STUDIES OF HETEROCYCLIC COMPOUNDS CONTAINING GROUP VI ELEMENTS :

I 4H-INDENO[2,1-d]AZOLIUM SALTS

II 6a-THIATHIOPHTHENES

being a Thesis

presented by

JOHN GREY DINGWALL, B.Sc.,

to the

University of St. Andrews

in application for

THE DEGREE OF DOCTOR OF PHILOSOPHY

DECLARATION

I declare that this thesis is based on the results of experiments carried out by me, that it is of my own composition and has not been submitted previously in application for a higher degree.

The research was carried out in the Department of Chemistry, St. Salvator's College, University of St. Andrews under the direction of Dr. D.H. Reid.

CERTIFICATE

I hereby certify that Mr. John Grey Dingwall, B.Sc., has spent eleven terms at research work under my supervision, has fulfilled the conditions of Ordinance No. 16 (St. Andrews), and is qualified to submit the accompanying thesis in application for the degree of Ph.D.

Research Supervisor.

UNIVERSITY CAREER

I entered the University of St. Andrews as a Matheson Scholar in October 1961 and subsequently graduated B.Sc. with First Class Honours in Chemistry in June, 1965.

From September, 1965 till June, 1968, as a Carnegie Scholar, I carried out the work which is embodied in this thesis.

ACKNOWLEDGEMENTS

It is with pleasure that I thank Dr. D.H. Reid for his continued interest and encouragement and for much stimulating discussion. I should like also to thank Drs. S. McKenzie, W.G. Salmond and K.O. Wade for the interest they have shown in this work. Finally I should like to thank Professor J.I.G. Cadogan for making available laboratory facilities, and the Carnegie Trust for the Universities of Scotland for the award of a Research Scholarship.

SUMMARY

STUDIES OF HETEROCYCLIC COMPOUNDS CONTAINING GROUP VI ELEMENTS :

I 4H-INDENO[2,1-d]AZOLIUM SALTS

Part A (Introduction).

A brief survey of the role of sulphur d-orbitals in bonding in organic compounds is given.

Parts B and C (Discussion and experimental).

(i) Two indeno[2,1-d]oxazolium salts and two indeno[2,1-d] selenazolium salts have been synthesised.

(ii) Acyl derivatives of one indeno-thiazolium anhydro-salt and one indeno-selenazolium anhydro-salt have been prepared.

(iii) The spectral properties of these acyl derivatives are discussed with reference to the bonding of the group VI element.

(iv) Vilsmeier salts have been prepared from a series of indeno[2,1-d]thiazolium salts.

(v) Some derivatives of 1-thiacycl[2,3,3]azine have been prepared.

II 6a-THIATHIOPHTHENES

Part A (Introduction)

A review of the chemistry of 6a-thiathiophthenes is given.

Parts B and C (Discussion and experimental)

(i) A new synthesis of 6a-thiathiophthenes from 3-methyl(ene)-1,2-dithiolium salts has been developed.

(ii) Oxygen and nitrogen containing isosteres of 6a-thiathiophthene have been prepared by the same method.

(iii) The properties of some 3,4(peri)-disubstituted 6a-thiathiophthenes are discussed.

(iv) It has been found that 6a-thiathiophthenes are rearranged to 4H-thiopyran-4-thiones by nucleophiles in dimethylformamide solution.

(v) Possible mechanisms for this and related rearrangements are discussed.

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PART A

INTRODUCTION

THE VALENCE SHELL EXPANSION OF SULPHUR.

I: The Atomic Orbitals of Sulphur. Sulphur belongs to the subgroup VIB and has the electronic configuration $3s^2$, $3p_x^2$, $3p_y^1$, $3p_z^1$ in the outer shell of the free atom. In its divalent state the $3p_y$ and $3p_z$ orbitals are filled by electron sharing. There remain five empty d-orbitals which could also be used in bond formation, with an expansion of the outer shell to accommodate more than eight electrons. Of these, the $3d_{xy,yz,zx}$ orbitals are of equal energy and have the correct symmetry for Π-bonding. A Π-bond arises when one of these orbitals is orientated with its positive and negative lobes equally inclined to the line of centres, and requires a $p\Pi$ (or $d\Pi$) orbital at the other centre (Fig.I).

Craig and co-workers[1], from calculations of overlap integrals, showed that the d-orbitals of atoms such as phosphorus and sulphur could be used for $p\Pi$-$d\Pi$ bonding. Calculations showed, however, that if the free sulphur atom was taken as a model for sulphur in its bonding state, the d-orbitals would be too diffuse to form useful bonds. In a later paper, Craig and Magnusson[2] proposed that these diffuse d-orbitals could contract as a result of polarisation by ligands, and so be more suited for bonding. In Π-bonding, however, the need for such perturbation is not so critical, as a diffuse $d\Pi$-orbital may overlap quite strongly with a compact $p\Pi$-orbital.

In divalent sulphur compounds the C-S-C bond angle lies between 90° and the tetrahedral angle, suggesting considerable s-admixture in the sulphur bonds and an approach towards sp^3 hybridisation[3]. Sulphonium salts, in which the sulphur atom is trivalent, can be

separated into optical isomers when substituted with three different groups[4]. This behaviour means that the bonding must be through the mutually perpendicular p-orbitals, the lone pair occupying the 3s-orbital.

II: Valence Shell Expansion in Acyclic Systems. The ability of sulphur to conjugate with a carbonium centre by pΠ-pΠ overlap is exemplified in the increased rate of solvolysis of α-chlorosulphides[5] over alkyl halides[6]. This reaction proceeds by a carbonium ion intermediate[7] which is stabilised by the adjacent sulphur atom. In this type of electron releasing conjugation there is no need to invoke the use of d-orbitals. However, to explain conjugation with a free radical centre (electron sharing conjugation) or with a carbanion centre (electron acceptor conjugation), d-orbital interaction must be introduced.

Price and co-workers have shown, from co-polymerisation studies involving vinyl sulphides[8,9] and vinyl ethers[10], that sulphur containing free-radicals are much more stable than the corresponding oxygen ones. This can be attributed to delocalisation of the odd electron utilising sulphur d-orbitals, which can take place by two mechanisms. Firstly, the odd electron in the carbon 2pΠ-orbital could be fed into a suitable 3dΠ-orbital of sulphur to form a 2pΠ-3dΠ bond. Alternatively, an electron from a sulphur 3p-orbital could be promoted to a 3d-orbital, overlap then occurring between a carbon 2pΠ-orbital and a sulphur 3pII-orbital to form a 2pΠ-3pΠ bond. Results from similar studies involving vinyl sulphones[8] and

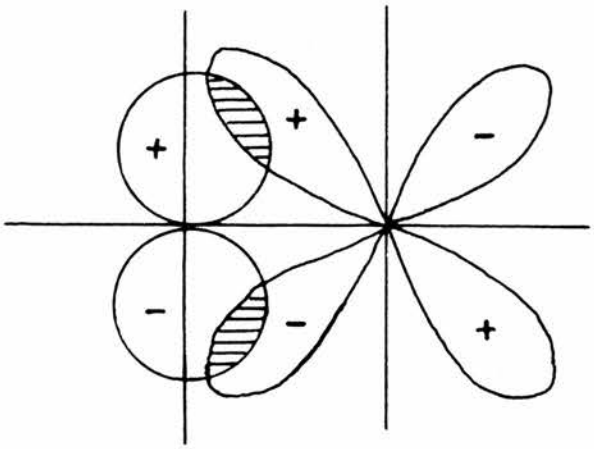


fig. 1 a 2p–3dπ bond

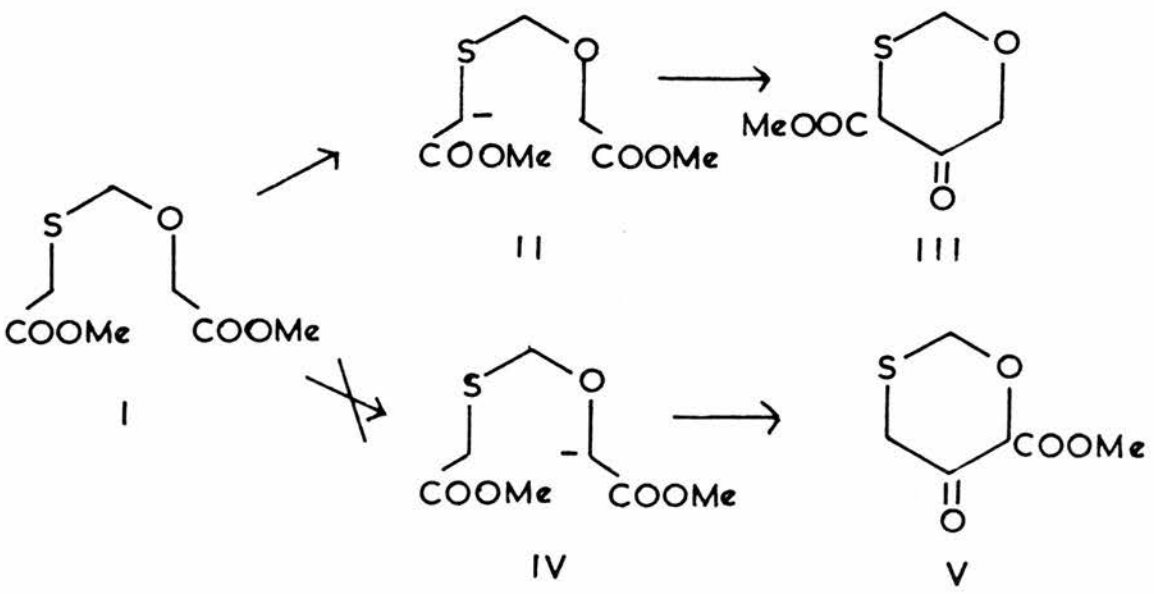
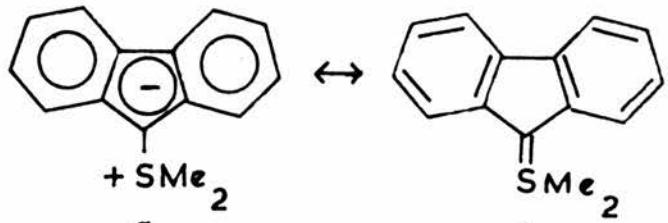


PLATE I

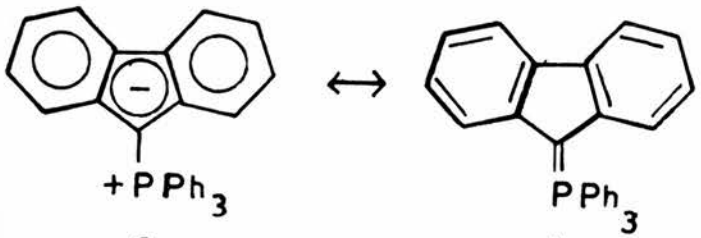
vinyl silanes[11] support the latter mechanism. The radicals derived from sulphones and silanes are less stable than those derived from sulphides. Although the former both have the necessary d-orbitals for pΠ-dΠ overlap, neither has an unshared pair of electrons from which an electron could be promoted to a 3d-orbital.

A sulphur atom can also stabilise carbanion sites. Dieckmann cyclisation of the compound (I) to give the product (III)[12], rather than compound (V), indicates that the intermediate carbanion (II) is more stabilised than the carbanion (IV). Again two mechanisms are possible for this conjugation, pΠ-dΠ overlap, or promotion from one of the sulphur p-orbitals followed by pΠ-pΠ overlap. That the latter mechanism is unimportant in the stabilisation of a carbanion is suggested by the fact that compound (VI) exchanges its deuterium, under basic conditions, about a thousand times faster than compound (VII)[13]. In the bicyclic compound (VI), formation of a 2pΠ-3pΠ bond is unlikely because of the impossibility of having the carbon and three sulphur atoms coplanar, whereas in compound (VII) coplanarity is possible. However, the steric requirements for pΠ-dΠ bonding are less than those for pΠ-pΠ bonding[14]. Perhaps compound (VI) might even be constrained in the geometry necessary for pΠ-dΠ overlap.

Craig and co-workers[1,2] predicted that d-orbital overlap would be most effective when the atom with the vacant d-orbitals carried a formal positive charge and was attached to very electronegative groups. Such is the situation in the sulphonium and phosphonium ylids



a VIII b



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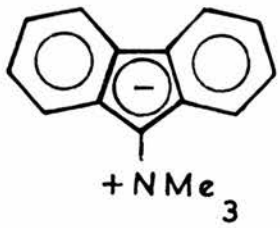
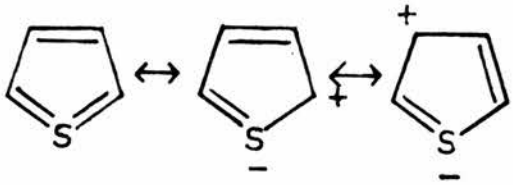
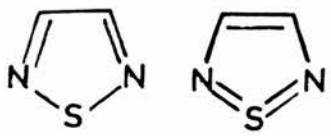


X

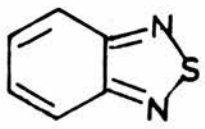


XI

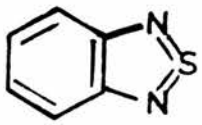


a b

XII

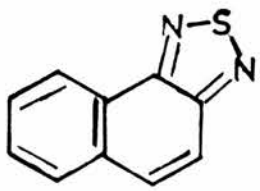


a



b

XIII



XIV

PLATE 2

(VIII) and (IX), whose stability and ease of formation, compared to the ammonium ylid (X)[17], has been attributed to valence shell expansion of the hetero-atom[18]. However the high values of the dipole moments of compounds (VIII)[19] and (IX)[20] indicate that structures (VIIIb) and (IXb) cannot be the major contributors to the resonance hybrids. Johnson[21] has estimated, from dipole moment data, that the contribution of structure (VIIIb) is approximately 30%.

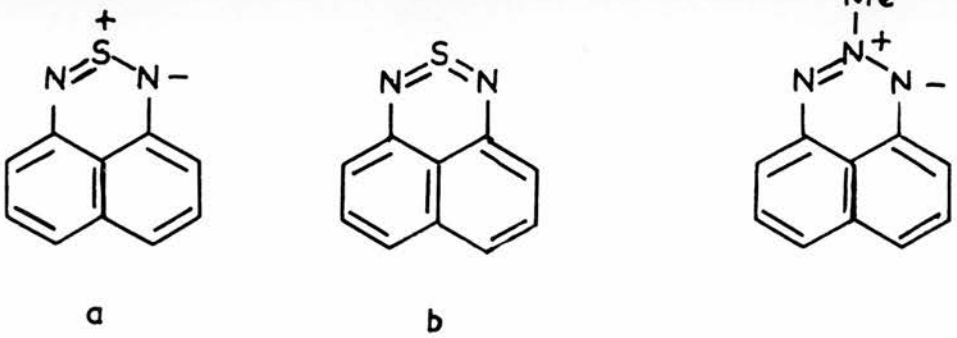
III: Valence Shell Expansion in Heterocyclic Systems. In 1939 Shomaker and Pauling[22] made the first reference to valence shell expansion of divalent sulphur, with reference to thiophene. They found that comparison of dipole moments, bond lengths and resonance energies of furan, pyrrole and thiophene suggested that structures (XI), involving more than eight electrons in the outer shell of the sulphur atom, were important contributors to the valence-bond description of thiophene. Ten years later Longuet-Higgins applied the method of molecular orbitals to thiophene and showed that the pronounced aromatic character of thiophene, compared with furan and pyrrole, could be explained by a model which utilised the 3d-orbitals of sulphur. In this model the σ-bond framework is set up using the sulphur sp^2 hybrid orbitals. The remaining $3p_z$-orbital and the $3d_{yz}$ and $3d_{xz}$-orbitals of sulphur are mixed to give three pd^2 hybrid orbitals, two of which have the proper energy and symmetry for Π-conjugation with the $2p_z$-orbitals of the neighbouring carbon atoms. Kreevoy[24], however, has shown that the properties of thiophene can

be explained theoretically without invoking valence shell expansion of the sulphur atom.

Metzger and Vincent[25] applied the method of Longuet-Higgins to the structure of thiazole, with improved agreement with experimental results over an earlier calculation[26] based on a purely p-model. However, Zahradnik and Koutecky[27] obtained even better correlation with experiment from calculations based on a p-model.

The reactions of 1,2,5-thiadiazole suggest that the structure (XIIb) is an important contributor to the resonance hybrid[28]. However structural parameters[29], obtained from physical measurements, are best represented by the structure (XIIa). Cava and Schlessinger[30] suggest that the stability of benzo[c]-1,2,5-thiadiazole (XIII)[31] and naphtho[1,2-c]-1,2,5-thiadiazole (XIV)[32] implies a significant degree of tetracovalent character in the sulphur atom of these compounds. They claim that crystal structure data[33] supports this view. Dietz[34], however, interprets the X-ray data as implying that the o-quinonoid structure (XIIIa) is important in the ground state. Such o-quinonoid structures are not possible for the thiadiazine (XV) which has a very similar U.V. spectrum to that of the isoconjugate triazine (XVI)[35], implying that structure (XVb) is unimportant. Cava and Schlessinger[30] claim that the thiadiazole analogue of anthracene (XVII) reacts predominantly as a tetracovalent sulphur species. This reactivity, like the reactivity of thiadiazole itself, may bear little relation to the ground state structure of the molecule.

