</u> and the unexpected rearranged compound <u>156</u> were obtained.



<u>150</u>

<u>151</u>

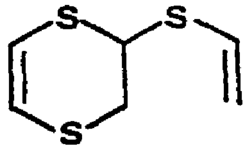
<u>152</u>

<u>156</u>

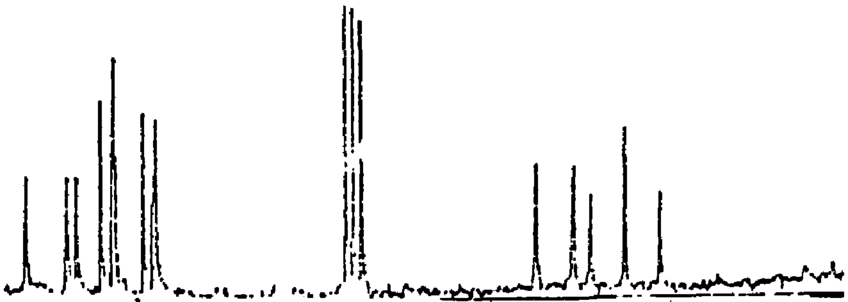
The proton NMR spectrum of diene 152 shows an AB quartet at δ6.67 and 6.38 for the olefinic protons, and a singlet at δ3.40 for the methylene protons.

The structural assignment of 156 was based on the proton NMR, the proton-decoupled and gated decoupled ^{13}C NMR, and the mass spectrum. The proton NMR exhibited a singlet at δ6.36 for the olefinic protons of the 6-membered ring, an ABX system at δ6.16 and δ5.47 typical for a vinylic sulfide protons($-S-CH=CH_2$), two multiplets at δ4.61 for the methine proton, and a multiplet at δ3.33 for the methylene protons. The proton-decoupled ^{13}C NMR spectra exhibited six singlets at 128.0, 116.7, 115.4, 113.4, 43.6, and 31.8 ppm as expected for the number of peaks and chemical shifts. The mass spectrum exhibited a molecular ion at m/e 176 and fragments at m/e 116(40 %), 84(87 %), 58(100 %). The gated decoupled ^{13}C NMR provided further confirmation for the assigned structure. The methine carbon gives rise to a doublet at 43.6 ppm, J_{CH}=158.7 Hz. The methylene carbon at 31.6 ppm appeared as a triplet with J_{CH}=145 Hz. The spectral data were fully consistent with the assigned structure. The carbon-13 spectra are shown on next page.

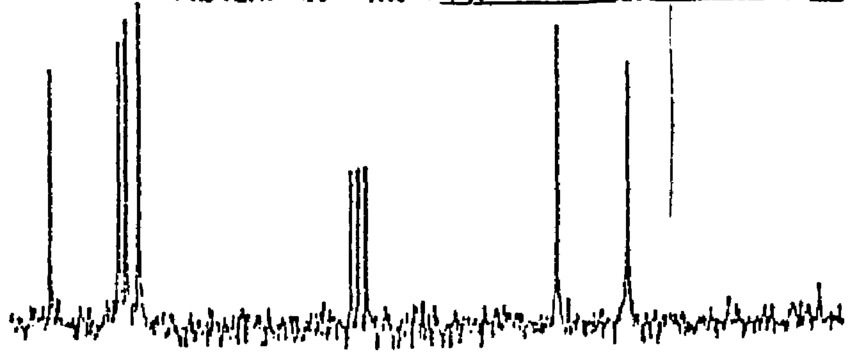
The formation of the rearranged compound 156 can be explained as the result of a transannular Pummerer reaction. An important feature in the medium-ring geometry is the existence of conformations in which opposite sides of the ring come into very close proximity with each other. The



156

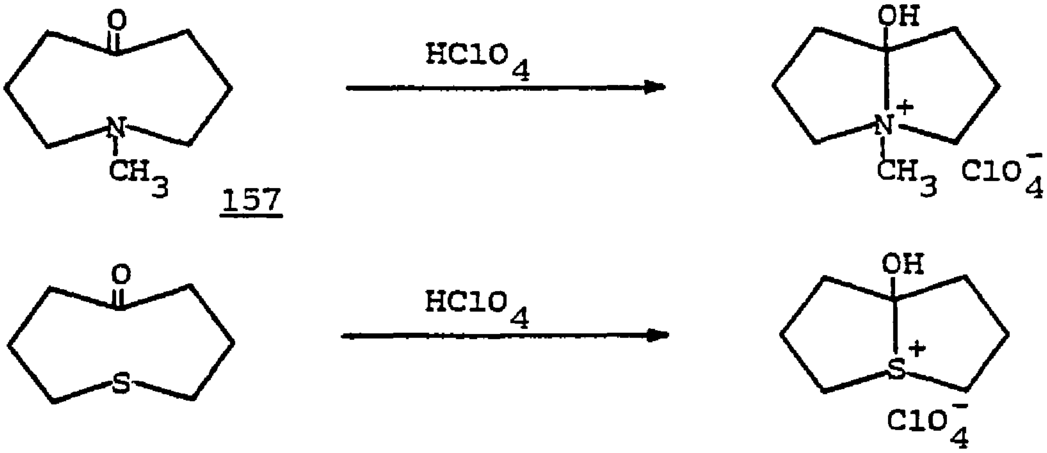


Gated decoupled ^{13}C NMR spectrum of 156



^{1}H NMR decoupled ^{13}C NMR spectrum of 156

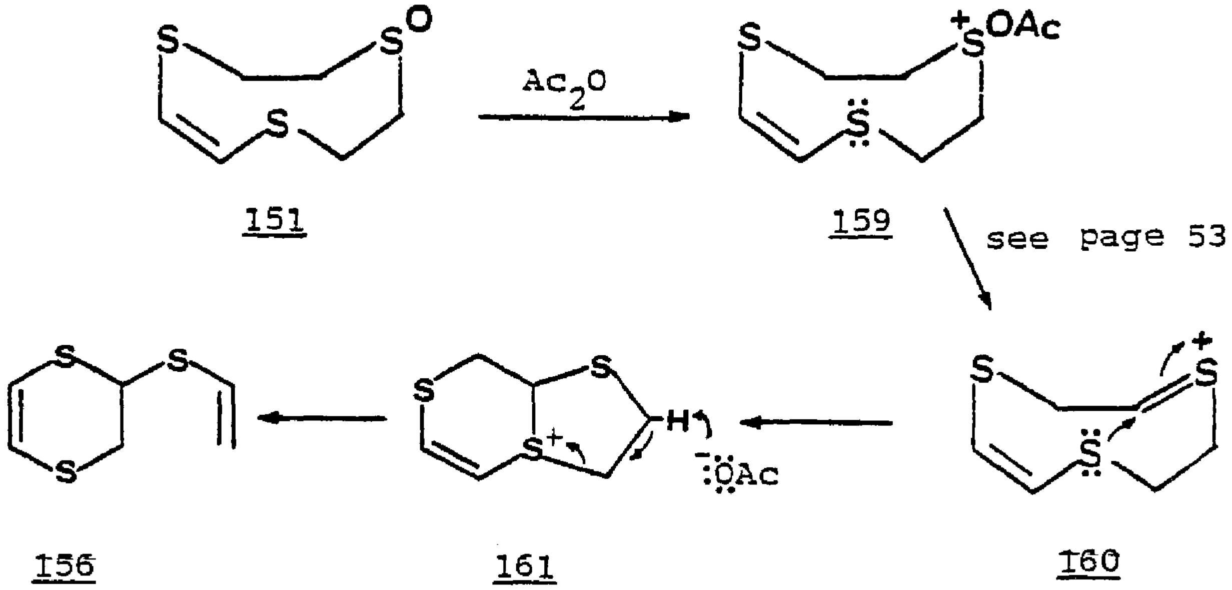
proximity effect is of considerable chemical significance. Leonard [135,136] has used spectral evidence to demonstrate interactions in compounds 157 [135] and 158 [136] between the free electrons of the nitrogen and sulfur atoms with the carbon atom of the carbonyl group. Other transannular interactions of medium-ring compounds are also well documented. [137]



157

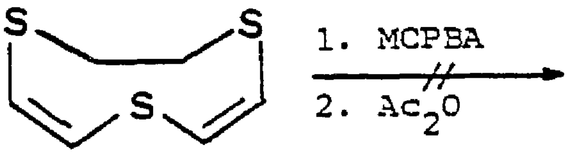
158

Therefore, the mechanism shown below for the formation of 156 from 151 may be proposed.



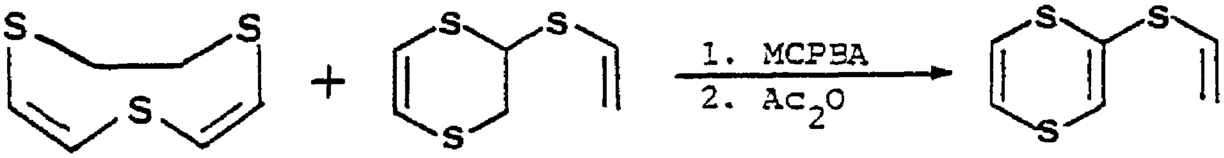
Conversion of 159, the initial intermediate of the Pummerer reaction, to the sulfonium salt 160 occurs via the pathway shown on page 53. This may be followed by a transannular interaction leading to the bicyclic intermediate 161, β-elimination by base then would give the ring opened compound 156.

With 152 in hand, conversion to 142 via Pummerer reaction of the corresponding sulfoxide was attempted. However, when 152 was oxidized and refluxed with acetic anhydride in the usual way, only polymerized material was obtained. The expected trithianin 142 could not be isolated. When the mixture of compounds 152 and 156 was oxidized and refluxed with acetic anhydride, only 162 was obtained, and no trace of the trithianin 142 was detected.



152

142



152

156

162

Clearly, 156 underwent the Pummerer reaction to give 162.[88]

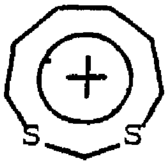
The structural assignment for 162 was based on the proton NMR spectrum, the proton-decoupled ^{13}C NMR and mass spectrum. The proton NMR($CDCl_3$,TMS) showed a doublet at δ6.35 for the olefinic proton(-SCH=CHS-), an ABX system at δ6.40 and 5.48 typical of vinylic protons and a singlet at δ6.30 for the isolated olefinic proton($-SCH{=}\overset{S}{C}S-$). The proton-decoupled ^{13}C NMR spectrum showed singlets at 130.1, 127.8, 123.0, 121.7 and 116.8 ppm as expected for the number of peaks and chemical shifts. The mass spectrum showed the molecular ion at m/e 174. The spectral data were fully consistent with the assigned structure 162.

The pure compound 156 was also oxidized and refluxed with acetic anhydride to afford as the sole product 162, identical with the one obtained from the mixture of 152 and 156 previously.

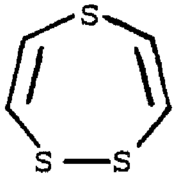
The observed reaction pattern of this novel transannular Pummerer reaction fits well into the known reactivity of nine-membered ring systems.

CONCLUSION

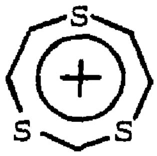
Compounds I, II, III, and V described in this thesis were expected to test the validity of Hückel's rule for 10π-heteroaromatic systems.



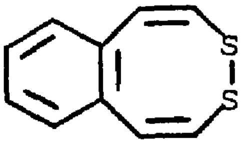
I



II



III



V

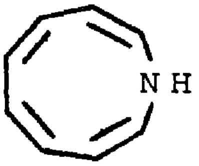
The synthesis of I has been attempted via the key intermediates 52-cis and 52-trans by several routes shown on page 43. Because of the inertness of dithiacarbonate 55, sulfur elimination in thiepin, resistence to dehydrobromination in 66 and the failure of the (2π+2π) photoaddition between 70 and 55, compound 52 was not obtained, and therefore the potential aromaticity of I could not be tested.

However, the first neutral 10π-electron sulfur heterocyclic aromatic system II has been synthesized during this thesis. Unambiguous assignments of II and its ideal reference model 83 by the proton NMR spectra, proton decoupled ^{13}C NMR and gated decoupled ^{13}C NMR spectra provided the necessary evidence for the aromaticity of II. With reference to table 6(page 73), while introducing a second double bond into cyclic sulfides changes the olefinic proton chemical shifts only slightly, large downfield shifts of the protons were found in II which are consistent with the presence of a diamagnetic ring current in II. Therefore, based on this, II may be considered an aromatic neutral 10π sulfur heterocycle in agreement with Hückel's rule.

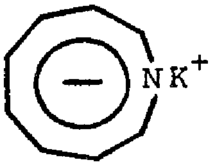
In the attempts to synthesize III, unexpected decomposition and polymerization reactions took place during the Pummerer reaction of 106 and the dehydrochlorination of 107. This decomposition could be due to transannular interaction in the medium-ring sulfur compounds. An unexpected β-elimination followed by fragmentation found when 106 was treated with n-butyllithium. All these factors made the synthesis of III not possible yet.

Starting with o-diethynylbenzene 134 followed by nucleophilic attack of sodium disulfide or of benzyl mercaptan, debenzylation, and oxidation was expected to give V, however, at temperatures of 10°C only naphthalene and sulfur were isolated, indicating a high reactivity for V, which is comparable to that of 3-benzothiepin 133.

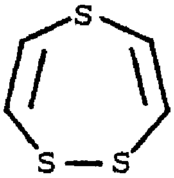
Among the 10π-electron heterocyclic systems, 1H-azonin 10a, the potassium salt of azonin 13, 1,2,5-trithiepin II, and 1,3-dithiepin anion 33 have been synthesized and shown to have aromatic character.



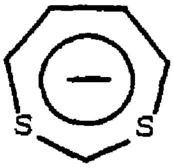
10a



13



II



33

In conclusion, the prediction of Hückel's rule for 10π-electron sulfur heterocyclic system have been documented for some molecules, however, further investigations are necessary in order to provide more information concerning the aromaticity of 10π-electron heterocyclic systems.

Therefore, summarizing proton NMR spectra of II indicated the presence of diamagnetic ring current, characterizing II is an neutral 10 π aromatic sulfur heterocycle.

However, current experimental data do not rigorously exclude the changes in the geometry as the cause for the downfield shift in going from 83 to II.

The high reactivity of V (10 π) comparable to that of 3-benzothiepin 133 (8π) prevented the measurements of the proton and carbon-13 NMR spectra and therefore the detection of the diamagnetic ring current.

EXPERIMENTAL

General

All boiling points are uncorrected. Melting points were obtained on a Buchi apparatus in a sealed capillaries. Infrared spectra were recorded on either a Perkin-Elmer 521 or 137 spectrophotometer. The proton NMR spectra were recorded on Varian A-60A or Hitachi R-24 instrument with Me_4Si as internal standard(δ 0 ppm). The proton NMR spectra at 220 MHz were taken on a Varian instrument at Rockefeller University. Carbon-13 NMR spectra were obtained on a JEOL Model PFT-100 Fourier transform instrument. UV spectra were recorded on a Cary 14 spectrophotometer. Vapor phase chromatographic analyses were performed on a Hewlett-Packard HP 5700 A using a 6 ft x $\frac{1}{4}''$ OV 17 glass column. Gas chromatographic mass spectra were obtained on a Finnegan 3300 instrument at Cornell University. Unless otherwise indicated all reactions were monitoried by thin layer chromatography.