In 1961 Price and his co-workers[36,37,38,39] prepared the stable,

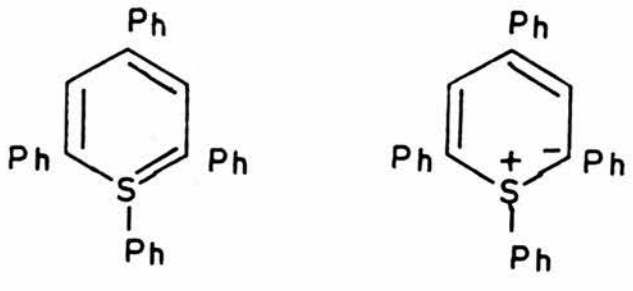


a b

XV

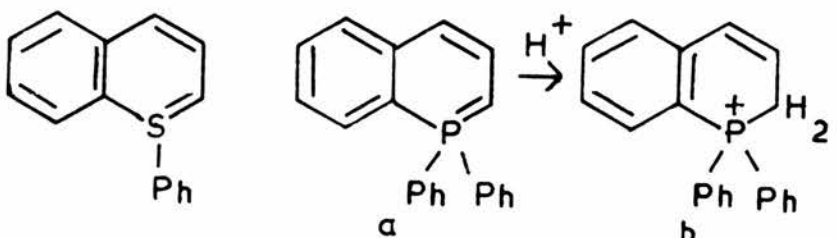
XVI

XVII



a b

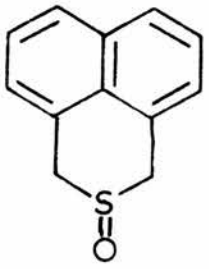
XVIII



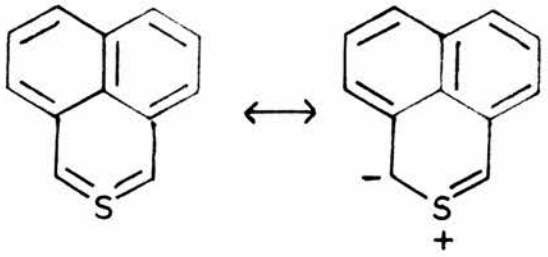
XIX XX

PLATE 3

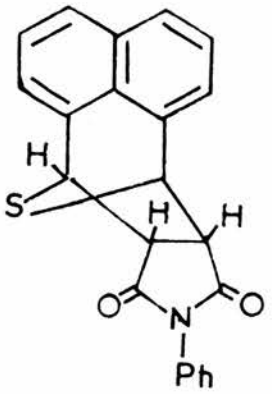
highly coloured thiabenzene derivative (XVIII) by reacting the corresponding thiopyrylium salt with phenyl lithium. The low value of the dipole moment (1.88D)[39] of the thiabenzene and its N.M.R. spectrum are consistent with the assigned covalent, aromatic structure (XVIIIa) rather than the ylid structure (XVIIIb). If this covalent structure is correct then the d-orbitals of the sulphur atom must be populated. This does not necessarily mean that pΠ-dΠ overlap is occurring: it is possible that an unshared pair of electrons is promoted into a 3d-orbital, aromatic delocalisation then occurring via 2pΠ-3pΠ overlap. The latter model receives support from a comparison of the behaviour of 1-phenyl-1-thianaphthalene (XIX)[39] and the analagous 1,1-diphenyl-1-phosphoranaphthalene (XXa)[40] with acid. In the phosphoranaphthalene all the valence electrons of phosphorus are involved in σ-bonding, so that any d-orbital interaction must be by pΠ-dΠ overlap. The phosphoranaphthalene is readily protonated to the phosphonium salt (XXb), even in aqueous media: the thianaphthalene is not protonated under these conditions, whereas acyclic sulphonium ylids will remove protons from water[41]. This is in accord with the view that the thiabenzene ring derives its stability from pΠ-pΠ rather than pΠ-dΠ overlap. Price and co-workers[39] have suggested that the fact that the thiabenzene and its naphthalene and anthracene analogues are highly coloured, while their U.V. spectra differ little from the related benzenoid compounds, may be attributed to an unshared pair of electrons in a d-orbital of the sulphur atom.



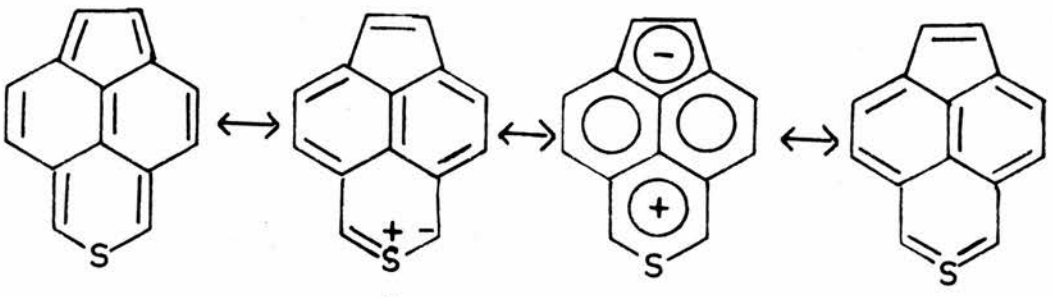
XXI



XXII



XXIII



a b c d

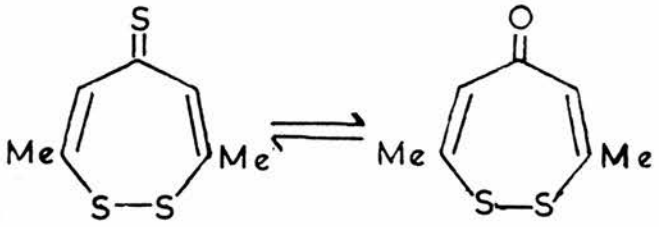
XXIV

PLATE 4

Excitation of one of these electrons to another 3d-orbital of only slightly higher energy may be responsible for the long wavelength transition, without having much effect on the cyclic conjugated Π-system. Significantly, the phosphorabenzenes are pale yellow.

Recently two groups of workers[42,43,44,45,46] have reported the transient existence of intermediates for which "the only uncharged resonance contributors are structures containing tetravalent sulphur"[42]. Dehydration of the sulphoxide (XXI)[43,44] in boiling acetic anhydride generated the intermediate 2-thiaphenalene (XXII) which was trapped in a Diels-Alder addition reaction with N-phenylmaleimide to give the adduct (XXIII). The mass spectrum[44] of the adduct gives rise to a retro-Diels-Alder-type fragmentation pattern with a peak corresponding to the parent heterocycle (XXII). Acenaphthyl[5,6-c,d]thiapyran (XXIV)[45] was generated by the same method. This heterocycle has (4n+2=14) peripheral Π-electrons and can be written in a number of resonance forms containing divalent sulphur (XXIVa and c). However its reactivity leads the authors to believe that it is best viewed as a tetracovalent sulphur species (XXIVd) with Π-electron delocalisation.

The foregoing account illustrates that the ability of a sulphur atom to permit through conjugation in a heterocyclic system, by expansion of its valence shell to accommodate a decet of electrons, remains a highly controversial topic.



XXV XXVI

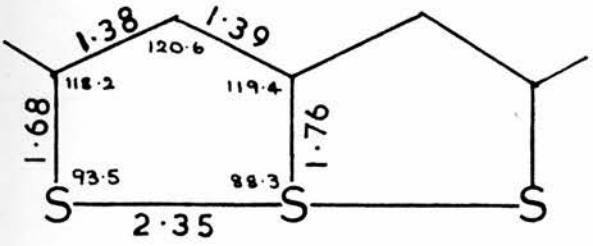


fig. 2

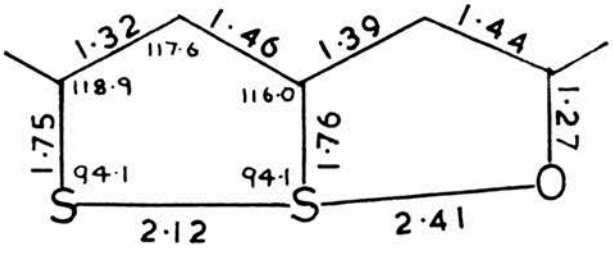
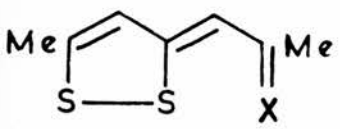


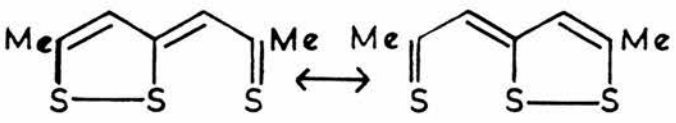
fig. 3



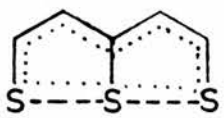
XXVII

a X=O

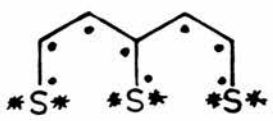
b X=S



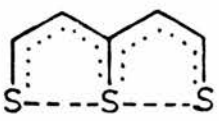
XXVIII



XXIX



XXX



XXXI

PLATE 5

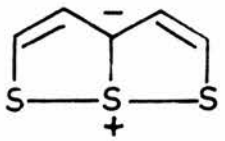
6a-THIATHIOPHTHENE.

In 1925 Arndt, Nachtwey and Pusch[47] isolated, from the reaction of diacetylacetone with phosphorus pentasulphide, a stable, orange, crystalline compound, $C_7H_8S_3$, which they formulated as 3,7-dimethyl-5H-1,2-dithiepin-5-thione (XXV). The chemical properties of this compound appeared to be in agreement with the proposed structure. Thus the reaction with 70% perchloric acid led to the replacement of one atom of sulphur by oxygen giving a yellow, crystalline product which was formulated as the dithiepin-5-one (XXVI)[48]. Treatment of this oxo-compound with phosphorus pentasulphide regenerated the thione (XXV). Arndt's structure appeared to be confirmed when Bothner-By and Traverso[49] reported that the N.M.R. spectrum of the thione (XXV) showed two singlets in the ratio 3:1, in agreement with the assigned symmetrical structure. Shortly afterwards Bezzi and co-workers[50,51,52] showed in an X-ray crystallographic study (Fig.2) that the assigned structure could not be correct. Guillouzo[53] had independently reached the same conclusion by an analysis of the I.R. spectrum of the oxo-compound (XXVI).

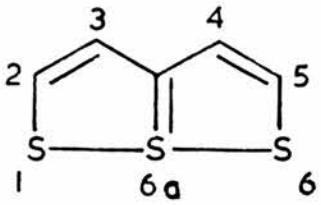
STRUCTURE. The X-ray data for the thione (Fig.2) are best examined alongside those for the corresponding oxo-compound[54] (Fig.3). The thione molecule is planar and symmetrical about the central carbon-sulphur bond. The three sulphur atoms are collinear and equally spaced at a distance of 2.35Å, compared with 2.10Å for a sulphur-sulphur bond in a cis-coplanar disulphide group[55] and 2.12Å in the oxo-compound.

The ring carbon-carbon bonds are all of the same length (1.38-1.39Å) compared with 1.397Å in benzene. The oxo-compound, however, has localised carbon-carbon double bonds. The length of the two outer carbon-sulphur bonds lies between that of a carbon-sulphur single bond (1.82Å) and that calculated for a carbon-sulphur double bond[56] (1.61Å). The central carbon-sulphur bond (1.76Å) is slightly shorter than a carbon-sulphur single bond. Obviously the thione structure cannot be adequately represented by a single formula such as (XXVIIb). Bezzi and co-workers[51], therefore, postulated a resonating 1,2-dithiole structure (XXVIII), the "no-bond resonance" conferring both symmetry and aromatic character on the molecule.

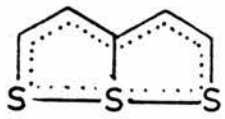
The electronic distribution corresponding tc the "no-bond resonance" structure has been studied by the molecular orbital method with the assumption that the d-orbitals of the central sulphur atom play no part in the bonding[57]. In this model (XXX) three sp^2-orbitals from each carbon atom and one $3p_y$-orbital from each sulphur atom form a localised σ-skeleton(—); the $3p_x$-orbitals of the three sulphur atoms(*), each containing a pair of electrons, form a delocalised σ-system and the remaining eight p_z-orbitals(•) form a delocalised 8Π-electron system. This model is represented by the formula (XXIX), the heavy broken line representing the delocalised σ-system and the dotted line representing the delocalised Π-system. Shustorovich[58] has used a variation of this model (XXXI) in which the delocalised Π-system is confined to the "backbone" of the molecule, the sulphur-sulphur bonds being purely σ in character.



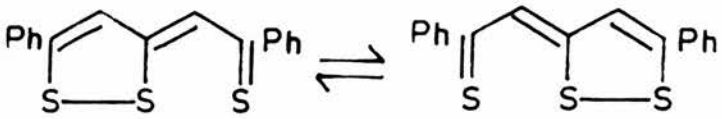
XXXII



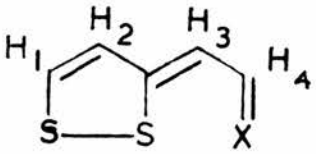
XXXIII



XXXIV



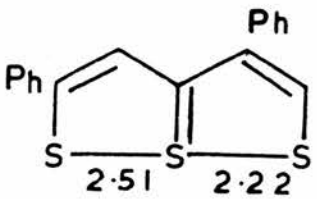
XXXV



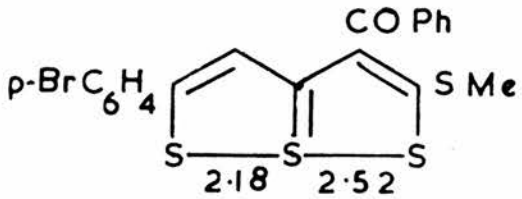
XXXVI

a X = O

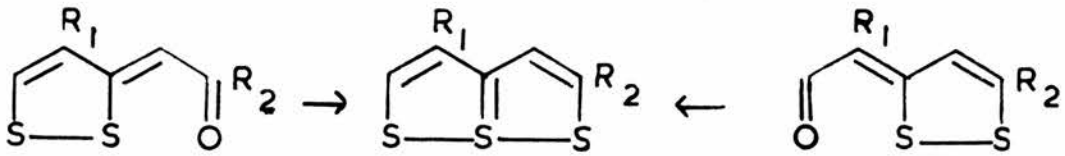
b X = S



XXXVII



XXXVIII



XXXIX XL XLI

Pfister-Guillouzo and Lozac'h[59] have proposed a model (XXXII) in which the central sulphur atom uses two sp_x hybrid orbitals for bonding to the other sulphur atoms; the $3p_y$-orbital is used in bonding to the central carbon atom and the $3p_z$-orbital contains the unshared pair of electrons. The carbanionic atom has the usual sp^2 hybridisation, the lone pair occupying a p-orbital. By utilising a d-orbital of the central sulphur atom the covalent structure (XXXIII) could be achieved. The authors liken this to the situation described (page3) for the sulphonium ylid (VIII), but are careful to point out that the sulphonium sulphur atom in their model does not have the usual pyramidal geometry of sulphonium compounds.

Maeda[60,61,62] has carried out molecular orbital calculations using a model in which the central sulphur atom uses its d-orbitals for bonding. One 3p-orbital and one 3d-orbital of the central sulphur atom are mixed to give two pd hybrid orbitals which overlap with the 3p-orbitals of the other two sulphur atoms to give two σ-bonds at 180° to each other. One of the remaining 3p-orbitals is involved in σ-bonding with the central carbon atom and the other in the delocalised Π-electron system: the five carbon atoms and the central sulphur atom each contribute one electron to the Π-system, the other two sulphur atoms each contributing two electrons to form a delocalised 10Π-electron system which confers aromatic character upon the molecule (XXXIII or XXXIV).

The forementioned models are essentially bicyclic in nature. Leaver[63] has adduced spectroscopic evidence to support a monocyclic

structure for the diphenyl compound (XXXV), symmetry coming from a rapid valence-isomerisation of the two 1,2-dithiole structures.

X-Ray studies[65,66] of the unsymmetrically substituted thiathiophthenes (XXXVII) and (XXXVIII) have shown that in these compounds the sulphur-sulphur bond distances are unequal, although the distance between the outer sulphur atoms remains constant (4.7Å). Each has a "long" bond(ca. 2.5Å) and a "short" bond(ca. 2.2Å), both bond lengths being much less than the van der Waals distance for two sulphur atoms (3.70Å). It is interesting to note that, considering the aryl groups in compounds (XXXVII) and (XXXVIII) as common reference points, the "short" and "long" bonds are reversed in the two compounds.

The most likely explanation for the unequal sulphur-sulphur bond distances is that the symmetrical thiathiophthene system is

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NOMENCLATURE. Formula (XXXIII) and the corresponding nomenclature for the system, 6a-thiathiophthene, will be used throughout this work. The nomenclature system proposed by Hertz, Traverso and Walter[64], though cumbersome, clearly indicates the relationship between 6a-thiathiophthenes and their oxygen analogues; thus the parent heterocycle is called meribicyclo-3,5-epidithio-2,4-pentadienethial and its oxygen analogue is 3,5-epidithio-2,4-pentadienal. This nomenclature is used for the oxo-compounds in the experimental part of this work. The oxo-compounds have also been referred to as furothiophthenes. Chemical Abstracts indexes the parent heterocycle as ethanethial,(1,2-dithiol-3-ylidene) and its oxygen analogue as ethanal, (1,2-dithiol-3-ylidene).