Attempted Diels-Alder reaction between vinylene dithiacarbonate 55 and α-pyrone 57

A mixture of α-pyrone 57(0.96 g, 10 mmol)[68] and vinylene dithiacarbonate 55(1.18 g, 10 mmol)[63,64,65,66] in 15 mL chlorobenzene was refluxed for 72 hr; no reaction occurred. Similarly, no reaction occurred when the mixture was heated to 180°C(o-dichlorobenzene as solvent) or 220°C (neat). After workup by column chromatography over silica gel, most of the starting materials were recovered.

Other Diels-Alder reactions between dithia compounds such as cis-dibenzylethylene dithia ether 59, vinylene trithiacarbonate, diethyl-2-thioxo-1,3-dithiole-4,5-dicarbonate 63(used as dienophiles) and tetraphenylcyclopentadienone, furan, cyclopentadiene, anthracene, 1,3-diphenylisobenzofuran 61, N,N-dimethyl-1,3-butadiene 62(used as dienes) under various conditions all gave negative results. The starting materials were recovered in all cases.

Attempted preparation of 1,2-Trithiacarbonyl-3,5-cyclohexadiene 65

A solution of potassium methyl xanthate was prepared by[71] dissolving 3.5 g(63 mmol) of potassium hydroxide and 5.7 g(75 mmol) of carbon disulfide in 20 mL methanol.

To this solution was added 2.35 g(25mmol) of an equilibrated mixture of benzene oxide-oxepin[69,70] dropwise at 5°C. The solution was allowed to stir at room temperature for 1 day. The mixture was poured into ice water, extracted with ether, dried($MgSO_4$), evaporated under vacuum to give only polymeric and decomposed materials instead of the desired diene 65.

Preparation of 1,2-Trithiacarbonyl-4,5-dibromocyclohexane 68

A solution of potassium methyl xanthate was prepared[71] by dissolving 0.7 g(12,5 mmol) of KOH and 1.14 g(15 mmol) of carbon disulfide in 5 mL methanol. To this solution was added 1.27 g(5 mmol) of 1,2-epoxy-4,5-dibromocyclohexane 66 dropwise at room temperature. The solution was allowed to stand at room temperature for 20 hr. The solid precipitate, most of which formed over the first 1 hr, was filtered and washed with several portions of water until the filtrate was colorless. More product was recovered from the filtrate. The combined yellow solid was recrystalized twice from the mixture of methylene chloride and pet. ether to afford 0.98 g (50 %) of 68 as yellow crystals,mp. 194-196°C. ^1H NMR: δ4.2-4.9(m, 4H, methine protons), δ2.3-2.8(m, 4H, methylene protons); IR(Nujol) shows the C=S absorptions at 1088(s), 1053(s) and 1031 cm^{-1}.[71]

Preparation of 1,2-dithiacarbonyl-4,5-dibromocyclohexane 69

Mercuric acetate (1 g, 3 mmol) in 15 mL of glacial acetic acid was added to a solution of 68(0.2 g, 0.6 mmol) in 15 ml THF. The yellow color was discharged in 2-3 min and a white solid was formed. The mixture was allowed to stir for 2 hr. The precipitate was filtered off,and the filtrate was diluted with ice water, extracted with ether, dried ($MgSO_4$) and evaporated to give 150 mg(75 %) of crude product, mp. 193-197°C. The crude product was recrystalized from chloroform to yield 120 mg (60 %) of desired dithiacarbonate 69, mp. 197-199°C. ^{1}H NMR: δ4.1-4.8(m, 4H, methine protons), δ2.1-2.9(m, 4H, methylene protons); IR(Nujol) shows a band at 1705 cm^{-1}(C=O), and no absorption at 1088, 1053 and 1031 cm^{-1} for C=S.

Attempted preparation of 1,2-Dithiacarbonyl-3,5-cyclohexadiene 52

To a solution of 69(70 mg, 0.2 mmol) in 3 ml of THF was added 0.14 g(0.8 mmol) of DBN at 0°C under N_2. The mixture was stirred for 2 hr at 0-5°C, then an additional 10hr at room temperature. The reaction mixture was then poured into ice water, extracted with ether, dried($MgSO_4$) and evaporated at reduced pressure. The crude product was purified by chromatography(over silica gel eluted with benzene) to give only monoene compound instead of the desired diene compound 52. The complete identification of the monoene was not attempted.

The dehydrobromination of 69 was also carried out using other bases such as potassium t-butoxide in THF, sodium methoxide in methanol, and a mixture of lithium chloride and lithium carbonate in HMPA at 85-95°C[74]; there was no evidence for the formation of diene 52 under any set of conditions.

[2 + 2] Cycloaddition of cis-3,4-dichlorocyclobutene 70 and vinylene dithiacarbonate 55

A mixture of cis-3,4-dichlorocyclobutene 70(1.23 g,[75] 10 mmol) and dithia carbonate 55(1.18 g, 10 mmol) in 200 ml dry ether in a Pyrex tube equipped with a drying tube was immersed into ice water. The mixture was irradiated with a 450 W Hanovia mercury lamp for 4 hr. After filtering off a yellow solid(sulfur insoluble in chloroform and acetone but soluble in carbon disulfide), the filtrate was concentrated, chromatographed over silica gel eluted with pet. ether to return most of dichlorobutene 70 and some dithiacarbonate 55.

The photolysis also failed in the presence of sensitizer.

Preparation of 1,2,5-Trithiepane 81

In a procedure similar to that of Field and Foster,[51] bis-(2-mercaptoethyl)sulfide 80 (30.8g,0.2 mole) in ether(400 ml) was added dropwise to a solution of $FeCl_3.6H_2O$(162 g, 0.6 mole) in ether(1500 mL) and acetic acid(200 mL) under reflux over 24 hr. The mixture was then kept under reflux for 2 days, after which the ether was distilled until the volume was 1200 mL. The mixture was then washed with 700 mL portions of water until the aqueous layer was neutral. The first two washes were back-extracted twice with 100 ml portions of ether. The ether layers were combined, and an aqueous solution of I_2-KI was added dropwise with vigorous stirring to remove unchanged 80 until a faint iodine color remained. An aqueous solution of sodium thiosulfate then was added dropwise until the iodine color disappeared. The resulting organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered and evaporated to give crude 81 as a viscous liquid. Distillation of the crude product using a Vigreux column gave 16.63g(55 %) of colorless 1,2,5-trithiepane 81, bp 61-63°C(0.2 mm). IR(neat) 2900 (s), 1410(s), 1280(s), and 830(s) cm^{-1}; ^1H NMR δ 3.1(s, in CCl_4) or δ2.7(s,in benzene) or δ3.05(s,in $CDCl_3$); Mass spectrum m/e 154(M^+); ^{13}C NMR two peaks at 37.6 and 31.2 ppm(from TMS); Gated decoupled ^{13}C NMR 37.6 ppm(t of t,C_A α to disulfide,$J_{C_A-H_A}=J_{C_A-H_{A'}}=140$Hz, $J_{C_A-H_B}=J_{C_A-H_{B'}}=2.6$ Hz), 31.2 ppm(t of m, C_B α to sulfide).

Preparation of 1,2,5-Trithiepane 5-Oxide 82

i) Via m-chloroperbenzoic acid

m-Chloroperbenzoic acid(5.70 g, 33 mmol) in 25 mL distilled chloroform was added to a solution of 1,2,5-trithiepane 81 (4.56 g, 30 mmol) in 80 mL $CHCl_3$ at 0°C. After stirring at 0-5°C for 2 hr, thin layer chromatography indicated that the starting material 81 had disappeared completely. The reaction mixture was then diluted with 100 mL $CHCl_3$, and to it was added slowly saturated $NaHSO_3$ solution to decompose the excess peracid. The organic layer was neutralized with cold saturated Na_2CO_3(or $NaHCO_3$) solution, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$ and the solvent evaporated under vacuum to give the crude product 82 (4.08 g, 81 %). Recrystalization from CCl_4 gave white crystal 3.2 g(60 % overall),mp 95-96°C(reported[51] mp 95-96°C).

ii) Via sodium periodate

In a procedure similar to that of Field and Foster,[51] a solution of sodium periodate (2.81 g, 13.15 mmol) in water(55 mL) was added to a stirred solution of 1,2,5-trithiepane 81 (2 g,13.15 mmol) in 150 mL of tetrahydrofuran. The temperature of the mixture was maintained at 0-9°C throughout the 30 minute addition and for 3 hr thereafter. Tetrahydrofuran(50 mL) then was added, and stirring was continued for 5 hr without cooling. The mixture was cooled to 0°C and filtered, and the residue was washed with THF. Evaporation of the combined filtrate gave a yellow oil suspended in an aqueous layer. The oil was extracted with chloroform. Evaporation of the extract left 1.45 g of yellow solid(66%), mp 84-89°C. Recrystalization of the crude product from CCl_4 gave white crystals, mp 95-96°C(40 % overall). IR(Nujol): 1025(s) and 1005(s) cm^{-1}; ^1H NMR($CDCl_3$,TMS) δ2.5-3.4(m), and 3.4-4.3(m).

Preparation of 6,7-Dihydro-1,2,5-Trithiepin 83

i) Via Pummerer reaction of 1,2,5-trithiapane 5-oxide 82

1,2,5-trithiepane 5-oxide 82 (1.52 g, 10 mmol) in 25 mL freshly distilled acetic anhydride was refluxed for 35 minutes under nitrogen. The dark brown mixture was poured into ice water and extracted with ether. The extract was then neutralized with saturated Na_2CO_3 solution, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$ and evaporated under vacuum. The crude product was purified by column chromatography over silica gel eluted with petroleum ether to give 0.29 g(20 %) of 105 as a pale yellow liquid 83. The crude product was also purified by vacuum distillation, bp 61.5°C/ 0.06 mm.

The preparation of the compound 105 was also carried out without the isolation of the corresponding sulfoxide 82 as follows: m-Chloroperbenzoic acid(7.5g,44mmol) in 100 mL chloroform was added to 1,2,5-trithiepane(6.08g, 40 mmol) in 80 mL chloroform at 0°C. The temperature of the mixture was maintained at 0-5°C for 2 hr thereafter. After the solvent was evaporated using a rotary evaporator, the residue was added to 45 mL freshly distilled acetic anhydride and refluxed for 30 minutes under nitrogen. It was worked up in the usual way to give compound 83 (0.77g, 12%). Both of the procedures described above gave 83 in the same yield(12 %) from compound 81.

ii) Via chlorination-dehydrochlorination

Recrystallized(from $CHCl_3$) N-chlorosuccinimide(16.3 g, 0.12 mole) was added to a solution of 1,2,5-trithiepane 81 (15.4 g, 0.1 mole) in 300 mL distilled CCl_4 at 0°C under nitrogen over a 30 minute period. The mixture was allowed to stir at 10-15°C for an additional 3 hr. A solid, succinimite, formed during this period. After filtration, the filtrate was evaporated under vacuum(water bath below 25°C), and the residue dissolved in 350 mL distilled benzene. To the solution was added triethylamine(40.4 g, 0.4 mole) at 0°C over 30 min period. The mixture was then heated at reflux for 40 hr, poured into 200 mL ice-cold 10 % HCl and extracted with ether. The extract was then washed with water, dried($MgSO_4$) and concentrated. The crude product was distilled under vacuum to afford 2.59 g(17 %) of 83, bp 61.5-62°C/0.06 mm. The pale yellow liquid is very stable for more than one year. It survives in GC up to 140°C without decomposition. The ^{1}H NMR($CDCl_3$,TMS) shows δ6.17 (H_B of AB quartet, 1H, J= 9 Hz, cis, proton α to sulfide), δ5.99(H_A of AB quartet, 1H, J= 9 Hz, cis, proton α to disulfide linkage), δ3.83(t, 2H, $-S-CH_2-$, J = 6 Hz) and δ3.11 (t, 2H, $-SS-CH_2-$, J = 6 Hz); IR(neat) 3020 cm^{-1}, 2920 cm^{-1}, 1530 cm^{-1}, 1410 cm^{-1}, 1270 cm^{-1}, 790 cm^{-1}, 600-700 cm^{-1}, and 400-500 cm^{-1}; UV: λ_{max}^{EtOH} 263 nm(2.5 x 10^3), 321 nm(2.7 x 10^3); MS(70 ev):m/e at 150(69.1 %, M^+), 105(100 %), 58 (45.3%) and 45(52.4 %); ^{13}C NMR($CDCl_3$, TMS):singlets at 126.6 ppm(carbon α to sulfide), 119.4 ppm(carbon α to disulfide), 33 and 35.7 ppm(methylene carbons); Gated decoupled ^{13}C NMR shows the resonance at 119.1 ppm(doublet of doublet, carbon α to disulfide linkage, $J_{C_A-H_A}$= 176.3 Hz, $J_{C_A-H_B}$= 3.65 Hz) and 126.6 ppm(two sets of quartets, carbon α to sulfide, $J_{C_B-H_B}$= 171 Hz, $J_{C_B-H_A}$=$J_{C_B-H_C}$=$J_{C_B-H_{C'}}$=5.8 Hz)

<u>Preparation of 1,2,5-Trithiepin II</u>

m-Chloroperbenzoic acid(1.81 g, 10.5 mmol) in 22 mL chloroform was added to 6,7-dihydro-1,2,5-trithiepin(1.5 g, 10 mmol) in 7 mL chloroform at 0°C under nitrogen. The temperature of the mixture was maintained at 0-5°C for 1 hr thereafter. After the solvent was evaporated using a rotary evaporator, the residue was added to 30 mL freshly distilled acetic anhydride and refluxed for 30 minutes under nitrogen. The dark brown mixture was poured into ice water and extracted with ether. The extract was then neutralized with saturated Na_2CO_3 solution, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$ and evaporated under vacuum. The crude product was purified by column chromatography over silica gel eluted with petroleum ether to afford 90 mg(6.1 %) of yellow liquid 1,2,5-trithiepin II. In another run the crude product was also purified by preparative TLC(CCl_4-petroleum ether 1:1) at 0°C under CO_2 giving a 6.1 % yield also. The compound is stable at 0°C for more than 5 months in solution but easily polymerized at room temperature without solvent. It survives in GC up to 140°C without decomposition; no 1,4-dithiin or thiophene was detected. The ^1H NMR shows resonances at δ7.24(AB quartet, 2H, J= 9 Hz, cis, proton α to sulfide), δ 6.57(AB quartet, 2H, J= 9 Hz, cis, proton α to disulfide linkage); IR(neat):3090-3200 cm^{-1}, 1560 cm^{-1}, 1290 $cm^{-1}$and 805-825cm^{-1} ; UV:$\lambda_{max}^{pet.\ ether}$ 263 nm(2.25×10^3), 296 nm(1.72×10^3), and 353 nm(1.40×10^3);GC-MS shows one peak and fragments as follow: m/e 148(29.9 %, M^+), 116(51.8 %, M-32), 103(100 %, M-45), 84(46 %, M-64), 64(14.9 %, M-84), 58(92 %, M-90), 57(48.6 %, M-91) and 45(86 %, M-103); ^{13}C NMR($CDCl_3$,TMS): singlets at 131.5 ppm(carbon α to disulfide linkage) and 128.6 ppm(carbon α to sulfide); Gated decoupled ^{13}C NMR shows the resonances at 131.5 ppm splitting into a doublet ($J_{C_A-H_A}$ = 179.7 Hz, carbon α to disulfide linkage) and 128.6 ppm splitting into two sets of quartets($J_{C_B-H_B}$ = 170.4 Hz, $J_{C_B-H_A}$ = 10.3 Hz and $J_{C_B-H_C}$ = 6.9 Hz, carbon α to sulfide).