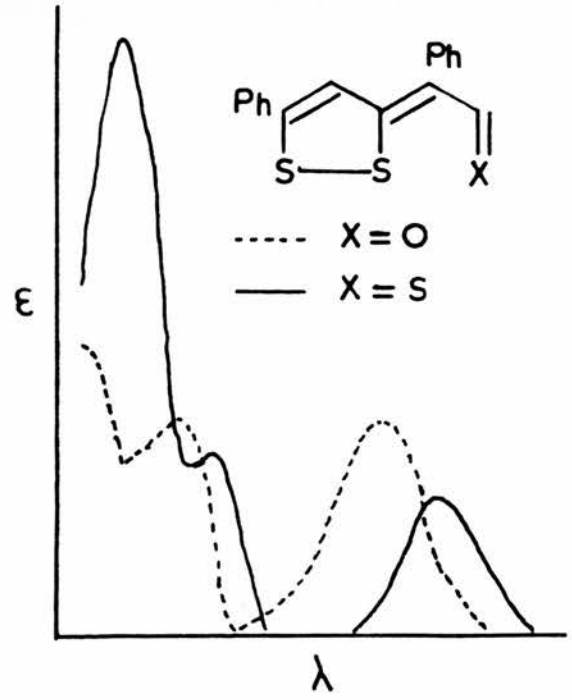


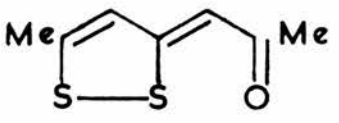
fig. 4

Benzophenone (EtOH)

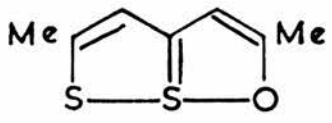
λ (mμ)	204	252	333
log ε	4.4	4.2	2.5

Thiobenzophenone (MeOH)

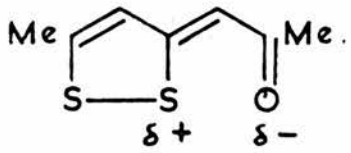
λ (mμ)	235	316	595
log ε	4.0	4.2	2.3



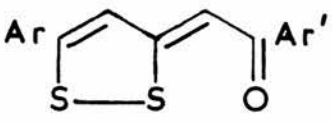
XLII



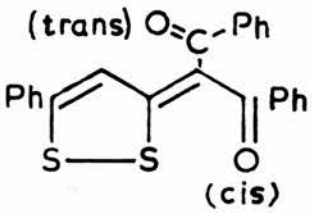
XLIII



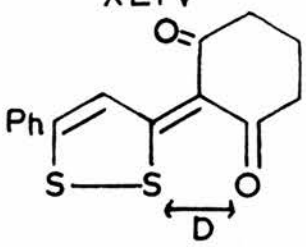
XLIV



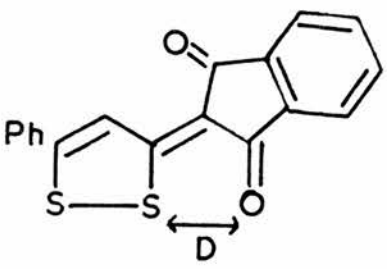
XLV



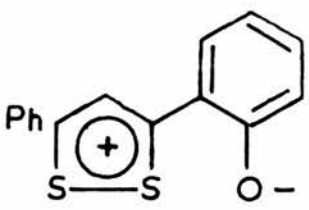
XLVI



XLVII



XLVIII



XLIX

PLATE 7

perturbed by unsymmetrical substition. However, in the light of these results, the interpretation of the X-ray data for 2,5-dimethyl-6a-thiathiophthene, in terms of a symmetrical molecular structure, has been questioned[109,118]. The equivalence of the outer sulphur atoms in the 6a-thiathiophthene system has been demonstrated chemically[59,67,68] by the formation of a single thiathiophthene (XL) from isomeric starting materials (XXXIX) and (XLI).

Thiathiophthenes are orange to purple crystalline solids which are stable at their melting points. The U.V. and visible spectra of thiathiophthenes and their oxygen analogues bear a characteristic relationship to one another[67,69,70]. The U.V. and visible spectra of 2,4-diphenyl-6a-thiathiophthene and its oxygen analogue are shown in fig. 4. When the oxygen atom is replaced by sulphur the visible absorption is shifted to longer wavelength and weakened and the ultra-violet absorption is shifted to shorter wavelength and greatly strengthened.The effect of replacing the oxygen atom of benzophenone by sulphur (see table in fig. 4) [71] is to cause a bathochromic shift of all the bands, the short wavelength absorption being appreciably weakened. Obviously the replacement of an oxygen atom by sulphur to form a thiathiophthene causes an important overall structural change.

The I.R. spectra of several thiathiophthenes have been determined[72,73] and are characteristic of an aromatic 10Π-electron system.

Sanesi and Traverso[74,75] have measured the dipole moments of

6a-thiathiophthene and 2,5-dimethyl-6a-thiathiophthene and find these to be in agreement with values calculated using electron densities from theoretical calculations. Interestingly, the agreement with experimental results is better when the electron densities used are those calculated using a d-model[60,61,62] rather than a p-model[57].

Nuclear magnetic resonance studies[49,76] have confirmed the symmetry of the thiathiophthene system. Thus 6a-thiathiophthene itself has only two types of proton, the spectrum showing a simple AB pattern. The coupling constant (6c/s) reflects the ring carbon-carbon bond angles of 120°. When the oxygen atom of compound (XXXVIa) is replaced by sulphur the protons H_1 and H_2 are deshielded by $>$1p.p.m., indicating the presence of a significant ring current in 6a-thia-thiophthene. Similarly the methyl group attached to the dithiole ring in compound (XXVIIa) is deshielded by 0.14p.p.m. when the oxygen atom is replaced by sulphur. The chemical shift of the methyl group in 2,5-dimethyl-6a-thiathiophthene has been used to give an indication of the size of the ring current in the thiathiophthene nucleus[77]. Calculations of the type used by Elvidge[78] to calculate the "aromaticity" of thiophene show that the ring current in 2,5-dimethyl-6a-thiathiophthene is approximately 65% of that in naphthalene.

The structure of furothiophthenes. Mammi and co-workers[54] concluded from X-ray crystallographic data (Fig.3) that the essential features of thiathiophthene are present in the oxygen analogue, but to a

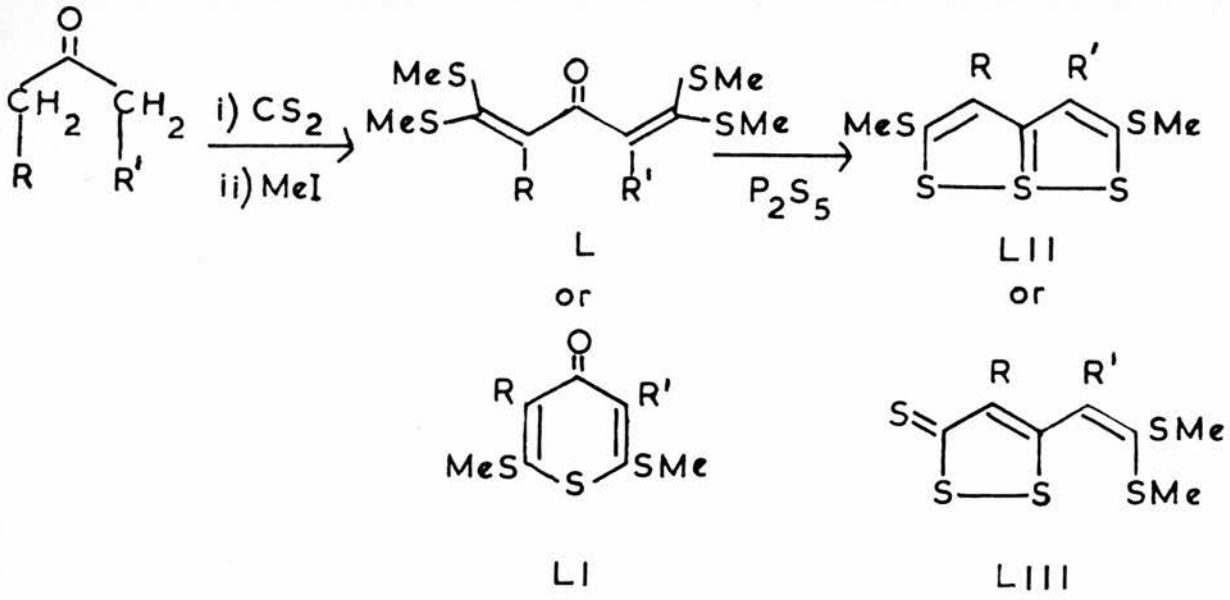
lesser extent, so that the electronic distribution is best represented by formula (XLII) with contributions from structure (XLIII) The abnormal sulphur-oxygen distance (2.41Å cf. single bond 1.70Å and van der Waals distance 3.25Å) is mainly due to the reluctance to distort the carbon-atom valence angles. The X-ray data could equally well be interpreted in terms of a polarised ketone (XLIV), the carbonyl group being held in the cis-coplanar configuration by electrostatic interaction rather than partial bonding. N.M.R. spectroscopy confirms the gross structure of the oxo-compounds[64]. Compound (XXXVIa) shows a typical peak for an aldehydic proton, indicating that sulphur-oxygen interaction is small. The dipole moments of the oxo-compounds (XXVIIa) and (XLII) have been measured[74,75], but, owing to the difficulty of calculating dipole moments for these structures, they give little structural information. The dipole moments of the oxo-compounds are higher than those of the corresponding thiathiophthenes, reflecting the decreased interaction between the oxygen and sulphur atoms[75].

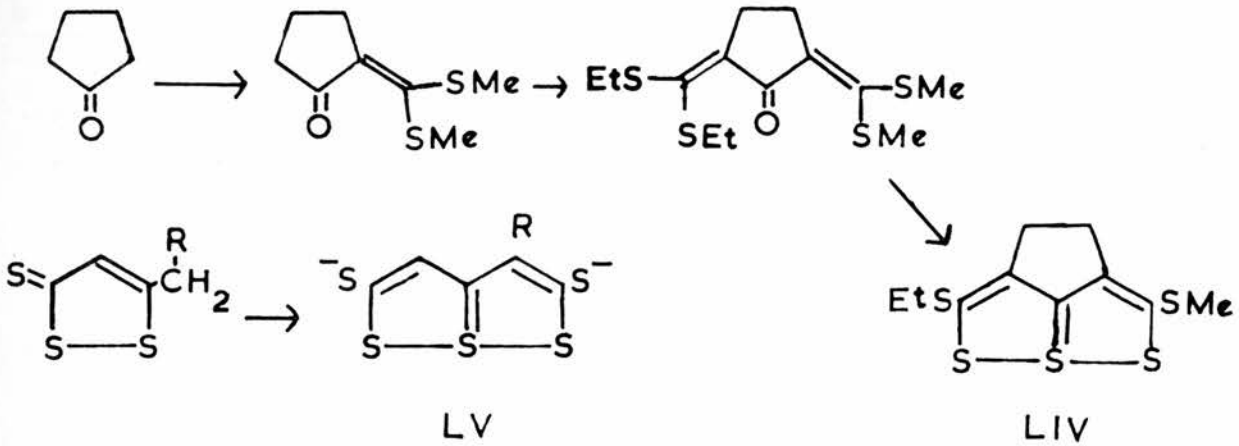
Lozac'h and colleagues[79,72,80] have made a detailed study of the I.R. spectra of the carbonyl compounds. Compound (XXVIIa) has a carbonyl stretching frequency of 1578cm^{-1} (KBr), which corresponds to a double bond character of 76% in the carbon-oxygen bond, in excellent agreement with the figure obtained from X-ray measurements (77%). The ketones (XLV) have carbonyl stretching frequencies between 1540 and 1560cm^{-1} (KBr). The 1,3-diketone (XLVI) has two carbonyl bands, one at 1633cm^{-1} (KBr) which is attributed to the trans-

carbonyl and one at 1535cm^{-1} which is attributed to the cis-carbonyl. On treatment of the diketone with phosphorus pentasulphide the cis-carbonyl oxygen is replaced by sulphur. The cyclohexanedione derivative (XLVII) shows the same pattern, with a cis-carbonyl stretching frequency of 1536cm^{-1} (KBr). In this latter compound the sulphur-oxygen distance (D=2.6Å) is the same as in the ketones (XLV). In the indanedione derivative (XLVIII) this distance is increased to ca. 3Å (cf. 3.25Å for the van der Waals distance) and the cis-carbonyl stretching frequency is 1637cm^{-1}, suggesting that the low value of the carbonyl stretching frequency in compounds (XLV), (XLVI) and (XLVII) may be due to partial bonding between the oxygen and sulphur atoms, which is greatly reduced when the sulphur-oxygen distance is increased. Recently Pinel, Mollier and Lozac'h[77] have reported the synthesis of the compound (XLIX). Consideration of dipole moment and N.M.R. data leads the authors to believe that there is partial bonding between the sulphur atom and the phenolic oxygen in this and related compounds.

SYNTHESES.

(a) From 1,3,5-triketones with phosphorus pentasulphide. As already mentioned, the first synthesis of a 6a-thiathiophthene involved the reaction of diacetylacetone with phosphorus pentasulphide[47]; 2,6-dimethyl-4H-thiopyran-4-thione and 2,6-dimethyl-4H-pyran-4-thione were also formed in the reaction. Stavaux and Lozac'h[81] have applied this reaction to a large number of 1,3,5-triketones and find yields between 5 and 55%.





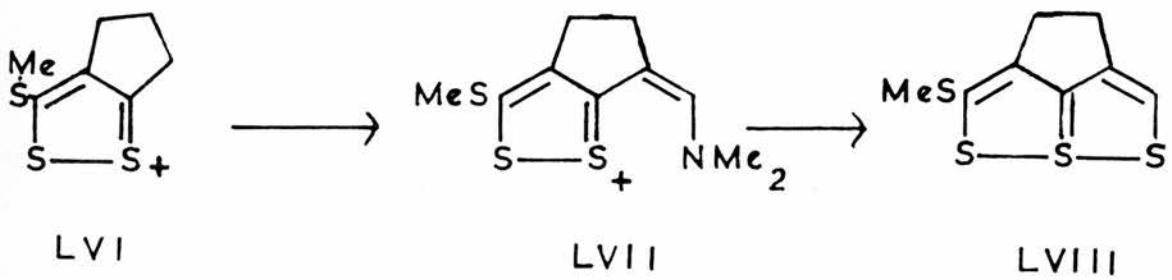


PLATE 8

(b) From ketones and carbon disulphide. In this synthesis, devised by Thuiller and Vialle[82], two molecules of carbon disulphide are condensed with one of ketone, using sodium t-amyloxide as condensing agent, and the product is alkylated with methyl iodide to give di(bis[methylthiomethylene]) compounds (L) in yields of 60-90%. The alkylated product is then treated with phosphorus pentasulphide to give a 2,5-dimethylmercapto-6a-thiathiophthene derivative (LII). That the product was the thiathiophthene and not the isomeric trithione derivative (LIII) was demonstrated for the reaction with cyclopentanone: the ketone was reacted with carbon disulphide stepwise using methyl iodide, then ethyl iodide as alkylating agents. The product (LIV) was shown to contain one methylthio- and one ethylthio- group; the corresponding trithione derivative would contain either two methylthio- or two ethylthio- groups.

In this reaction a thiopyrone (LI) can be produced as a by-product. When R and R' are parts of a five, six, seven or eight membered ring this is no longer possible. However, when the ring size is increased to fifteen carbon atoms the thiopyrone can again be formed.

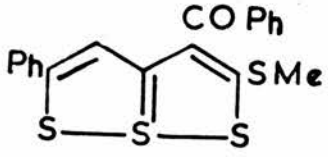
(c) From 5-methyl-1,2-dithiole-3-thiones and carbon disulphide. A methyl or methylene group in the 5-position of a 1,2-dithiole-3-thione is known to be acidic[83] and will condense with carbon disulphide in the presence of base[84,85]. Alkylation of the resulting dianion (LV) with methyl iodide gives a 2,5-dimethylmercapto-6a-thiathiophthene. The reaction of 3-methyl- or 3-methylene-1,2-dithiolium salts with carbon

disulphide in presence of base proceeds similarly to give 6a-thiathiophthene derivatives[86].

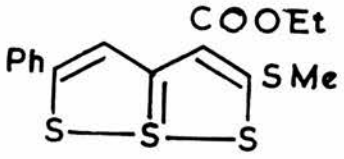
(d) From 3-methyl-1,2-dithiolium salts and methyl dithiobenzoate. A methyl group in the 3-position of the 1,2-dithiolium cation is extremely acidic, reacting rapidly with p-dimethylaminobenzaldehyde in acetic acid[87]. 3-Methyl-5-phenyl-1,2-dithiolium perchlorate reacts with methyl dithiobenzoate to give 2,5-diphenyl-6a-thiathiophthene.[63]

(e) From 3-methylene-1,2-dithiolium salts using the Vilsmeier reaction. The 3-methylene-1,2-dithiolium salt (LVI) reacts in a Vilsmeier-type reaction with dimethylformamide and phosphorus oxychloride, giving the the dimethylaminovinyl intermediate (LVII). This intermediate salt is solvolysed by aqueous sodium hydrogen sulphide to give the 6a-thiathiophthene (LVIII)[86].

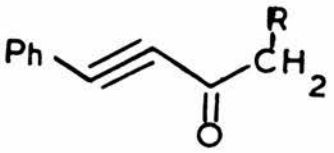
(f) From 3-methylmercapto-1,2-dithiolium salts and derivatives of methyl dithioacetate. Beer and co-workers[88] found that when 3-methylmercapto-5-phenyl-1,2-dithiolium methosulphate is heated in pyridine a small amount of the 6a-thiathiophthene (LIX) is formed. They attributed this product to a reaction between the dithiolium salt and methyl benzoyl dithioacetate, generated from the dithiolium salt with pyridine by nucleophilic attack at the 5-position. The structure of the thiathiophthene (LIX) was confirmed by an unambiguous synthesis from the dithiolium salt and an authentic sample of methyl benzoyl dithioacetate. This reaction can easily be extended to other derivatives of methyl dithioacetate: particularly useful is the reaction with methyl



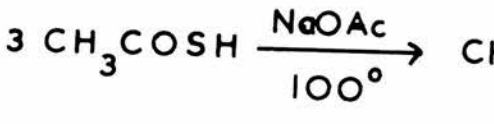
LIX



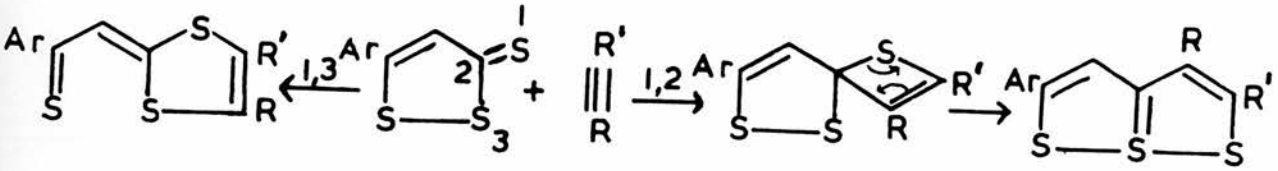
LX



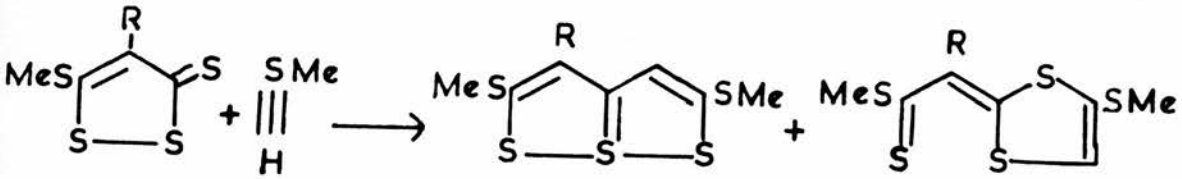
LXI



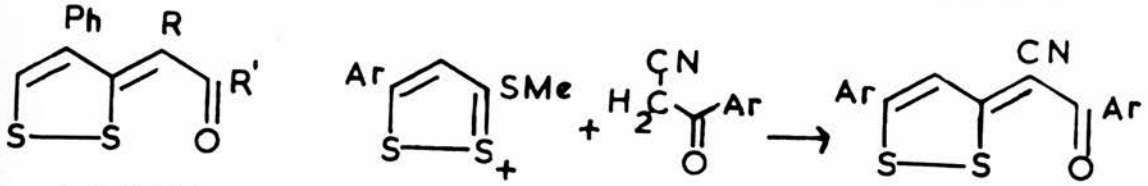
LXII



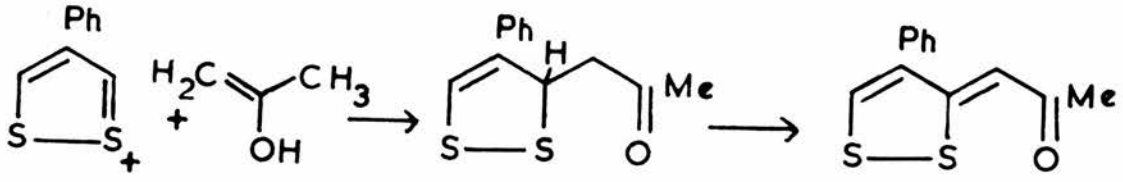
LXIII LXIV LXV



LXVI LXVII



LXVIII LXXI



LXIX LXX

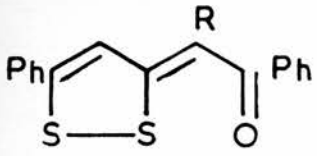
ethoxycarbonyl dithioacetate[85] which proceeds in almost quantitative yield. The product (LX) can then be hydrolysed and decarboxylated to give 2-methylmercapto-5-phenyl-6a-thiathiophthene.

(g) From 1,3-diketones or α-acetylenic ketones and thiolacetic acid. Acetylacetone reacts with thiolacetic acid in the presence of sodium acetate to give 2,5-dimethyl-6a-thiathiophthene[90]. α-Acetylenic ketones (LXI), having the same oxidation level as 1,3-diketones, react similarly to give 6a-thiathiophthenes having a methyl group in the 2-position. In this reaction thiolacetic acid supplies an acetyl or thioacetyl group and acts both as a sulphur-donor and an oxidising agent. The potential of thiolacetic acid as a sulphur-donor and oxidising agent is demonstrated in its reaction with sodium acetate at 100° to give acetaldehyde diacetyl dithioacetal (LXII)[91].

(h) From trithiones and acetylenic compounds. Acetylenes react with trithiones in a 1,3-dipolar addition reaction to give the thiones (LXIII)[84,92,93,94,95]. Behringer[92,93] found that in two cases the product was not the expected thione but the isomeric 6a-thiathiophthene (LXV) which is presumably formed by rearrangement of the spiro-intermediate (LXIV), derived from a 1,2-addition of the acetylene to the trithione. Vialle[84,95] investigated the reaction of mono-aryl acetylenes with 5-aryl-1,2-dithiole-3-thiones and found that mixtures of the two products were formed, the proportions depending on the reaction conditions. When the reactions were carried out in dry xylene the major products were the 6a-thiathio-

phthenes; in xylene, in the presence of hydrochloric acid gas, the major products were the thiones (LXIII). Further, the thiones could be isomerised to the thiathiophthenes by treatment with phosphorus pentasulphide in decalin. The reaction of 5-methylmercapto-1,2-dithiole-3-thione with methylmercapto acetylene proceeds in a similar manner[84], mixtures of the two products (LXVI) and (LXVII) being formed. Again the thiones (LXVII) can be isomerised to the 6a-thiathiophthenes (LXVI) by treatment with phosphorus pentasulphide.

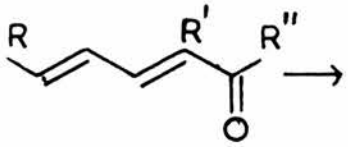
(i) From 4-phenyl-1,2-dithiolium salts and ketones. The condensation of 4-phenyl-1,2-dithiolium salts[96] with methyl and methylene ketones proceeds smoothly and in good yield to give acylmethylenedithioles (LXVIII) which are converted into the corresponding 6a-thiathiophthenes by treatment with phosphorus pentasulphide[67,69]. The mechanism of this reaction is illustrated by the condensation of 4-phenyl-1,2-dithiolium perchlorate with acetone[69]. Attack of the electrophilic dithiolium cation on the enol or anionoid form of acetone gives the acylmethyldithiole (LXIX) which can be isolated and then dehydrogenated to the acylmethylenedithiole (LXX) with chloranil. The acylmethyldithioles from alkyl-aryl ketones are not isolable, being dehydrogenated during the reaction by the excess of the 1,2-dithiolium salt. Acetaldehyde itself does not react but ethyl vinyl ether does so readily[69]. This reaction also proceeds with 3-phenyl-1,2-dithiolium salts but yields are poor.



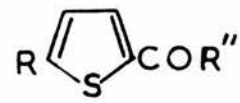
LXXII

a R=H

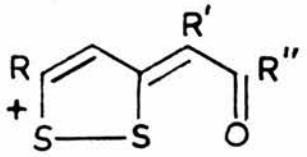
b R=CN



R'=H, COOEt

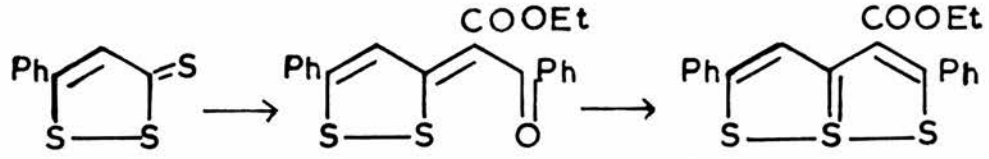


LXXIII

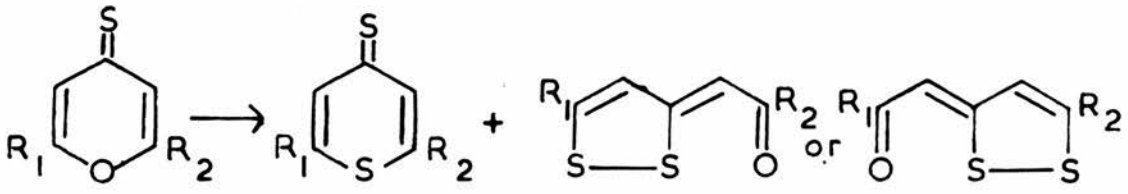


LXXIV

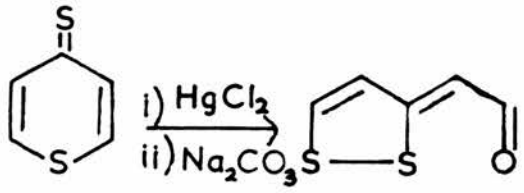
LXXV



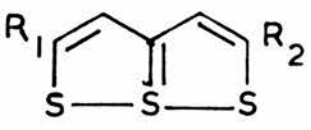
LXXVI LXXVII



LXXVIIIa



LXXIX



LXXVIIIb

R_1=Ph, R_2=H, Me

(j) From 5-aryl-3-methylmercapto-1,2-dithiolium salts and activated methylene ketones. The condensation of 3-methylmercapto-1,2-dithiolium salts with cyanmethyl ketones proceeds in good yield to give the acylmethylenedithioles (LXXI)[67,68] which are converted to 3-cyano-2,5-diaryl-6a-thiathiophthenes by treatment with phosphorus pentasulphide. The cyano group can then be removed by successive hydrolysis and decarboxylation. The reaction of 3-methylmercapto-5-phenyl-1,2-dithiolium perchlorate with the sodium enolate of ethyl benzoyl acetate gives the ketone (LXXIIa) in good yield, hydrolysis and decarboxylation of the ester occurring during the reaction.[63]

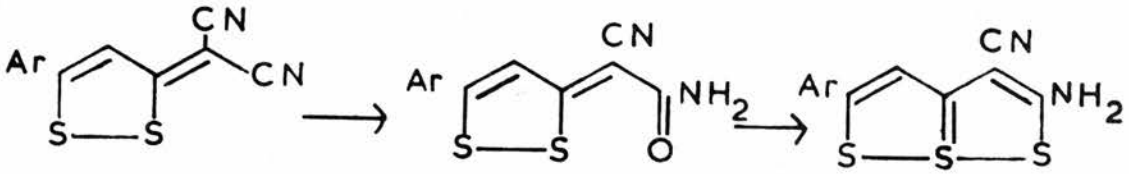
(k) From 5-phenyl-1,2-dithiole-3-one and activated methylene ketones. 5-Phenyl-1,2-dithiole-3-one reacts with benzoyl acetonitrile in phosphorus oxychloride to give the ketone (LXXIIb)[67] which is converted into 2,5-diphenyl-6a-thiathiophthene as previously described. 5-Phenyl-1,2-dithiole-3-one reacts with diazoacetophenone in a melt to give ketone (LXXIIa) in low yield[63]. A similar reaction with 5-p-methoxyphenyl-1,2-dithiole-3-thione gives the corresponding ketone in 30% yield[106].

(l) From α,γ-diethylenic ketones and sulphur. The action of sulphur at elevated temperatures on α,γ-diethylenic ketones gives a mixture of 2-acyl-thiophenes (LXXIII) and the ketones (LXXIV)[59,97]. The latter react with phosphorus pentasulphide to give the corresponding 6a-thiathiophthenes. When R"=COOEt the ester group can be removed by successive hydrolysis and decarboxylation.

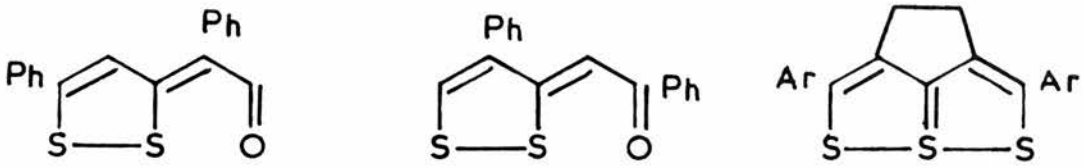
(m) From 2-aroyl acetoacetic esters and phosphorus pentasulphide. Trebaul and Teste[98] found that when ethyl-2-benzoyl-acetoacetate was heated with phosphorus pentasulphide in pyridine the product was neither of the expected 4-acyl-trithiones (LXXV), but a mixture of 5-phenyl-trithione and the thiathiophthene (LXXVII). They suggested that the first stage in the reaction was a deacetylation of the ester to give ethyl benzoyl acetate which reacts with phosphorus pentasulphide to form 5-phenyl-trithione; condensation of the trithione with more ethyl benzoyl acetate gives the ketone (LXXVI) which is then converted into the thiathiophthene by reaction with phosphorus pentasulphide.

(n) From 4H-pyran-4-thiones. Traverso[99,100,101,102] found that treatment of 4H-pyran-4-thiones with alkali sulphide or hydrosulphide gives acylmethylenedithioles (LXXVIIIa) in addition to the expected 4H-thiopyran-4-thiones, the nature of the product depending on the substituents R_1 and R_2. Alkaline hydrolysis of the mercuric chloride complex of 4H-thiopyran-4-thione converted it into the unsubstituted aldehyde (LXXIX) and so by this method Traverso was able to prepare the parent heterocycle, 6a-thiathiophthene[103].

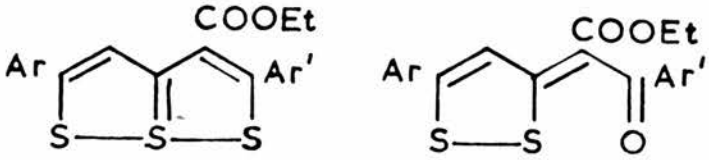
(o) Synthesis of 2-amino-6a-thiathiophthenes. The dinitrile (LXXX) can be prepared from malonitrile by method (k) above[69], or by a 1,2-dipolar addition of tetracyanoethylene to 5-aryl-trithiones[104]. Hydrolysis of the dinitrile gives the amide (LXXXI) which is



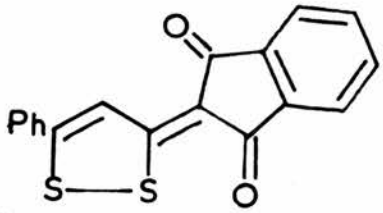
LXXX LXXXI LXXXII



LXXXIII LXXXIV LXXXV

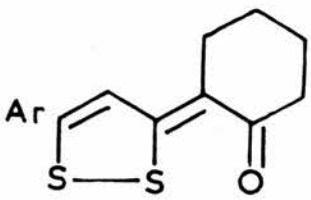


LXXXVI LXXXVII

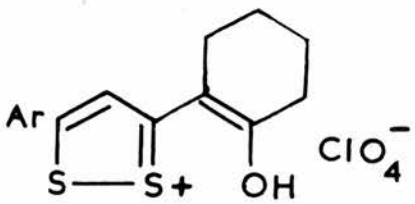


XC

LXXXVIII LXXXIX



XCI



XCII

PLATE II

converted to the 2-amino-6a-thiathiophthene (LXXXII) by treatment with phosphorus pentasulphide[69]. Compound (LXXXII) can also be prepared directly from the dinitrile by treatment with hydrogen sulphide in pyridine in the presence of triethylamine[104]. The condensation between 5-phenyl-3-methylmercapto-1,2-dithiolium iodide and cyano thioacetamide gives 2-amino-3-cyano-5-phenyl-6a-thiathiophthene directly[105].

REACTIONS.

(a) Carbonyl reactions. The aldehyde (LXXIX) readily forms a 2,4-dinitrophenylhydrazone[76]; under the same conditions 6a-thiathiophthene does not react. Since one might expect a thioaldehyde to be more reactive than the corresponding aldehyde[107], this confirms the interaction of the three sulphur atoms in the thiathiophthene system. The aldehyde (LXXXIII) readily forms a 2,4-dinitrophenylhydrazone while the isomeric ketone (LXXXIV) does not[67]; the methyl ketone (XXVIIa) reacts slowly[76]. The thiathiophthenes (LXXVIIIb) react with hydroxylamine with evolution of hydrogen sulphide, the colour of the solution changing from red to yellow-brown[99], presumably with formation of the corresponding oximes.

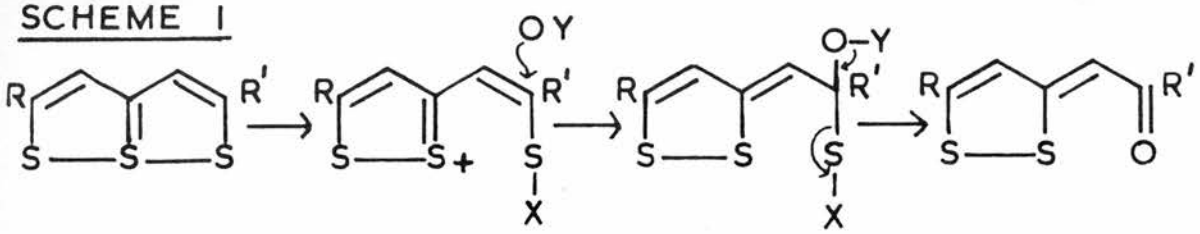
Thiathiophthenes show typical thione properties in their reactions with mercuric compounds. Thus compounds (LXXVIIIb) form complexes with mercuric chloride[99]. The reaction of thiathiophthenes with mercuric acetate in acetic acid at room temperature leads to the replacement of one atom of sulphur by oxygen. This reaction

is highly specific: thus 2,4-diphenyl-6a-thiathiophthene, prepared from ketone (LXXXIV), gives the aldehyde (LXXXIII) in quantitative yield[67]. Under the same conditions 2,5-diphenyl-6a-thiathiophthene does not react. The thiathiophthenes (LXXXV) react instantaneously with mercuric acetate in boiling acetic acid[81]. When the thiathiophthenes (LXXXVI) react with mercuric acetate the products are the β-ketoester derivatives (LXXXVII)[98].

2,5-Dimethyl-6a-thiathiophthene reacts with 70% perchloric acid or conc. sulphuric acid with evolution of hydrogen sulphide to give the oxygen analogue (XLII). When the thiathiophthenes (LXXVIIIb) are treated with concentrated acid, hydrogen sulphide is evolved and the resulting solutions have the yellow colour typical of the oxygen analogues[99]. The product from the reaction of 2-methyl-5-phenyl-6a-thiathiophthene with concentrated acid has been shown by Raney nickel desulphurisation[108] to be the methyl ketone (LXXXVIII). There was no evidence for the presence of the isomeric phenyl ketone (LXXXIX). The structures of these isomeric ketones can be readily differentiated by I.R. and N.M.R. spectroscopy[79]. An interesting reaction occurs when the ester (LXXXVI, Ar=Ar'=Ph) is treated with conc. sulphuric acid, the product being the indanedione derivative (XC)[97], formed by acid catalysed cyclisation of the ester onto the ortho-position of the benzene ring.