Preparation of 1,3,6-Trithiacyclooctane 106

Bis(2-mercaptoethyl)sulfide(15.4 g, 0.1 mole) in 75 mL absolute ethanol and 75 mL dried THF was added to the solution of sodium(4.83 g, 0.21 mole) in 500 ml absolute ethanol. The mixture was refluxed for 30 min to reach equilibrium. A solution of dibromomethane(18.81 g, 0.103 mole) in 75 mL THF was added dropwise to the above mixture at reflux temperature over a 4 hr period under nitrogen. The mixture was then kept under reflux for 20 hr, after which the solvent was distilled until the volume was 200 ml. The mixture was poured into ice water, extracted with ether, dried($MgSO_4$), filtered and evaporated to give a crude liquid product. The crude product was purified by column chromatography over silica gel eluted with 10 % benzene in petroleum ether to afford pure colorless liquid 1,3,6-trithiacyclooctane 106 in 32 % yield, bp 98-101°C/ 0.31 mm. ^{1}H NMR($CDCl_3$,TMS) shows resonances at δ4.30(s, S-CH_2-S, 2H) and δ2.93(s, 4H, -S-CH_2CH_2-S-); ^{13}C NMR shows three singlets at 38.8, 35.5 and 31.2 ppm as expected; IR(neat): 2950,1430 cm^{-1}; GC-MS(70 ev) exhibits fragment ions at m/e 106(100%), 78(55%), 60(64%) and 45(94%).

Attempted preparation of 7,8-dihydro-1,3,6-trithiocin 104

i) Via Pummerer reaction from 1,3,6-trithiacyclooctane 96

m-Chloroperbenzoic acid(4.52 g, 28 mmol) in 70 mL chloroform was added to 1,3,6-trithiacyclooctane 96 (4.1 g, 25 mmol) in 25 mL chloroform at 0°C under N_2. The temperature of the mixture was maintained at 0-5°C for an additional 2 hr. After the solvent was evaporated at reduced pressure, the residue was dissolved in 50 ml of freshly distilled acetic anhydride and refluxed for 30 min under nitrogen. The dark brown mixture was poured into ice water, neutralized with cold 10 % NaOH solution, and extracted with ether. The extract was then dried over anhydrous $MgSO_4$ and evaporated under vacuum giving no expected compound 104 but decomposed materials which were not identified further.

ii) Via the intermediate 107

Bis-divinylmercaptomethane 126 obtained from the methods reported by Overberger[109], Bransma,[110] and Grohmann[41] was used as one of the starting materials. Another starting material, sulfur dichloride, was purified by vacuum distillation to remove chlorine, followed by distillation at atmospheric pressure.

To a stirred solution of bis-divinylmercaptomethane (9.24 g,75 mmol) in 250 mL of dry tetrahydrofuran was added dropwise a solution of freshly distilled sulfur dichloride (7.73 g, 75 mmol) at 0°C over 20 min period under nitrogen. The mixture was allowed to stir at 5-10°C for an additional 1.5 hr. During this period the reaction mixture was monitored by GC and ^{1}H NMR to ensure the complete disappearance of bis-divinylmercaptomethane 126 and the formation of 4,8-dichloro-1,3,6-trithiacyclooctane 107. The formation of 107 was detected by ^{1}H NMR : δ5.49 (t, 2H, J= 7 Hz), δ4.18(s, 2H, $-SCH_2S-$) and δ3.35(d, 4H, J = 7 Hz). To the clear solution, decanted from the polymeric material, was added potassium t-butoxide(33.6 g, 0.3 mole) at -10°C for 30 min under N_2. The mixture was allowed to stir at room temperature for an additional 15 hr. The dark brown mixture was poured into ice water, neutralized with 10 % hydrochloric acid, extracted with ether, washed with water, dried ($MgSO_4$) and evaporated under vacuum to give decomposed and polymeric materials, and none of the expected diene 104. Repetition of the reaction using powdered KOH, triethylamine, DBN and diisopropylethylamine as bases still gave none of expected compound 104, but only decomposed material.

Preparation of 2,2'-dimethyl-1,3,6-trithiacyclooctane 110

To a solution of 3 mL of $BF_3 \cdot Et_2O$ in 250 mL chloroform was added dropwise a 1:1 mixture of bis(2-mercaptoethyl)-sulfide 80 (4.62 g, 30 mmol) and 2,2'-dimethoxypropane (3.13 g, 30 mmol) in 150 mL chloroform at reflux over a 10 hr period. The mixture was allowed to reflux for an additional 5 hr and was poured into ice water. The resulting mixture was neutralized with 10 % $NaHCO_3$ and extracted with ether. The extract was washed with water, dried over anhydrous $MgSO_4$ and concentrated at reduced pressure to give 3 g of crude product 110. The crude product was chromatographed over silica gel(eluted with 15 % benzene in petroleum ether) to give 1.16 g(20 %) of colorless liquid product 110. The ^1H NMR shows resonances at δ3.07 (s, 8H, $-S-CH_2CH_2-S-$) and δ 1.61(s, 6H, CH_3); IR(neat): 2980, 1430 and 1370 cm^{-1}.

Attempted preparation of 2,2'-dimethyl-7,8-dihydro-1,3,6-trithiocin 111

To a solution of 2,2'-dimethyl-1,3,6-trithiacyclooctane 110(1.16 g, 6.5 mmol) in 15 mL $CHCl_3$ was added m-chloroperbenzoic acid(1.23 g, 7.1 mmol) in 20 mL $CHCl_3$ at 0°C. The temperature of the mixture was maintained at 0-5°C for an additional 2 hr. After the solvent was evaporated at reduced pressure, the residue was added to 35 mL of freshly distilled acetic anhydride , refluxed for 30 min under N_2, and worked up as described as page 124. The crude product was chromatographed over silica gel eluted with a mixture of petroleum ether and CCl_4(1:1)to give none of the expected product 111 but 1,2,5-trithiepane 81 instead.