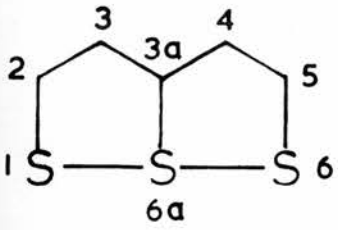
The ketones (XCI) form stable perchlorates (XCII)[77] and so might be expected to react with alkylating agents. There is no evidence for the formation of stable perchlorates from thiathio-

SCHEME I



conc. acid reaction X=H , OY=H_2O

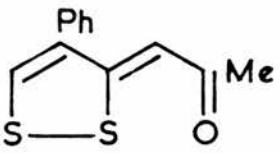
mercuric acetate reaction X= HgOAc, OY=CH_3COO^-



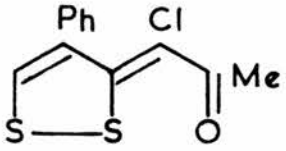
Atom	Net Charge
1	+0.04
2	−0.10
3	−0.20
3a	−0.12
6a	+0.64

(ref.57)

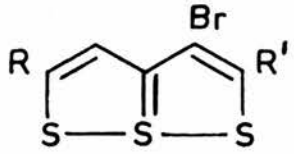
fig. 5



XCIII

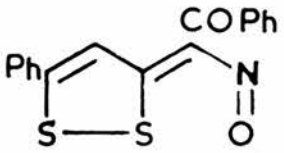


XCIV

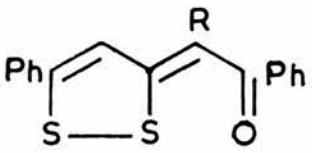


XCV

R= R'= Me or Ph



XCVI



XCVII

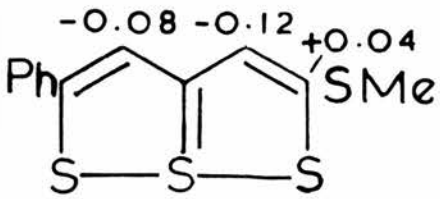
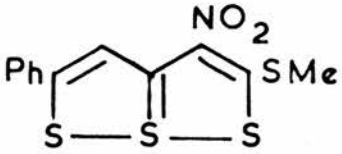
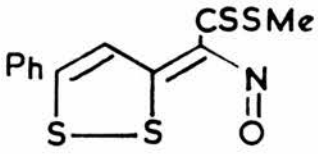


fig. 6



XCVIII



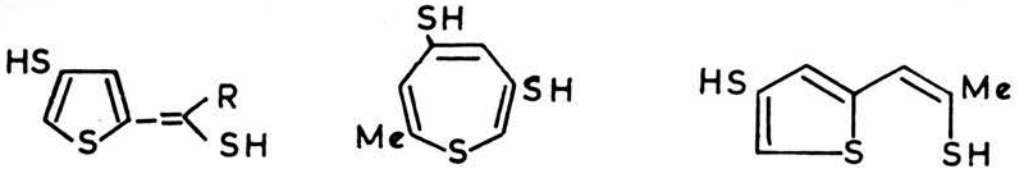
XCIX

phthenes, which are also resistant to alkylating agents such as dimethyl sulphate[67].

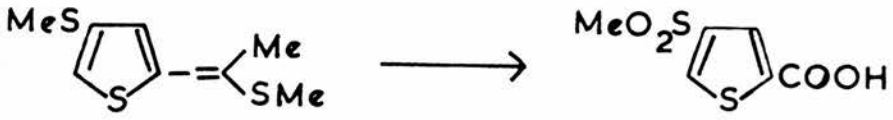
A comparative study of the above reactions with variously substituted thiathiophthenes might provide much useful information. Consideration of the likely mechanisms for the reactions of thiathiophthenes with mercuric acetate and with concentrated acid (scheme 1), suggests that these reactions should follow parallel courses.

(b) Substitution reactions. The charge densities calculated for the thiathiophthene system (fig.5) indicate that electrophilic substitution should occur at the 3-position. Attempts to chlorinate 2-methyl-5-phenyl-6a-thiathiophthene with sulphuryl chloride failed[69]. However, the oxygen analogue (XCIII) was readily chlorinated to give compound (XCIV), which did not react with phosphorus pentasulphide. 2,5-Dimethyl- and 2,5-diphenyl-6a-thiathiophthenes react readily with bromine in inert solvents to give the monobromo compounds (XCV)[85]. 2-Methyl-5-phenyl-6a-thiathiophthene is brominated at the 3-position, in agreement with calculated charge densities for this compound[109]. Attempted nitration and nitrosation of 2,5-diphenyl-6a-thiathiophthene both yielded the nitroso compound (XCVI)[109], which could also be obtained by nitrosation of the ketone (XCVII, R=H). Structure (XCVI) is preferred to the isomeric structure (XCVII, R=NO) on the basis of visible and I.R. spectra.

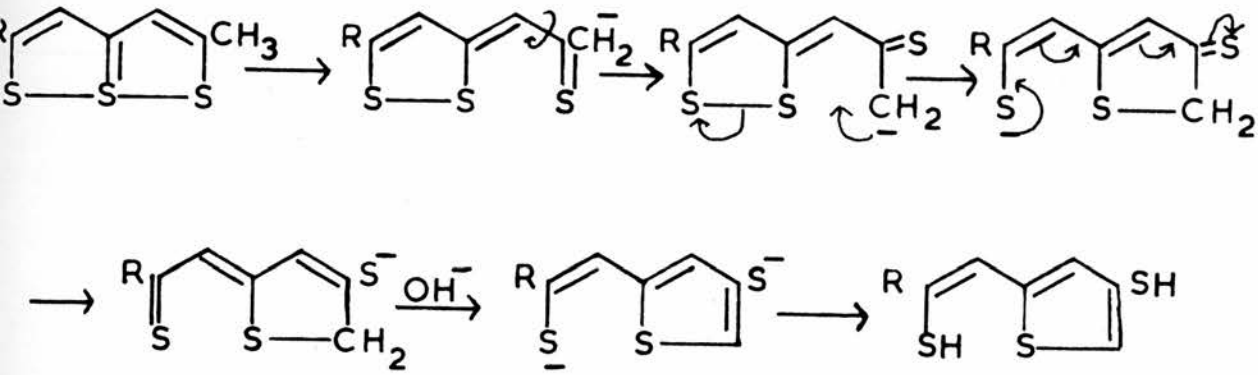
The charge densities calculated for 2-methylmercapto-5-phenyl-



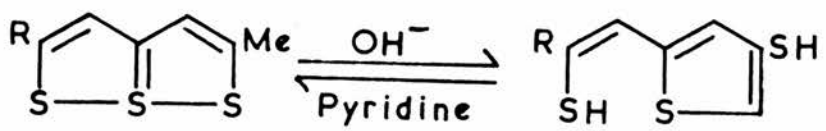
C CI CIV



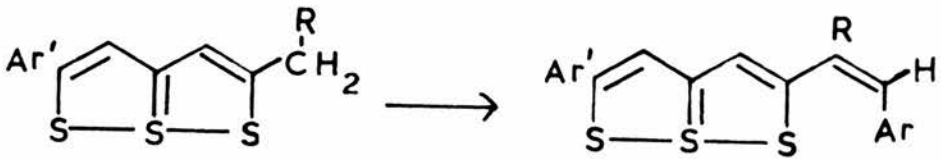
CII CIII



SCHEME 2



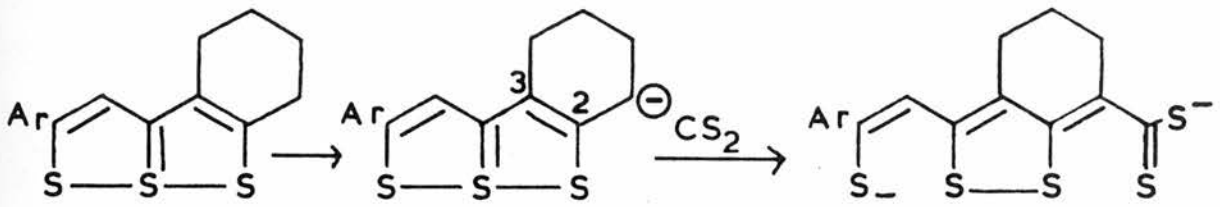
CV



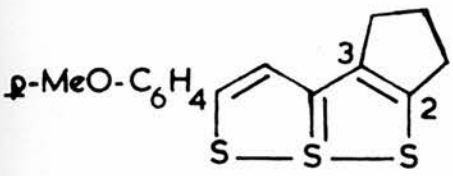
CX

6a-thiathiophthene[109] are shown in fig. 6. In agreement with these calculations, bromination and nitration take place at the 3-position. The structure of the nitration product (XCVIII) was confirmed by an unambiguous synthesis from 3-methylmercapto-5-phenyl-1,2-dithiolium methosulphate and methyl nitrodithioacetate. Nitrosation also takes place at the 3-position; the authors believe that the nitroso compound is best formulated as structure (XCIX). The methylmercapto group in 2-methylmercapto-5-phenyl-6a-thiathiophthene is slowly replaced by nucleophiles such as ethoxide ion and primary aliphatic amino groups. The calculated positive charge density at the 2-position is in accord with these findings.

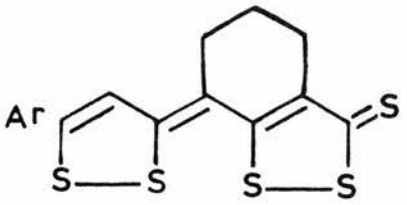
(c) Side chain reactivity. Thiathiophthenes with a methyl (or methylene) group in the 2-position are rearranged by hot methanolic potassium hydroxide to unstable products[48,110], whose chemical properties are consistent with the dimercapto thiophene structures (C). Thus with dimethyl sulphate they give dimethyl thioethers. Oxidation of the dimethyl thioethers gives disulphones, indicating that one of the sulphur atoms is involved in an aromatic system such as thiophene. The dimethyl thioethers react with mercuric chloride in a manner typical of thiophenes with a free 2-position. Bothner-By and Traverso[112] reported that the N.M.R. spectrum of the rearrangement product from 2,5-dimethyl-6a-thiathiophthene was consistent with the dimercapto thiepin structure (CI), which had earlier been suggested by Arndt[111] as an alternative to the



CVI CVII CVIII

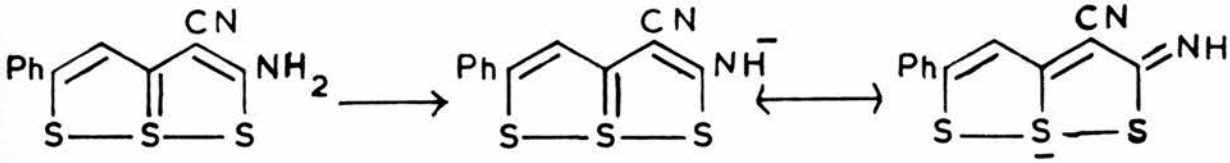


CXI

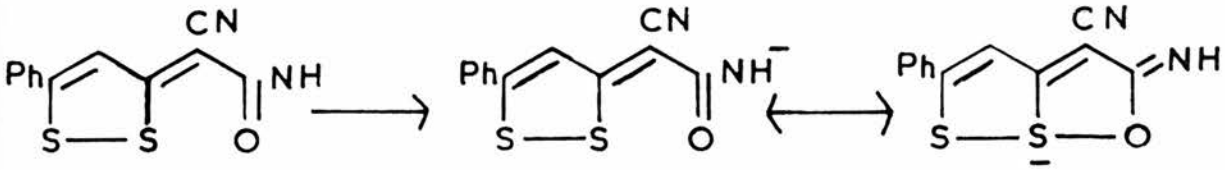


CIX

CXII



CXIII CXIV



CXV CXVI

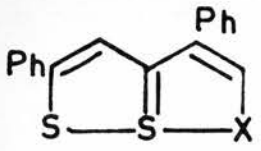
thiophene structure. Arndt and Walter[113] have presented chemical evidence in favour of the thiophene structure: oxidation of the dimethyl thioether (CII) gives a carboxylic acid whose equivalent weight corresponds to the thiophene carboxylic acid (CIII). An X-ray crystallographic study[114] has shown conclusively that the rearrangement product from 2,5-dimethyl-6a-thiathiophthene has the planar thiophene structure (CIV), the general configuration of the molecule being similar to 2,5-dimethyl-6a-thiathiophthene. The accepted mechanism for this reaction [115,116] (scheme 2) involves, as its first step, the removal with base of a proton from the methyl group, which must therefore be acidic. The rearrangement is reversed by heating the dimercaptans in pyridine[48,110], the thiathiophthenes being regenerated in good yield. This reversible rearrangement could be regarded as an equilibrium (CV), strong base favouring the thiophene structure and weak base favouring the thiathiophthene. These reactions require further investigation, and in particular, the unusual colour changes which accompany the reverse reaction.

Stavaux and Lozac'h[116], in attempting to condense the methyl group of 2-methyl-5-phenyl-6a-thiathiophthene with carbon disulphide in strongly basic medium, found that the above rearrangement was occurring. However, with the thiathiophthene (CVI) the carbanion formed (CVII) cannot undergo the rearrangement as the necessary rotation about the C_2-C_3 bond is not possible. This carbanion reacts with carbon disulphide to give the dianion (CVIII) which can be

oxidised to the thione (CIX). The same authors[117] have condensed a series of 2-methyl- and 2-methylene-6a-thiathiophthenes with aromatic aldehydes to give the styrene derivatives (CX). Attempts to condense 3-methyl-2,5-diphenyl-6a-thiathiophthene with benzaldehyde were unsuccessful, the methyl group in the 3-position being unreactive. Similarly the cyclopenteno derivative (CXI) reacts with one molecule of benzaldehyde, the methylene group in the 3-position being unreactive. The authors suggest that the acidity of the methyl group in the 2-position indicates that structures (CXII) in which the 2-position carries a positive charge, may be more important than hitherto assumed.

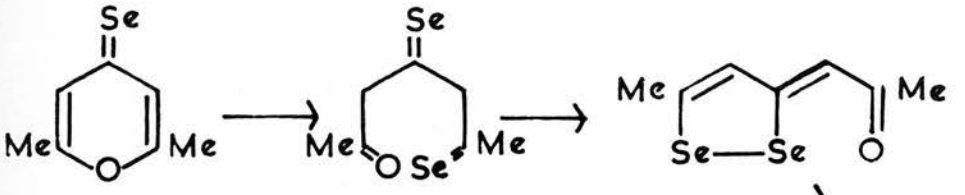
2-Amino-6a-thiathiophthenes. These compounds show typical thiathiophthene U.V. and visible spectra[69]. The 2-amino-6a-thiathiophthene (CXIII) is acidic rather than basic and is unexpectedly stable to alkali. A likely explanation for this is that the anion (CXIV) is stabilised by electron delocalisation onto the central sulphur atom. The related amide (CXV) is also acidic and stable to alkali. The U.V. spectra of compounds (CXIII)and (CXV) are entirely different in neutral solution, but in alkaline solution they are almost identical, indicating stabilisation of the anion (CXVI) by electron delocalisation via sulphur-oxygen bonding.

Selenium analogues of 6a-thiathiophthene. The aldehyde (LXXXIII) reacts with phosphorus pentaselenide to give the selenium analogue (CXVIIa)[118]. X-Ray crystallography confirms the structure. The two



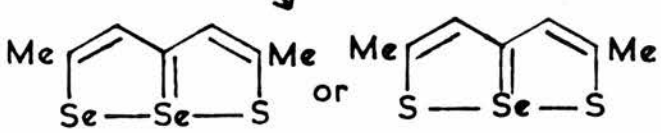
		S–S	S–X
a	X=Se	2.49	2.33
b	X=S	2.51	2.22

CXVII

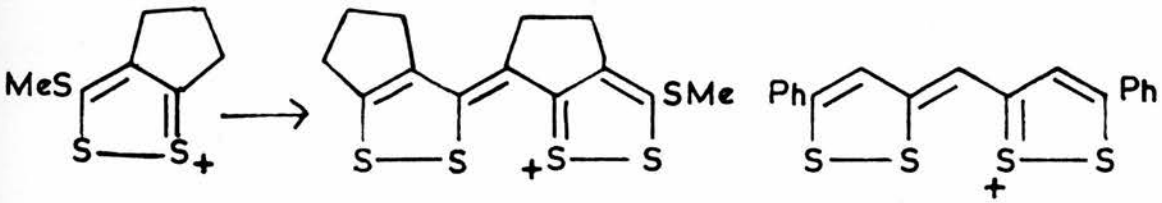


CXVIII

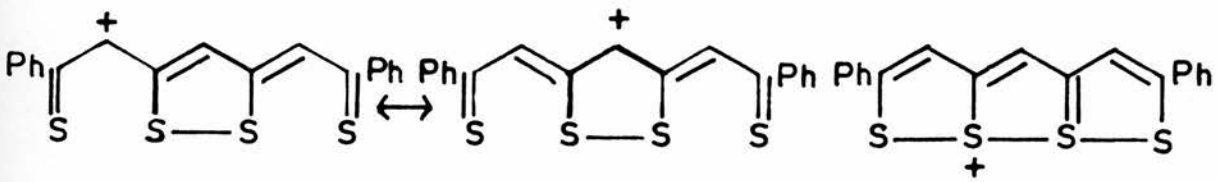
CXIX



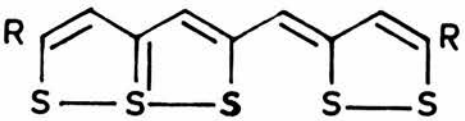
CXX CXXI



CXXII CXXIII CXXIV



CXXV CXXVI

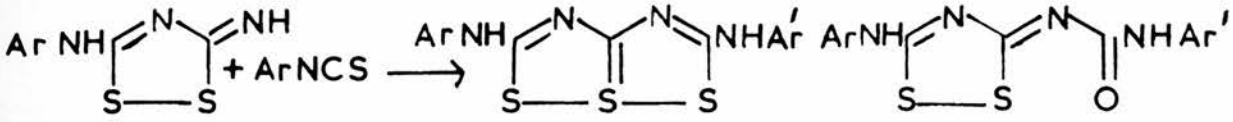


CXXVII

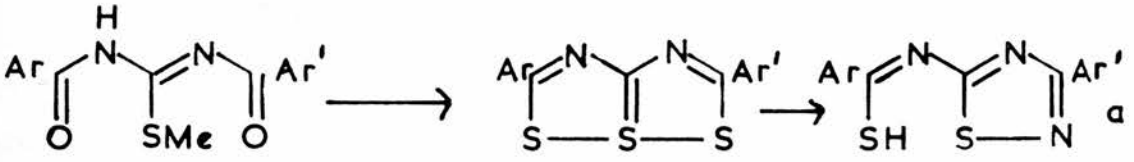
PLATE 15

rings of the heterocycle are inclined at an angle of 6.6° to one another. The sulphur-sulphur bond distance (2.49Å) is similar to that reported for the corresponding distance in the thiathiophthene (2.51Å), indicating that replacement of one atom of sulphur by selenium has little effect on the other sulphur-sulphur bond. The sulphur-selenium bond distance is 2.33Å, compared with the sum of the single-bond covalent radii (2.21Å)[56]. Subtraction of the difference in single-bond covalent radii for sulphur and selenium from the sulphur-selenium bond distance gives a figure of 2.21Å, almost identical to the "short" sulphur-sulphur distance in the thiathiophthene. The thiathiophthene and its selenium analogue are obviously closely related structurally. The U.V. and visible spectra of the selenium compound and the aldehyde (LXXXIII) show a relationship similar to that found for the thiathiophthene and the aldehyde. Similarity to the thiathiophthene is also shown in the elimination of selenium on treatment with mercuric acetate.