Preparation of cis-methylmercapto-(2-methylmercapto)ethylmercaptoethylene 127

Sodium(0.35 g, 15 mmol) was added in small portions to a solution of 6,7-dihydro-1,2,5-trithiepin 83 (0.9 g, 6 mmol) in dry liquid ammonia(100 ml) at -78°C. The solution was allowed to stir for an additional 2 hr. Excess methyl iodide (4.26 g, 30 mmol) was then added to the above solution, which was allowed continue stirring at -50°C for 1 hr, 0°C for 2 hr and room temperature for 1 hr. Ammonium chloride was added and the solvent was allowed to evaporate followed by addition of ice water. The ether layer was separated and the aqueous layer was extracted with ether. The combined extract was dried($MgSO_4$) and evaporated at reduced pressure to give crude 127 which was purified by column chromatography over silica gel using 10 % benzene in petroleum ether, to give the pure yellow liquid 127(0.86 g, 80 %). The ^1H NMR($CDCl_3$,TMS) shows resonances at δ6.30(AB quartet, 2H, olefinic protons), δ2.8-3.15(m, 4H, methylene protons), δ2.4(s, 3H, $-CH{=}CHSC\underline{H}_3$) and δ2.20 (s, 3H, $-CH_2CH_2SC\underline{H}_3$); ^{13}C NMR shows six singlets at 127.2, 121.6, 34.7, 33.6, 16.9 and 15.4 ppm. IR(neat): 3030, 2980, 1550, 1430, 1340, 830 and 730 cm^{-1}; GC-MS(70 ev) exhibits peaks at m/e180(M^+, 14 %), 75(100 %), 61 (54.4 %), 45(39.8 %) and 47(37.5 %).

Preparation of 2-methoxy-1,3,6-trithiacyclooctane 108

Bis(2-mercaptoethyl)sulfide(5.4g, 40 mmol) in 50 mL absolute ethanol was added to a solution of sodium(2.3 g, 100 mmol) in 250 mL absolute ethanol. The mixture was refluxed for 30 min to reach equilibrium. A solution of α,α'-dichloromethylmethyl ether(4.6 g, 40 mmol) in 20 mL distilled CH_3CN was added to the above mixture at $0^\circ C$ under nitrogen. The resulting mixture was allowed to reflux for 10 hr, after which the solvent was distilled until the volume was 80 mL. The mixture was poured into ice water, extracted with ether, dried($MgSO_4$), filtered and evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel to afford 108 as a white solid,mp $65-66.5^\circ C$(0.22 g,12 %). The ^1H NMR($CDCl_3$, TMS) shows resonances at $\delta 6.60$(s, 1H, methine proton), $\delta 3.5$ (s, 3H, methyl protons) and $\delta 2.9-3.2$(m, 8H, methylene protons).

Preparation of 2-methoxy-7,8-dihydro-1,3,6-trithiocin 128

i) Via the cyclization of compound 129

To a solution of 6,7-dihydro-1,2,5-trithiepin 83 (1.5g, 10 mmol) in 180 mL of dry liquid ammonia at $-78^\circ C$ was added sodium(0.58 g, 25 mmol) in small portions. The mixture was kept stirring for an additional 2 hr at $-78^\circ C$ under nitrogen and the ammonia allowed to evaporate. The residue was dissolved in 175 mL CH_3CN followed by addition of α,α'-dichloromethylmethyl ether(1.16 g, 10 mmol) in 2 mL CH_3CN dropwise at 0°C under nitrogen. The resulting solution was stirred at room temperature for 20 hr. The reaction mixture was poured into ice water, extracted with ether, dried($MgSO_4$) and evaporated at reduced pressure. The residual yellow oil was chromatographed over silica gel(eluted with 10 % benzene in petroleum ether) to afford 0.18 g(9.1 %) of yellow liquid product <u>128</u>. ^1H NMR($CDCl_3$,TMS):δ6.73(AB quartet, 1H, J= 9 Hz, cis), δ6.10(AB quartet, 1H, J = 9 Hz, cis), δ6.10(s,1H, methine proton), δ3.50(s,3H, methyl protons) and δ2.76-3.30(m, 4H, methylene protons).

ii) Via Pummerer reaction from compound <u>108</u>

m-Chloroperbenzoic acid(1.06 g, 6 mmol) in 15 mL chloroform was added to 2-methoxy-1,3,6-trithiocin <u>108</u>(0.98 g, 5 mmol) in 8 mL chloroform at 0°C under N_2. The temperature of the mixture was maintained at 0-5°C for an additional 2 hr. After the solvent was evaporated under vacuum, the residue was dissolved in 15 mL of freshly distilled acetic anhydride and refluxed for 35 min under N_2. The dark brown mixture was poured into ice water, neutralized with cold 10 % NaOH solution and extracted with ether. The extract was then dried over anhydrous $MgSO_4$ and evaporated under vacuum giving none of the expected compound <u>128</u> but only decomposed material.

Preparation of Diphenyl keteneacetal of 1,3-dithia-4-cyclohexene 120

m-Chloroperbenzoic acid(1.47 g, 83 mmol) in 15 mL chloroform was added to a solution of diphenyl ketene acetal of 1,3-dithiacyclohexane 117(1.9 g, 67 mmol)[106] in 15 mL chloroform at 0°C under N_2. The temperature of the mixture was maintained at 0-5°C for 2 hr. After the solvent was evaporated, the residue was dissolved in 30 ml freshly distilled acetic anhydride and refluxed for 40 min under nitrogen. It was worked up in the usual way to give crude solid product 120 which was purified by preparative TLC(benzene + pet. ether 1:1) to give 66 mg of pure 120 (4.5 %) as white solid.

^1H NMR($CDCl_3$,TMS): δ7.30(m, 10H, aromatic protons), δ6.3 (m, 2H, olefinic protons) and δ3.2(d,2H,methylene protons).

Preparation of diphenyl keteneacetal of 1,3-dithiacycloheptane 121

To a solution of 2-trimethylsilyl-1,3-dithiacycloheptane(0.8 g, 1.9 mmol) in 40 mL dry THF was added a solution of 2.4 M n-butyllithium(1.6 mL, 1.9 mmol) in n-hexane at -78°C under N_2. The mixture was allowed to stir at room temperature for 1 hr. To the resulting reaction mixture was added a solution of benzophenone(0.8 g, 4.4 mmol) in

6 mL of dry THF. The mixture was then stirred for 1 hr and poured into ice water, and extracted with ether. The combined extract was dried over anhydrous $MgSO_4$ and evaporated at reduced pressure. The residue was chromatographed over silica gel eluted with 15 % benzene in pet. ether to give 0.4 g of 121 as solid,which was recrystalized from benzene-pet. ether to afford 0.30 g(53 %) of 121 as white crystals, mp 162-163°C. ^1H NMR δ7.22(broad s, 10H, aromatic protons), δ2.8-3.1(m, 4H) and δ1.85-2.2(m, 4H).

Preparation of diphenyl keteneacetal of 1,3-dithia-cyclohepta-4,6-diene 122

m-Chloroperbenzoic acid(4.32 g, 25 mmol) in 20 ml of chloroform was added to diphenyl ketenethioacetal 121(3.55 g, 12 mmol) in 20 mL of $CHCl_3$ at 0°C under N_2. The mixture was allowed to stir at 0-5°C for an additional 2 hr. After the solvent was evaporated at reduced pressure, the residue was dissolved in 70 mL freshly distilled acetic anhydride and refluxed for 50 min under N_2. The brown mixture was then poured into ice water, neutralized with cold 10 % NaOH solution and extracted with ether. The combined extract was then dried($MgSO_4$) and evaporated to give crude material,which was chromatographed over silica gel eluted with petroleum ether to afford 0.18 g of pure 122 (5 %) as yellow crystals,mp 88-89°C(reported mp. 88-89°C from different route[106]). ^{1}H NMR($CDCl_3$,TMS): δ7.26(s, 10H, aromatic protons), δ6.35(AA'BB', 4H, olefinic protons).