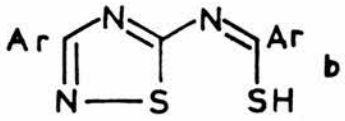
Traverso has described a synthesis of the thiathiophthene analogue(CXX) containing two selenium atoms[119]. Treatment of 2,6-dimethyl-4H-pyran-4-selenone with sodium selenide followed by careful acidification gives α,β-diseleno-diacetylacetone (CXVIII) which undergoes aerial oxidation to the ketone (CXIX). Treatment of this ketone with phosphorus pentasulphide gives the thiathiophthene analogue. In a later paper[75] this product is formulated as the structure (CXXI) which has only one selenium atom; no details are given.

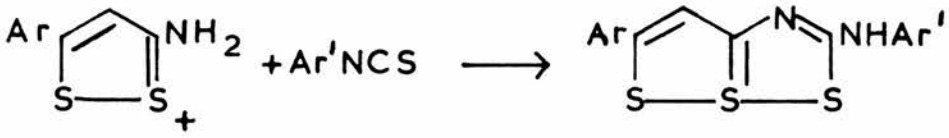


CXXVIII CXXIX

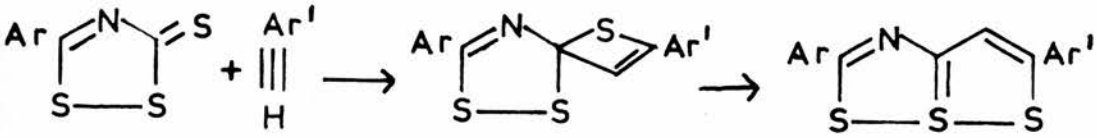


CXXX + CXXXI

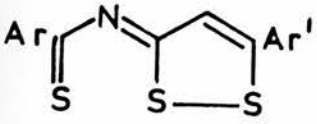




CXXXII



CXXXIII



CXXXIV

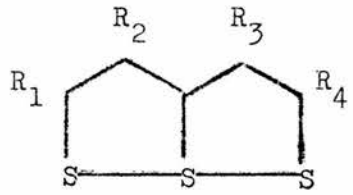
PLATE 16

Thiathiophthene homologues containing four collinear sulphur atoms. Self-condensation of the methylmercapto dithiolium salt (CXXII) gives the dithiolocyanin (CXXIII)[120]. The dithiolocyanin (CXXIV) was prepared by a condensation reaction between 3-methyl-5-phenyl-1,2-dithiolium perchlorate and the corresponding 3-methylmercapto compound[121,122]. X-Ray crystallography[123] shows the molecule (CXXIV) to be planar, the four sulphur atoms being nearly collinear. The distance between the internal sulphur atoms (3.0-3.1Å) is shorter than the van der Waals distance for two sulphur atoms (3.70Å). This led Klingsberg[121] to formulate the compound as a resonance hybrid to which structures of type (CXXV) contribute. Leaver[122], however, regards the interannular bonding as a consequence of valence shell expansion of the internal sulphur atoms giving structures such as (CXXVI). The homologue of thiathiophthene containing five collinear sulphur atoms (CXXVII) has not yet been synthesised.

Aza-analogues of 6a-thiathiophthene. The reaction of 5-amino-3-arylimino-1,2,4-dithiazoles with aryl isothiocyanates gives products which are formulated as derivatives of 2,5-diamino-3,4-diaza-6a-thiathiophthene (CXXVIII)[70]. Compounds (CXXVIII) and their oxygen analogues (CXXIX) show a relationship in their U.V. spectra similar to that shown by thiathiophthenes and their oxygen analogues. Further resemblance to the 6a-thiathiophthene system is shown by the synthesis of a single 3,4-diaza-6a-thiathiophthene from isomeric starting materials. The reaction of N,N-diaroyl-S-methyl-isothioureas

with phosphorus pentasulphide gives 2,5-diaryl-3,4-diaza-6a-thiathiophthenes (CXXX)[124]. The authors have presented further chemical proof of the symmetrical nature of the system: thus the diaza-thiathiophthene (CXXX) gives two products (CXXXIa) and (CXXXIb) with ammonia, indicating the equivalence of the two outer sulphur atoms. The reaction of 3-amino-5-aryl-1,2-dithiolium salts with aryl isothiocyanates gives compounds which are formulated as derivatives of 3-aza-6a-thiathiophthene (CXXXII)[125]. Related compounds (CXXXIII) are obtained from addition reactions of aryl acetylenes to 5-aryl-1,2,4-dithiazole-3-thiones[126]. The authors formulate these compounds as the thiobenzamide derivatives (CXXXIV).

Substituted 6a-Thiathiophthenes.*



R_1	R_2	R_3	R_4	Synthesis Method	Yield (%)	M.p. (°C)	Ref.
H	H	H	H	n		114	103
Me	H	H	Me	a	15-40	183-184	47, 59, 90
				g	9		90
Et	H	H	Et	a		56	101
Et	$-CH_2-CH_2-CH_2-$		Et	a	59	70-71	68
Ph	H	H	H	n	20-50	135-136	79, 99, 100
H	Ph	H	H	i	32	61-63	69
Ph	H	Ph	H	i	30	129-131	67
Ph	H	H	Ph	a	39-47	162	90, 100
				d			63
				h	30	165	95
				j	9-35		63, 67, 68, 72
				k	23	166-168	67
				l	3	165	59, 97
Ph	Ph	Ph	H	i		178-180	67
Ph	Ph	H	Ph	a	30	188	81
				h	41	185-186	93
Ph	Ph	Ph	Ph	a	5	262	81

* Compounds which differ only in that they carry a substituent in a benzene ring are not included. Intermediate cyano- and (m)ethoxycarbonyl derivatives are not included.

R_1	R_2	R_3	R_4	Synthesis Method	Yield (%)	M.p. (°C)	Ref.
-=-=-		H	Ph	j	28	130-132	68
Ph	H	H	3-pyridyl	a	26	151	81
Ph	H	H	Me	a	28	169	81, 100
				g	36		90
				n	18,52	169	79, 99
Me	H	Ph	H	i	38	82.5-83.5	69
Ph	H	H	Et	a	43	109	117
Ph	H	Me	Me	g	39	150-151	90
Ph	Me	H	Ph	a	30	157	81
				h	50	156	95
Ph	H	Ph	Me	g	81	147-148	90
Ph	Me	Me	Ph	a	10	184	81
Ph	Me	Ph	Ph	a	15	176	81
Ph	$-CH_2-CH_2-$		Ph	a	26	233	81
Ph	$-CH_2-CH_2-CH_2-$		Ph	a	22	153	81
Ph	H	$-(CH_2)_4-$		i	24	154	72
Ph	Me	$-(CH_2)_4-$		i	15	168	72
Ph	$-CH_2-CHMe-CH_2-$		Ph	a	17	164	81
Ph	H	$-CH_2-CH_2-C_6H_4-$		i		158	165
Ph	H	H	Ph-CH=CH-	a	17	233	81
Ph	COPh	H	Ph	i		175	72
				j			105
SMe	$-CH_2-CH_2-$		H	e		163	86
SMe	H	H	SMe	c	15	97	84, 85
				b	13		84
SMe	Me	H	SMe	c	34	100	84
				h	42		84
SMe	Et	H	SMe	b	50	110	82
				c	27		84

R_1	R_2	R_3	R_4	Synthesis Method	Yield (%)	M.p. (°C)	Ref.
SMe	$-CH_2-CH_2-$		SMe	b	42	169-170	82
				c	40	150	84
SMe	$-(CH_2)_3-$		SMe	b	58	148-149	82
				c		149-151	86
SMe	$-(CH_2)_4-$		SMe	b	35	154-155	82
				c	17	156	84
SMe	$-(CH_2)_5-$		SMe	c	26	218	84
SMe	Ph	H	SMe	c	65	139-140	84, 85
				f			85
				h	15		84
Ph	H	H	SMe	f		125-126	85
Ph	H	COPh	SMe	f	80	163-164	88

PART B

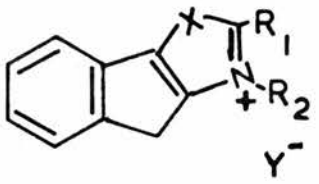
DISCUSSION

The Synthesis and Reactions of Some 4H-Indeno[2,1-d]azolium Salts.

Reid and Salmond[127] have synthesised a series of 4H-indeno[2,1-d]thiazolium salts (1, X=S). Reaction of these salts with base generates a carbanion site in the five-membered carbocyclic ring (2a, X=S)[128]. The charges can be delocalised within the framework of the five-membered rings to give the dipolar structure (2c, X=S). Alternatively, if charge neutralisation occurs, then structure (2b, X=S) is achieved in which the d-orbitals of sulphur must be utilised in bonding. These deprotonation products are themselves unstable, but they react readily with electrophiles to give stable acyl derivatives (3, X=S). Spectroscopic investigation of these derivatives indicates that they exist in the dipolar state (3a, X=S). This, however, does not rule out the possibility of a contribution from structure (3b, X=S) to the ground state of the molecule.

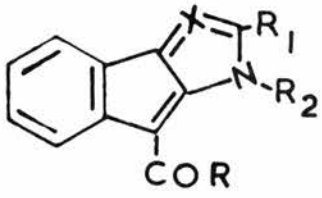
In an attempt to clarify the situation, the synthesis of the oxygen and selenium analogues (3, X=O,Se) was undertaken. It was hoped that comparison of the spectral properties of the oxygen, sulphur and selenium compounds would help to resolve the problem, since the oxygen atom, unlike sulphur and selenium, cannot expand its valence shell.

The primary objective was to synthesise the oxygen and selenium analogues of the thiazolium salt (4, X=S). The selenazolium salt was successfully synthesised, as were its acyl derivatives. However, attempts to synthesise the oxygen analogue were unsuccessful. Attention was then turned to the compounds (5, X=O,S,Se). All three azolium salts were synthesised, the selenazolium salt in low yield. The acyl



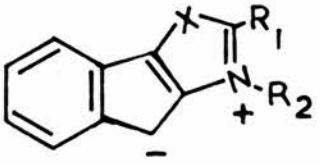
1

a

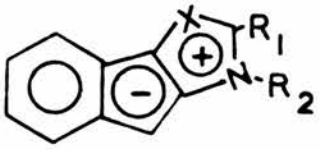


b

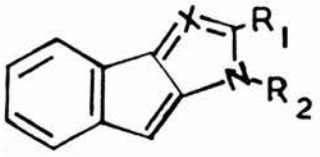
3



a

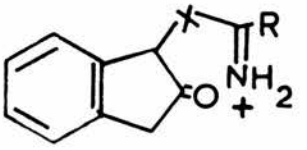


c



b

2



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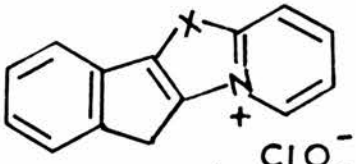

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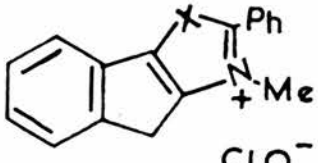

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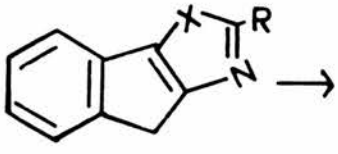

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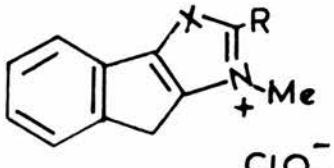

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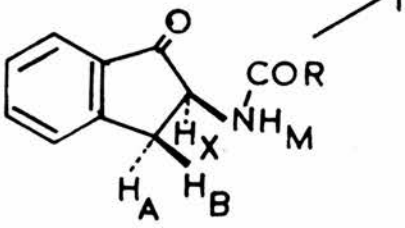

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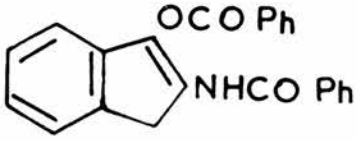


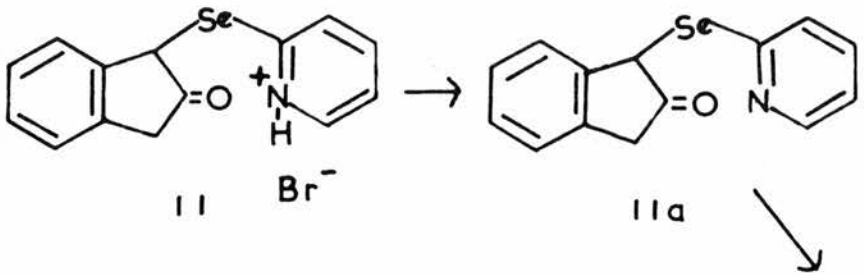
8

PLATE 17

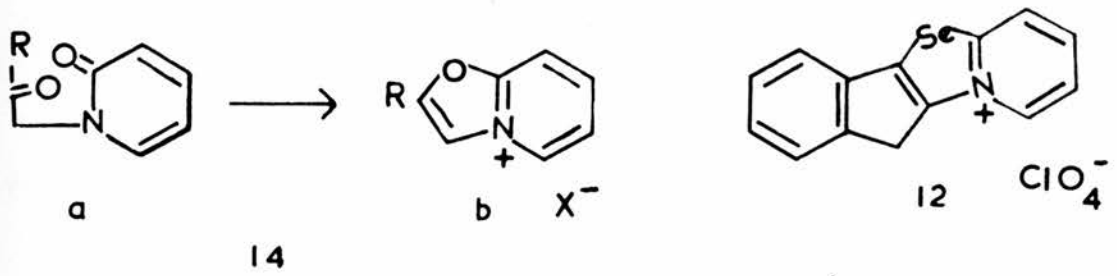
derivatives (3, X=S, R_1=Ph, R_2=Me) of the thiazolium salt (5, X=S) were prepared, but attempts to prepare similar acyl derivatives of the oxazolium salt (5, X=O) were unsuccessful; the only products isolable from the reactions of the oxazolium salts were orange polymeric materials, presumably formed by ring opening of the oxazolium salt with base.

1-Bromoindan-2-one reacted smoothly with thio- and selenobenzamide and 2-selenopyridone, giving the intermediate thiolimidate and selenolimidate salts (6, R=Ph, X=S,Se) and (11). N.M.R. spectroscopy (table A 1) indicates that these compounds exist in the ketonic form in trifluoroacetic acid solution and I.R. spectroscopy indicates that they exist in the enolic form in the solid state. In the I.R. spectra there is no absorption in the carbonyl region. There is, however, strong absorption in the 1100 $cm.^{-1}$ region, attributable to C-O stretching in enols, and broad absorption in the 2500-3400 $cm.^{-1}$ region, where both N-H and O-H stretching vibrations occur. The mechanism of this tautomerism has been investigated in a series of closely related compounds[128], and the evidence indicates that when the enol form is dissolved in trifluoroacetic acid a proton is transferred from nitrogen to carbon (13), rather than from oxygen to carbon as is usual in keto-enol tautomerism.

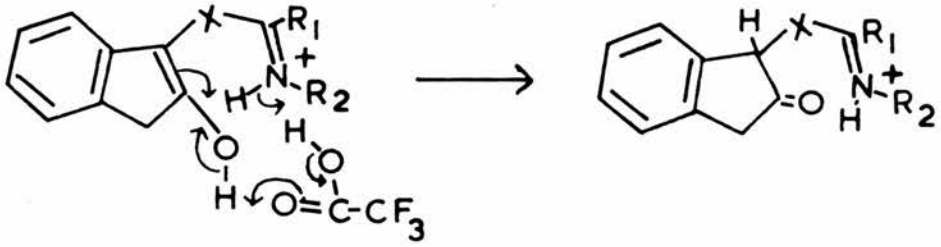
The salts (6, R=Ph, X=S,Se) were cyclised to the azoles (9, R=Ph, X=S,Se) with thionyl chloride in dimethylformamide[127]. Quaternisation of the azoles with methyl-p-toluenesulphonate gave the corresponding azolium salts (10). Attempts to cyclise the salt (11) with phosphorus



11 Br^- 11a



a 14 b X^- 12 ClO_4^-



13

$$AmONO + HCl \rightleftharpoons Am\overset{+}{\underset{H}{O}}NO \rightleftharpoons AmOH + NOCl$$

$$Cl^-$$

SCHEME 1

$$\Updownarrow$$

$$AmOH + NO^+ + Cl^-$$

pentachloride in boiling nitromethane[127] led to decomposition. However, the conjugate base (11a) was readily cyclised with phosphorus pentachloride in a mixture of nitromethane and methylene chloride to the selenazolium salt (12).

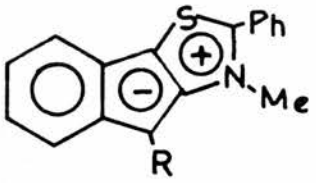
Attempts to prepare the oxygen analogue (4, X=O) by condensation of 1-bromoindan-2-one with 2-pyridone or its sodium salt were unsuccessful. 2-Methoxypyridine is quaternised by α-bromoketones[129], giving the diketones (14a) which can be cyclised to the oxazolium salts (14b) with concentrated sulphuric acid. This reaction failed with 2-bromoindan-1-one. The oxazolium salts (10, X=O) were synthesised by an alternative route. The reported method of preparation of 2-oximino-indan-1-one using amyl nitrite[130] gave poor results. It was found that nitrosation of indan-1-one occurred readily when nitrosyl chloride was added to a cold solution containing the ketone and an alcohol (amyl alcohol or ethanol). It would appear that the nitrosonium cation is more readily formed from nitrosyl chloride and amyl alcohol than from amyl nitrite and hydrochloric acid gas (scheme 1).

Attempted benzoylation of 2-aminoindan-1-one hydrochloride in a two-phase aqueous system led to reaction at both the nitrogen and oxygen atoms, giving the dibenzoyl compound (8). Reaction of the amine hydrochloride with benzoyl chloride and pivaloyl chloride in a mixture of acetonitrile and pyridine gave the amides (7), whose structure was readily confirmed by N.M.R. spectroscopy (table A 4). The spectra show an ABX splitting pattern, the signals due to H_X being further split by the proton on nitrogen (H_M). The cis, trans

assignments are made on the basis of coupling constants, the larger coupling being attributed to the cis-hydrogens. Attempts to cyclise these amides with concentrated sulphuric or polyphosphoric acid[131] failed. They were successfully cyclised to the oxazoles (9, X=O), however, by boiling phosphorus oxychloride. Quaternisation of the oxazoles with methyl-p-toluenesulphonate gave the 4H-indeno[2,1-d] oxazolium salts (10, X=O).

The azoles (9, R=Ph, X=O,S,Se) show a blue-violet U.V. fluorescence which is characteristic of 2,5-diphenylazoles. The U.V. spectra (table C 1) show the typical pattern for the replacement of oxygen by sulphur and selenium in heterocyclic systems[132]. Thus replacement of oxygen by sulphur and selenium respectively causes a bathochromic shift of the long wavelength transition from 326 to 343 to 352 mμ. In addition a weak absorption shifts from 246 to 260 to 272 mμ and is strengthened. The N.M.R. spectra of these azoles (table A 2) show some interesting variations. When oxygen is replaced by sulphur and selenium respectively, the signals due to the ortho-protons of the phenyl group move to slightly higher field, due to the decrease in electronegativity of the hetero-atom. The signal for the methylene protons occurs at higher field in the oxazole (δ3.59) than in the thiazole (δ3.86) and selenazole (δ3.83). This is probably due to the increased ring-current deshielding in the more aromatic thiazole and selenazole rings. A similar trend is shown in the N.M.R. (table A 3) and U.V. spectra (table C 1) of the azolium salts (10, R=Ph).

Reaction of the indenothiazolium salt (10, X=S, R=Ph) and the



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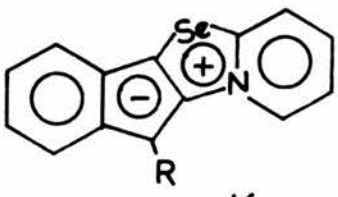

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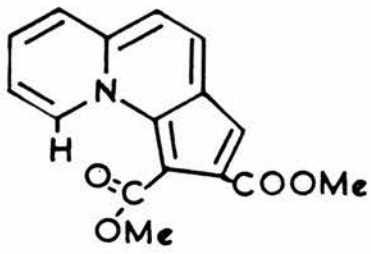
R=H, CHO, COMe, COOMe



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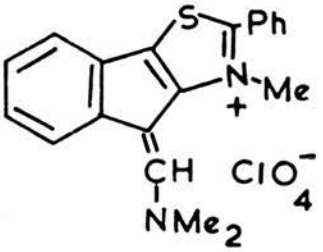

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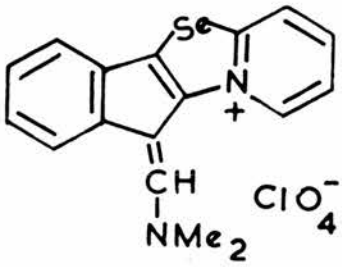

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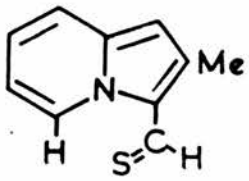

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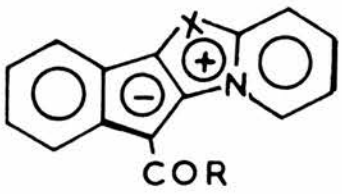

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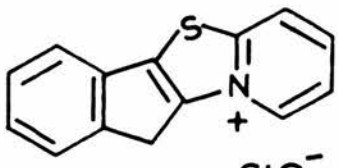

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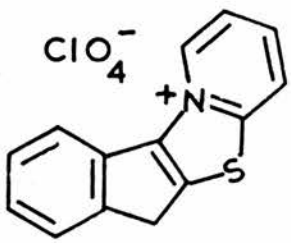

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PLATE 19

indenoselenazolium salt (12) with base generated the unstable, highly-coloured intermediates (15 and 16, R=H) which, by virtue of the high charge density in the five-membered carbocyclic ring, reacted readily with electrophiles (acetic anhydride, methyl chloroformate) to give the stable acetyl and methoxycarbonyl derivatives (15 and 16, R=COMe, COOMe). The aldehydes (15 and 16, R=CHO) were readily obtained by hydrolysis of the Vilsmeier salts* (17) and (18) with dilute alkali.

The acyl derivatives of the selenazolium salt (12) and their sulphur analogues show almost identical spectral properties. The U.V. and visible spectra are very similar, the selenazolium compounds showing a bathochromic shift of some of the peaks (table C 2). The colour of the acyl derivatives (16) is solvent dependent, ranging from red to violet in non-polar solvents, such as cyclohexane, to orange to yellow in polar solvents, such as methanol; these compounds show a bathochromic shift of the visible transition of about 100 mμ on changing solvent from methanol to cyclohexane (table C 2), the figures being almost identical to those measured for the sulphur analogues[128]. This phenomenon can be interpreted in terms of a transition to an upper state which has a lower dipole moment than the ground state[135]. This implies that the ground state is highly dipolar; the more polar ground state is stabilised by solvation in polar

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* Salts whose cation can be represented by formula (a) or (b) are called Vilsmeier salts in this work.

$$\underset{(a)}{Ar\text{-}CH{=}N^{+}Me_2} \qquad \underset{(b)}{Ar{=}CH\text{-}N^{+}Me_2}$$

carries a partial negative charge. Because of electrostatic interaction between the negatively charged oxygen atom and the positively charged pyridinium ring the carbonyl group will tend to take up the orientation with the oxygen atom directed towards the pyridinium ring. At the same time, due to delocalisation of charge from the five-membered ring, the exocyclic carbon-carbon bond attains a measure of double bond character: this will restrict rotation about this bond and so tend to maintain the orientation of the carbonyl group towards the pyridinium ring. Similar deshielding has been observed in the cyclopenta[c]quinolizine derivative (19)[136] and in 2-methyl-3-thioformylindolizine (20)[137]. In trifluoroacetic acid solution (table A 6) the acyl derivatives (16) again have similar N.M.R. spectra to their sulphur analogues. The acetyl and methoxycarbonyl derivatives show a sharp singlet at δ 5.62 and 5.48, indicating that protonation is occurring on the ring carbon atom to which the acyl group is attached. The aldehyde shows no peak in this region, indicating protonation at oxygen to give a hydroxymethylene salt.

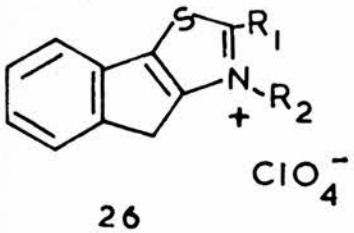
The accumulated spectroscopic evidence is consistent with the assigned dipolar structure (21) for the acyl derivatives (16) and their thiazolium analogues. The negative charge associated with the five-membered carbocyclic ring is delocalised into the carbonyl group. In this system the selenium atom does not expand its valence shell, to permit through conjugation, more readily than the sulphur atom.

The acyl derivatives (15) show the same spectral characteristics as described above. In the U.V. and visible spectra the long

wavelength absorptions show bathochromic shifts of 70-80 mμ when the solvent is changed from methanol to cyclohexane. The larger solvent shifts observed for the pyridinium compounds (ca. 100 mμ) must be a consequence of delocalisation of the positive charge into the pyridinium ring, thus increasing the charge separation, and consequently, the dipole moment of the ground state. The more polar ground state will be more stabilised by solvation and hence the solvent shifts will be larger.

I.R. solvent shift studies have shown that the carbonyl stretching absorptions of compounds (15, R=CHO, COMe, COOMe) occur at 1588, 1562 and 1640 $cm.^{-1}$ respectively. The N.M.R. spectra in trifluoroacetic acid solution show that the acetyl and methoxycarbonyl derivatives are protonated on the ring carbon atom, whereas the aldehyde is protonated on oxygen. One further interesting point arises from the N.M.R. spectra in deuterochloroform solution. The chemical shift of the N-methyl group occurs at lower field (δ4.5-4.6) than that of the N-methyl group of the parent indeno-thiazolium salt (δ4.32 in trifluoroacetic acid solution). That this is not a solvent effect was demonstrated by recording the spectrum of the salt (5, X=S) and the acetyl derivative (15, R=COMe) in deuterodimethylsulphoxide solution, the chemical shifts for the N-methyl groups being δ4.29 and 4.54 respectively. This difference is probably caused by the same carbonyl deshielding mechanism which operates in the pyridinium compounds.

The indeno-thiazolium salts (22) and (23) react with dimethylformamide in boiling acetic anhydride to give the dimethylaminomethylene



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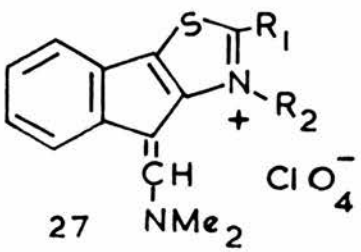


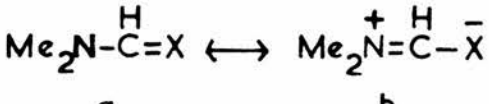
27

a $R_1 = R_2 = Ph$

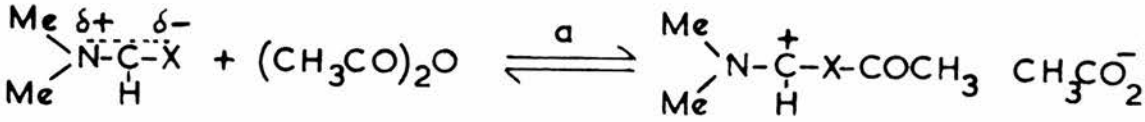
b $R_1 = Bu^t$, $R_2 = Ph$

c $R_1 = Ph$, $R_2 = Me$

d $R_1 = Bu^t$, $R_2 = Me$



31 X = O, S



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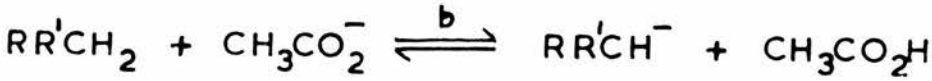
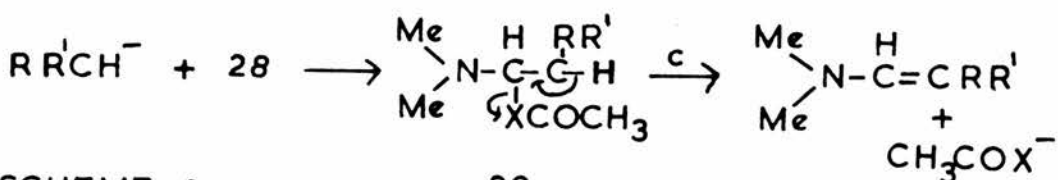
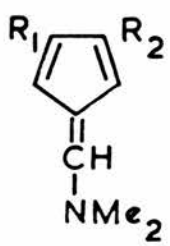




29 30

SCHEME 2



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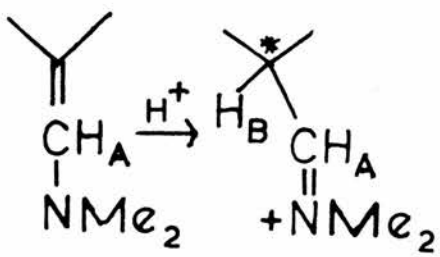
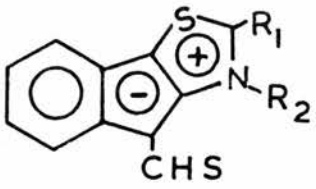


33

(Vilsmeier) salts (24) and (25)[128]. The indeno-thiazolium salts (26) react only slowly with dimethylformamide, but rapidly with dimethylthioformamide in acetic anhydride, giving the Vilsmeier salts (27). The reactions of the indeno-azolium salts (22) and (12) with dimethylformamide and dimethylthioformamide illustrate the greater reactivity of the latter; after 10 minutes reaction of the salts (22) and (12) with dimethylthioformamide the yields of the Vilsmeier salts (24) and (18) were 93 and 85% respectively; after 30 minutes reaction of the salt (22) with dimethylformamide the yield of the Vilsmeier salt (24) was 60%, and after 2 hours reaction with dimethylformamide the yield of Vilsmeier salt (18) was 33%. The condensation with dimethylthioformamide in acetic anhydride is particularly useful because it avoids prolonged reaction times and the accompanying decomposition. A reasonable mechanism[138], which accounts for the greater reactivity of dimethylthioformamide over dimethylformamide in this reaction, is shown in scheme 2. The carbon-sulphur double bond is more polarisable than the carbon-oxygen double bond[139], and so will conjugate more readily with the dimethylamino group. Hence the contribution from the dipolar form (31b) will be more important in dimethylthioformamide than in dimethylformamide. This is confirmed by variable temperature N.M.R. studies which show that the energy barrier to rotation about the carbon-nitrogen bond in dimethylthioformamide (28 k.cal./mole)[140] is much higher than the value for dimethylformamide (10 k.cal./mole)[141]. Because of the greater negative charge on the sulphur atom, dimethylthioformamide will react more readily as a nucleophile to give the

intermediate complex salt (28). Electrophilic attack of this complex salt on the carbanion derived from the reactive methylene group gives the intermediate (29). Conversion of this intermediate to the dimethylaminomethylene compound (30) requires the breaking of a carbon-oxygen or a carbon-sulphur bond, the latter being weaker and so more readily broken. Which of steps (a) and (c) is rate determining is open to question, but in either case the greater reactivity of dimethylthioformamide in this reaction can be rationalised.

The Vilsmeier salts show characteristic N.M.R. spectra (table A 7). The following discussion deals in particular with the Vilsmeier salt (27c). In dimethysulphoxide solution this salt shows a singlet at δ8.45 for the olefinic proton (H_A in part formula 33) and a singlet for the two methyl groups of the dimethylamino function which are, therefore, magnetically equivalent. This indicates that, at the temperature of the N.M.R. probe, there is free rotation about the carbon-nitrogen bond. Restricted rotation of this type has been observed in the closely related fulvene derivatives (32)[142], the coalescence temperature being -17°. When the orange Vilsmeier salt is dissolved in trifluoroacetic acid the resulting solution is colourless. The methyl groups are now magnetically non-equivalent. The low field signal now appears as a doublet (J=9.7 c/s), and a further one proton doublet appears atδ5.96 (J=9.7 c/s). The Vilsmeier salt is protonated at the ring carbon atom (33). The methyl groups in the protonated structure are intrinsically non-equivalent. When the spectrum is run in deuterotrifluoroacetic acid solution the doublet at δ5.96 disappears



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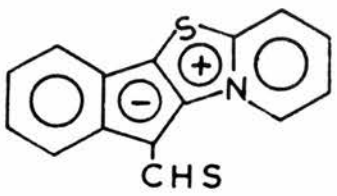

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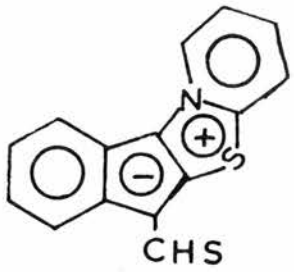
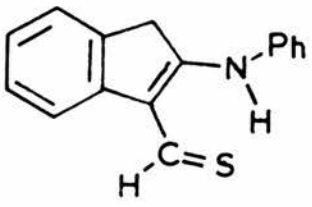


36

a $R_1 = Bu^t$, $R_2 = Me$

b $R_1 = Bu^t$, $R_2 = Ph$



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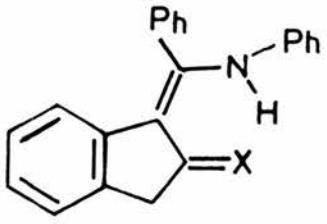
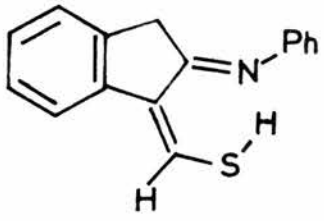


38

a X = O

b X = S



39

UV and visible spectra of compounds 37 and 38b

	λ(mμ)	log ε
37	454, 295, 274, 222 sh	(4.11, 4.29, 4.34, 4.21)
38b	451, 278, 226 sh	(4.08, 4.32, 4.34)

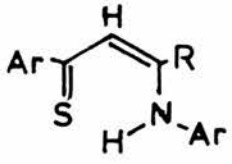


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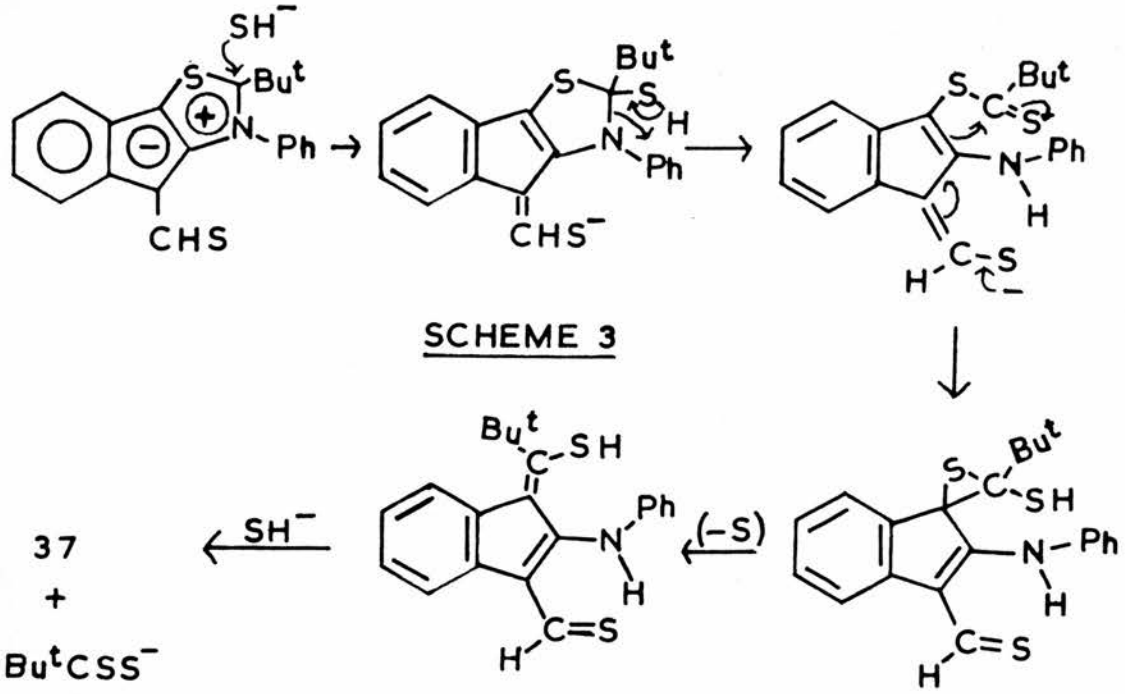
PLATE 21

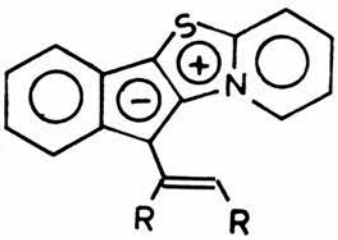
and the doublet at δ8.26 collapses to a singlet, confirming that the doublet at δ5.96 is due to the added proton. This pattern in trifluoroacetic acid solution is repeated throughout the series of Vilsmeier salts, the low field doublet usually being obscured by the aromatic signals.