Attempted preparation of 2-Trimethylsilyl-1,3,6-trithiacyclooctane 123

To a stirred solution of 1,3,6-trithiacyclooctane 106(2.49 g, 15 mmol) in 60 mL dried THF was added a solution of 2.5 M n-butyllithium(7.5 mL, 16.5 mmol) in n-hexane at -78°C under nitrogen. The reaction mixture was allowed to warm to room temperature and 3 hr thereafter. To the resulting mixture was added an excess of distilled trimethylsilyl chloride(3.25 g, 30 mmol) at -78°C and was allowed to stir at room temperature for 1 hr. The reaction mixture was then poured into ice water, extracted with ether, dried($MgSO_4$) and evaporated at reduced pressure to give an oil. Chromatography of the oil over silica gel eluted with 2 % ether in pet. ether to afford the unexpected 2-mercaptoethylvinyl sulfide 124(0.9 g, 50 %) instead of the desired silylated compound 123. The structure assignment of 124 was mainly based on ^{1}H NMR and IR shown below. The ^{1}H NMR($CDCl_3$, TMS) shows resonances at δ6.3(AB_2 vinylic, 1H), δ5.25(AB_2 vinylic , 2H),centered at δ3.5 and 2.9(m, 4H, methylene protons) and δ1.3(t, 1H, thiol proton).

Preparation of 2-methylmercaptoethylvinyl sulfide 125

In order to confirm the formation of compound 124 in the attempted preparation of 123, the preparation of 125 was carried out as follow. To a stirred solution of 1,3,6-trithiacyclooctane 106(2.49 g, 15 mmol) in 60 ml dry THF was added a solution of 2.5 M n-butyllithium(7.5 ml, 16.5 mmol) in n-hexane at -78°C under N_2. The reaction mixture was allowed to warm to room temperature and 3 hr thereafter. To the resulting mixture was added an excess of methyl iodide(4.26 g, 30 mmol) at -78°C under N_2. The mixture was allowed continue stirring at room temperature for 3 hr, poured into ice water, and extracted with ether. The combined extract was then dried($MgSO_4$) and evaporated under vacuum to give an oil which was distilled and chromatographed over silica gel(eluted with 5 % benzene in pet. ether) to afford 1.1 g(52 %) of 125 as a pale yellow liquid. ^1H NMR($CDCl_3$, TMS):δ6.3(AB_2 vinylic, 1H), δ5.32 (AB_2 vinylic, 2H), δ2.7-3.0(m, 4H, methylene protons) and δ2.15(s, 3H, methyl protons); IR(neat): 3020, 2960, 1590 and 1430 cm^{-1}.

Preparation of o-bis(β-chlorovinyl)benzene 135

Triphenylphosphine(13.12 g, 25 mmol) was placed in a 500 mL three-neck flask equipped with an addition funnel, stirrer and dry ice-acetone condenser topped with a N_2 inlet tube. Anhydrous ether(200 ml) and methylene chloride (4.95 g, 28 mmol) were added. The mixture was stirred rapidly while 18.4 ml of 2.4 M n-butyllithium(22 mmol) in n-hexane was added dropwise over a 30 min period at -40°C. After the addition had been completed, the solution was orange, and a considerable amount of yellow solid was present. When recrystalized o-phthaldehyde(2.68 g, 20 mmol) in 20 ml anhydrous ether was added the orange solution immediately turned light yellow and more solid was formed. The mixture was heated at reflux for 10 hr; subsequently the ether was removed by distillation. The residue dissolved completely in 200 ml of THF, and this solution was heated at reflux for 6 hr. The reaction mixture was poured into ice water and extracted with ether. The combined extract was dried($MgSO_4$) and concentrated under vacuum. After triphenylphosphine oxide was removed from the residue,the filtrate was distilled to give 1.60 g,(40 %) of pale yellow liquid 135 consisted of three isomers, a 1:1:1 mixture of EE, ZE and ZZ stereoisomers(bp 70-76°C/0.1 mm). The presence of these isomers with the correct molecular weight was confirmed by GC-MS.

The chloromethyltriphenylphophonium chloride obtained from commercial material(recrystallized from methylene chloride or a mixture of ethanol and ether before use) or prepared from triphenylphosphine, hydrogen chloride and paraformaldehyde, was used to prepare 135 giving a better yield. (50 %). ^{1}H NMR($CDCl_3$,TMS) δ7.2-7.7(m, 4H, aromatic protons), δ6.2-6.9(m, 4H, olefinic protons); IR(neat) 3020-3080, 1600, 930, 820, 730 cm^{-1}(mixture of cis and trans); MS(70 ev): m/e 199(M^+).

Preparation of o-diethynylbenzene 134

To a solution of o-bis(β-chlorovinyl)benzene 135(2 g, 10 mmol) in 80 mL of distilled benzene was added potassium t-butoxide(4.5 g, 40 mmol) at 10°C,and the mixture was heated at reflux for 6 hr. The reaction was monitored by GC and NMR to detect the formation of o-diethynylbenzene 134 and the disappearance of 135. The reaction mixture was poured into ice water, neutralized with dilute HCl, and extracted with ether. The combined extract was dried ($MgSO_4$), evaporated and distilled to afford 0.76 g(60 %) of o-diethynylbenzene 134 as a colorless liquid , bp 80-82°C/14 mm. (reported bp 80-82 C/14 mm[118]). IR(neat):3312, 2107, and 756 cm^{-1}; ^{1}H NMR δ7.15-7.6(m, 4H, aromatic protons) and δ3.40(s, 2H, acetylene proton); ^{13}C NMR shows 5 singlets at 81.8, 81.4, 78.4, 77.2 and 75.9 ppm as expected.

Preparation of o-bis(cis-β-benzylmercaptovinyl)benzene 136

Benzylmercaptan (0.8g, 6.4 mmol) in 4 mL of THF was added to a solution of sodium(0.15 g, 6.4 mmol) in 5 of absolute ethanol. The mixture was refluxed for 20 min to reach equilibrium. The o-diethynylbenzene 134(0.2 g, 1.6 mmol) in 4 mL of absolute ethanol was added to the above mixture and maintained at reflux for 2.5hr. The reaction mixture was poured into ice water, extracted with ether, dried($MgSO_4$) and evaporated to give a solid material which was recrystalized from pet. ether to yield 0.42 g 136(70 %) of pure white needles, mp 73-74°C. ^1H NMR ($CDCl_3$, TMS):δ7.2-7.6(m, 4H, aromatic protons), δ6.5 and 6.2(AB quartet, 4H, J= 10 Hz, cis); IR(Nujol):3100, 2920, 1540, 1430, 1370, 745 cm^{-1} and no trans double bond at 925 cm^{-1}.[121] ; ^{13}C NMR shows 10 singlets at 137.4, 134.9, 128.9, 128.5, 128.4, 127.2, 127.1, 126.7, 124.2 and 38.9 ppm.

Attempted preparation of 5,6-benzo-1,2-dithiocin V

i) Via the addition of sodium disulfide to o-diethynylbenzene 134

o-Diethynylbenzene(100 mg, 0.8 mmol) in 4 mL of dry DMF was added to a mixture of $Na_2S\cdot9H_2O$(192 mg, 0.8 mmol) and sulfur(26 mg, 0.8 mmol) in 5 mL of dry DMF. The solution was heated under reflux for 0.5 hr and then poured into ice water. The mixture was extracted with hexane and the aqueous phase was acidified with dilute HCl and extracted with hexane. The combined extract was washed with water, dried and concentrated on a rotary evaporator. The resulting solid was recrystallized from petroleum ether to afford 70 mg of naphthalene(69 %), the sulfur extrusion product of 5,6-benzo-1,2-dithiocin V. Since V seems unstable at high temperature, the reaction was also carried out at 20°C for 3 days, 70°C for 3 days and 95°C for 5 days, but no reaction took place. When the temperature was increased to 105°C for 2 days, the o-diethynylbenzene 134 disappeared completely and only naphthalene was detected, with no trace of V. The above reaction was monitored by GC, TLC and ^{1}H NMR.

ii) Via debenzylation of 136 followed by acidification and oxidation

Sodium(0.22 g, 9.2 mmol) was added in small portions to a solution of 136(0.85 g, 2.3 mmol) in 3 mL THF and 30 mL dry liquid ammonia at -78°C. The solution was allowed to stir for an additional 3 hr. After the ammonia was evaporated, the residue was dissolved in 20 mL methanol and acidified with cold dilute H_2SO_4 at 0°C. To the mixture was added $FeCl_3 \cdot 6\ H_2O$(1.8 g, 6.9 mmol) at 0°C and the mixture was allowed to stir at 15°C for 6 hr. After workup, only naphthalene (73 mg, 25 %) was formed.

Attempted preparation of 3-benzothiepin 133

o-Diethynylbenzene(100 mg, 0.8 mmol) in 4 mL absolute ethanol was added to Na_2S $9H_2O$(192 mg, 0.8 mmol) in 4 mL of absolute ethanol;the solution was heated under reflux for 15 hr. The reaction was monitored by gas chromatography and TLC. The reaction mixture was poured into ice water, acidified with dilute HCl, extracted with ether, dried($MgSO_4$) and evaporated on a rotary evaporator. The resulting solid was recrystallized from pet. ether to give 76 mg of naphthalene(59 %). The result was consistent with that of Vogel and Buschken,[128] who also reported that 133 decomposed above -5°C to give naphthalene and sulfur.

Preparation of Cis-1,4,7-trithiacyclonona-2-ene 150

This preparation was carried out under high dilution conditions. Bis-(2-mercaptoethyl)sulfide(15.4 g, 0.1 mole, 300 mL absolute ethanol) and cis-1,2-dichloroethylene(9.7 g, 0.1 mole, 140 mL absolute ethanol) in two separate additional funnels, were simultaneously added dropwise to a solution of sodium(5.29 g, 0.23 mole) in 1200 mL absolute ethanol at reflux over 4 hr. The mixture was allowed to reflux for another 15 hr, after which the solvent was distilled until the volume was 350 mL. The mixture was then poured into ice water, neutralized with dilute HCl, extracted with ether, dried($MgSO_4$) and evaporated under vacuum. The residue was chromatographed over silica gel eluted with 4 % benzene in pet. ether to afford 2.04 g(4 %) of the desired compound 150 as a colorless liquid. ^1H NMR($CDCl_3$, TMS):δ6.30(s, 2H, olefinic protons), δ3.4(t, 8H, methylene protons); IR(neat): 3020, 2960, 1550, 1430, 1370, 810 cm^{-1}; ^{13}C NMR shows three singlets at 124.7, 37.9 and 33.3 ppm.

Preparation of Cis-1,4,7-trithiacyclonona-2-ene 7-oxide 151

m-Chloroperbenzoic acid(1.89 g, 11 mmol) in 30 mL distilled $CHCl_3$ was added to a solution of 151(1.78 g, 10 mmol) in 20 mL $CHCl_3$ at 0°C. The mixture was allowed to stir for an additional 2 hr at 0-5°C. The reaction mixture was then diluted with 100 mL $CHCl_3$ and added slowly with saturated $NaHSO_3$ solution to decompose the excess peracid. The organic layer was neutralized with cold dilute NaOH solution, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$ and the solvent evaporated at reduced pressure to give crude 151. Chromatography of the product over silica gel using 1:1 ether-petroleum ether gave 1.04 g (55 %) of the expected sulfoxide 151 as an off-white liquid. ^1H NMR($CDCl_3$, TMS):δ6.4(s, 2H, olefinic protons), δ3.4(t, 4H) and δ3.2-3.7(m, 4H); IR(neat): 3030, 1550, 1430, 1370, 1050, 810 cm^{-1}.

Preparation of 8,9-Dihydro-1,4,7-trithianin 152

Sulfoxide 151(1.75 g, 9 mmol) in 30 mL of freshly distilled acetic anhydride was refluxed for 35 min under nitrogen. The mixture was poured into ice water, extracted with ether, neutralized with cold dilute NaOH solution, dried($MgSO_4$),and evaporated under vacuum. The residue was chromatographed over silica gel(eluted with 2 % benzene in pet. ether) to give 140 mg of the desired diene 151(9 %) as a pale yellow liquid and 148 mg of 2-vinylmercapto-2,3-dihydro-1,4-dithiin 156(9 %) as a pale yellow liquid. The ^1H NMR($CDCl_3$, TMS) of 152 shows resonances at δ6.67 and 6.38(AB quartet, 4H, J= 9 Hz, cis). The structure assignment of 156 was based on the following spectral features. ^1H NMR($CDCl_3$,TMS):δ6.36(s, -SCH=CHS-, 2H), δ6.16(AB_2 vinylic, 1H, -SC$\underline{H}$=CH_2), δ5.47(AB_2 vinylic, 2H, -SCH=C$\underline{H}_2$), δ4.61(d of d, 1H, methine proton) and δ3.33 (m, 2H, methylene protons); MS(70 ev):at m/e 176(M^+) and fragment ions at 116(40%), 84(57%) and 58(100%); IR(neat): 3020, 2900, 1590, 1550, 1416, 960, 916, 820 and 725 cm^{-1}; ^{13}C NMR shows six singlets at 128, 116.7, 115.4, 113.4, 43.6 and 31.8 ppm as expected; gated decoupled ^{13}C NMR shows the resonances at 43.6 ppm(d, J=158.7 Hz) for the methine carbon, and 31.8 ppm(t, J=144 Hz and 14.6 Hz) for the methylene carbon.

Attempted preparation of 1,4,7-Trithianin 142

To a solution of 8,9-dihydro-1,4,7-trithianin 152 (140 mg, 0.8 mmol) in 6 mL $CHCl_3$ was added 145 mg(0.84 mmol) of m-chloroperbenzoic acid in 8 ml $CHCl_3$ at 0°C. The mixture was then allowed to stir at 0-5°C for 2 hr thereafter. After evaporation of the solvent,the residue was refluxed in 20 ml freshly distilled acetic anhydride under N_2 for 30 min. When worked up in the usual way only the polymeric and decomposed material, without any indication of the extected triene 142, could be found.

Preparation of 2-vinylmercapto-1,4-dithiin 162

m-Chloroperbenzoic acid(145 mg, 0.84 mmol) in 6 mL $CHCl_3$ was added to a solution of 5,6-dihydro-5-vinylmercapto-1,4-dithiin 156(140 mg, 0.8 mmol) in 8 mL $CHCl_3$ at 0°C. The mixture was allowed to stir for another 1.5 hr. After evaporation of the solvent,the residue was refluxed in 20 ml of freshly distilled acetic anhydride for 30 min under nitrogen. After workup, chromatography over silica gel eluted with pet. ether afforded 16.8 mg (12 %) of the expected 2-vinylmercapto-1,4-dithiin 162 as a yellow liquid. ^1H NMR($CDCl_3$, TMS):δ6.40(AB_2 vinylic, 1H, $-SC\underline{H}=CH_2$), 5.48(AB_2 vinylic, 2H, $-SCH=C\underline{H}_2$), δ6.30(s, 1H, $-SCH=\overset{S}{C}-S-$) and 6.35(d, 2H, -SCH=CHS-); MS(70 ev): at m/e 174(M^+); ^{13}C NMR exhibits signals as singlets at 130, 127.8, 123, 121.7 and 116.8 ppm. IR(neat): 3030, 1580, 1540, 970, 915, 820 and 760 cm^{-1}.

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