The salts (17) and (18) are hydrolysed by aqueous sodium hydroxide to give the aldehydes (15 and 16, R=CHO). Solvolysis of the appropriate Vilsmeier salts with aqueous sodium hydrogen sulphide[137] gave the stable thioaldehydes (34), (35) and (36). These thioaldehydes owe their unusual stability to the polarisation of the carbon-sulphur double bond, produced by electron delocalisation from the carbocyclic five-membered ring which carries a negative charge. In the N.M.R. spectra of compounds (34a) and (36) the chemical shift of the thioaldehyde proton occurs at ca. δ10.2 (table A 8). This is a characteristic value for a CHS proton in a highly polarised thioaldehyde[137]. An interesting by-product isolated in the course of preparing the thioaldehyde (34b) was shown by mass spectrometry and N.M.R. spectroscopy to have the thioformyl structure (37). Confirmatory evidence comes from a comparison of the U.V. and visible spectrum of compound (37) with that of the thione (38), obtained by treatment of the corresponding ketone[128] with phosphorus pentasulphide. The chromophore is virtually the same in both compounds and the spectra are very similar. The thione-enamine structure (37) is preferred to the isomeric thiolmethylene-imine structure (39) from a consideration of the N.M.R. spectrum, which shows a singlet at δ10.58 (CHS) and a broad peak at δ15.10 (NH, hydrogen bonded). The

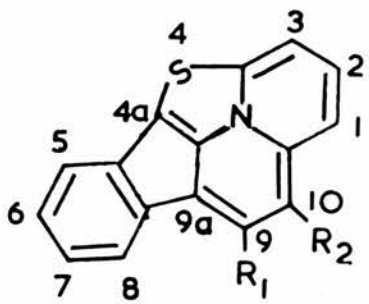


SCHEME 3

37 + Bu^tCSS^-



41 R=COOMe

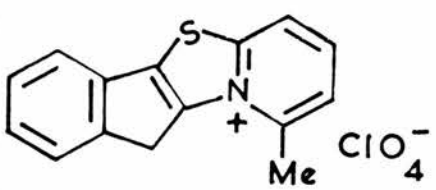


42

a $R_1 = R_2 = COOMe$

b $R_1 = R_2 = H$

c $R_1 = Me$, $R_2 = COMe$

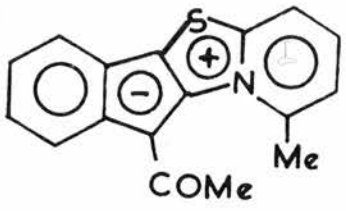


43

PLATE 22

presence of an abundant ion in the mass spectrum, corresponding to the loss of SH, does not necessarily mean that this compound exists in the thiol form, since the latter can readily be obtained from the thial by a 1,5 hydrogen shift. Related acyclic compounds (40) have been described[143,144], the authors preferring the thione structure from spectral considerations. The thioaldehyde (37) is formed by further reaction of the initially formed thioaldehyde (34b) with aqueous sodium hydrogen sulphide. A tentative mechanism is suggested in scheme 3.

The indeno-thiazolium salt (22) reacts with dimethylacetylene-dicarboxylate in the presence of triethylamine to give the diester (41) which on heating in boiling nitrobenzene is cyclised, the cyclised product then disproportionating to give the thiacyclazine derivative (42a)[128]. When the indeno-thiazolium salt (43) is heated in acetic anhydride in the presence of triethylamine the initially formed red solution rapidly turns green and the green thiacyclazine derivative (42c) is isolated. When the same reaction is carried out in acetonitrile the red solution slowly turns green. Work up of the red solution gives a mixture of the red acetyl derivative (44) and the green thiacyclazine derivative (42c). The acetyl derivative (44) is readily cyclised to the thiacyclazine derivative by boiling acetic anhydride; in the presence of triethylamine the yield is much higher. The acetyl group in the thiacyclazine (42c) could be introduced either before or after cyclisation. The failure to bring about cyclisation of compound (44) in the absence of acetic anhydride



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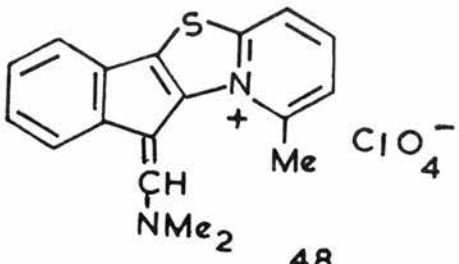

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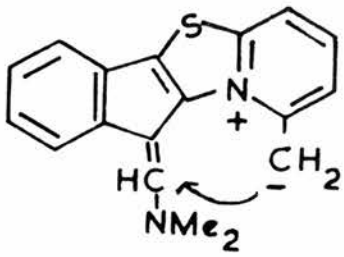
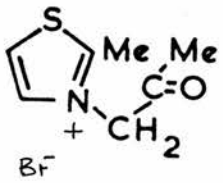


42b + $NHMe_2$ ←



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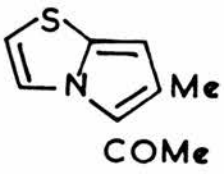
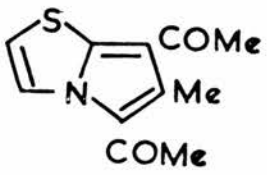


46

+



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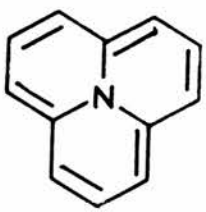

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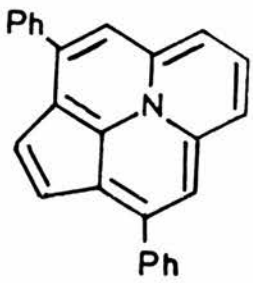
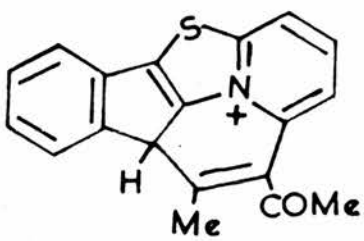


50



51

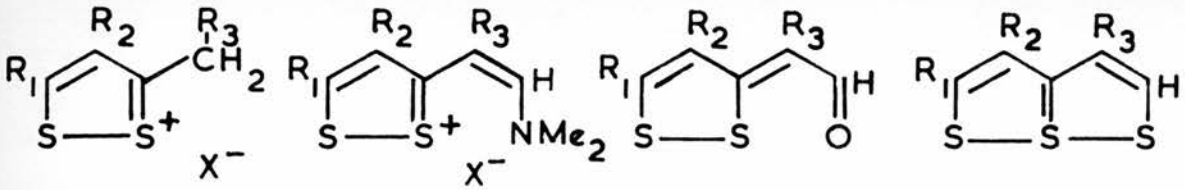
PLATE 23

would suggest that the acetyl group is introduced prior to cyclisation: acetylation of the pyridinium methyl group would activate it for cyclisation. The failure of the unsubstituted thiacyclazine (42b) to acetylate under the conditions used for cyclisation is further evidence for acetylation prior to cyclisation. A precedent exists for this type of reaction in the synthesis of pyrrolo[2,1-b] thiazoles[145]. The cyclisation of 3-acetonyl-2-methyl-thiazolium bromide (45) in acetic anhydride in the presence of sodium acetate gives a mixture of the mono and diacetyl pyrrolo[2,1-b]thiazoles (46) and (47) in a molar ratio of 2:5. Acetylation of 6-methyl-pyrrolo[2,1-b]thiazole under the same conditions as used for cyclisation gives less than 5% of the diacetyl compound (47). This indicates that the acetyl group in the 7-position of the pyrrolo[2,1-b] thiazole must be introduced prior to cyclisation.

The salt (43) condenses with dimethylformamide in acetic anhydride giving, at optimum conditions, a mixture of the starting salt and the Vilsmeier salt (48) in a molar ratio of 6:4. The low reactivity of this indeno-thiazolium salt is probably a consequence of steric inhibition by the adjacent methyl group; condensations of this type are known to be very sensitive to steric factors[146]. A pure sample of the Vilsmeier salt could be isolated from the mixture by utilising the different reactivities of the two components towards triethylamine. In dimethylformamide solution, in the cold, the salt (43) is deprotonated by triethylamine to give a methylene chloride soluble product; the Vilsmeier salt does not react under

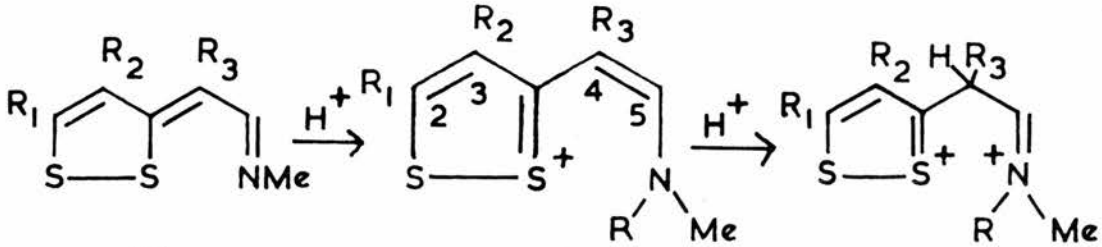
these conditions and is insoluble in methylene chloride, so a separation can be achieved. The Vilsmeier salt is cyclised to the parent indeno[1,2,3-b,c]-1-thiacycl[2,3,3]azine (42b) by triethylamine in dimethylformamide.

Compounds (42) are of interest because they are thia-analogues of cycl[3,3,3]azine (49)[147], a derivative (50) of which has been prepared[148]. Compound (42b) is in fact a ring homologue of the system contained in compound (50), a sulphur atom replacing a carbon-carbon double bond. Compounds (42) and (50) all form dark green solutions and their U.V. and visible spectra (table C 3) are similar. Compounds (42b) and (42c) are basic, being protonated in a 1% solution of perchloric acid in methanol. The N.M.R. spectrum of compound (42c) in trifluoroacetic acid shows a one proton singlet at δ 5.66; a likely site for protonation is at the five-membered carbocyclic ring, giving structure (51). The N.M.R. spectrum of compound (42b) in trifluoroacetic acid shows two groups of ill-defined signals centred on δ4.8 and 5.8, indicating that protonation is occurring at more than one site. Possible sites for protonation are carbon atoms 4a, 9a, 1, 3 and 10. Protonation at the first two sites would give rise to a methine signal and protonation at the other three sites would give a methylene signal. The signals at δ4.8 and 5.8 can be attributed to the methylene and methine protons respectively. Chemical evidence supports the above interpretation: when a solution of compound (42b) and p-dimethylaminobenzaldehyde in acetic acid is boiled for a few minutes the solution turns deep purple. Thin layer chromatography



52 53 54 55

	R_1	R_2	R_3
a	H	H	H
b	Me	H	H
c	H	Me	H
d	Bu^t	H	H
e	COOEt	H	H
f	H	$-CH_2CH_2-$	
g	H	$-CH_2CH_2CH_2-$	
h	Ph	H	H
i	H	Ph	H
j	Ph	H	Me
k	Ph	H	Ph
l	H	Ph	Ph



56

57 R=H
53 R=Me

58 R=H
59 R=Me

PLATE 24

shows three highly coloured components. Protonation at three of the five possible sites gives rise to compounds with methylene groups which can condense with p-dimethylaminobenzaldehyde.

The Synthesis and Spectral Properties of 6a-Thiathiophthenes and Related Compounds.

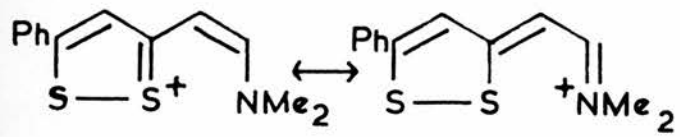
This work on 6a-thiathiophthenes arose from our group's interest in the synthesis and spectral properties of thioaldehydes[137]. The 6a-thiathiophthenes were synthesised by a modification of the Vilsmeier reaction. 3-Methyl(ene)-1,2-dithiolium salts condense with dimethylthioformamide in acetic anhydride to give the Vilsmeier salts(53), which are readily solvolysed by nucleophiles. With aqueous sodium hydroxide they give the aldehydes (54), with aqueous sodium hydrogen sulphide the 6a-thiathiophthenes (55), and with aqueous methylamine the aldimines (56).

The required 1,2-dithiolium salts were synthesised by a modification of the method developed by Leaver and co-workers[149] and later used by Schmidt and Schulz[150]. Leaver's method involved the reaction of appropriate 1,3-diketones with hydrogen disulphide (H_2S_2)[151] in benzene solution saturated with hydrochloric acid gas, over a prolonged period at room temperature. Schmidt and Schulz found that the reaction proceeded with hydrogen polysulphide (H_2S_x), reaction times being of the order of 1-2 weeks. In this work the reaction of 1,3-diketones with hydrogen disulphide was carried out in glacial

acetic acid using concentrated perchloric or hydrobromic acid instead of hydrochloric acid gas; reaction times of 5-10 minutes at 60-70° were sufficient, the dithiolium salts being obtained in good yield. The dithiolium salt (52e) was unstable and could only be isolated as an oil which rapidly turned purple in contact with air. The N.M.R. spectra (table A 10) confirm the structures of these dithiolium salts.

3-Methyl(ene)-1,2-dithiolium salts having a substituent in the 5-position condense with dimethylthioformamide in boiling acetic anhydride to give crystalline Vilsmeier salts (53). When the 5-position does not carry a substituent the yield of the Vilsmeier salt is low, the dithiolium salt being largely decomposed under these conditions. An exception to this is the dithiolium salt (52l) which does give a crystalline Vilsmeier salt in good yield. This decomposition of the 1,2-dithiolium salts is probably due to nucleophilic attack by acetate ion or by dimethylthioformamide at the 5-position, leading to ring opening[152]. However, using a mixture of phosphorus oxychloride and dimethylthioformamide as the Vilsmeier reagent, Vilsmeier salts can be formed from those dithiolium salts which do not react satisfactorily with dimethylthioformamide in acetic anhydride. These Vilsmeier salts are not isolated but are utilised at once for further reaction.

N.M.R. spectra of the Vilsmeier salts (table A 11) were recorded in trifluoroacetic acid containing perchloric acid. The spectra show that the Vilsmeier salts are protonated at C-4 (53) to give compounds (59) which show a methine or (when R_3=H) a methylene signal. The N-methyl groups are magnetically non-equivalent. This situation is very



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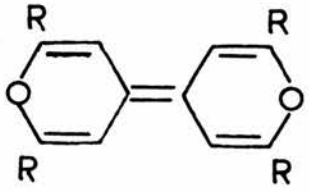
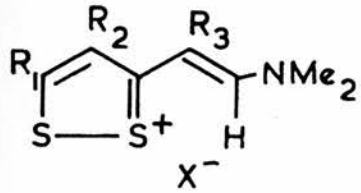
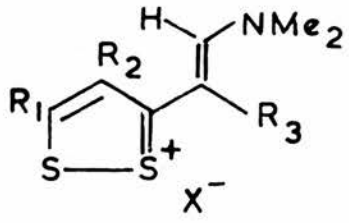


62 R=COOEt

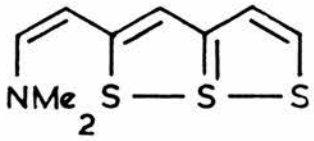


A

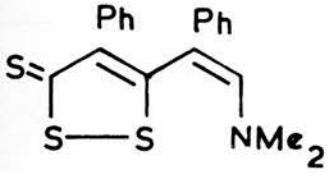


B

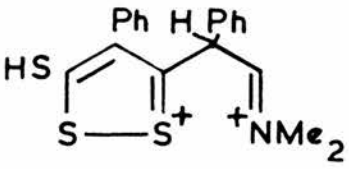
61



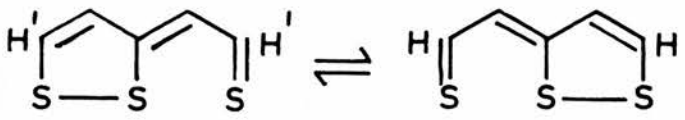
63



64

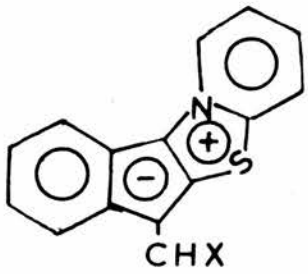


65



A B

66



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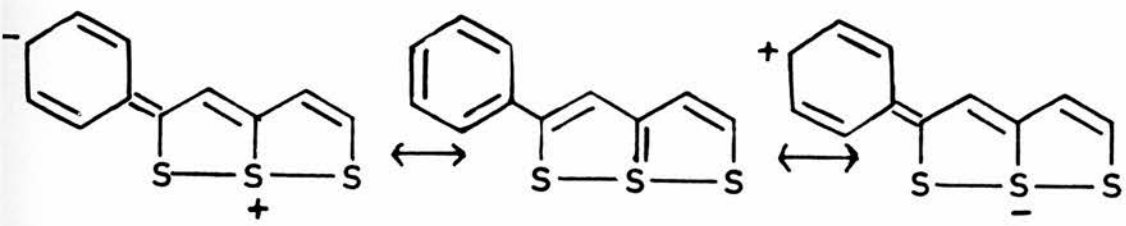

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PLATE 25

similar to that previously described (page 43) for the Vilsmeier salts in the indeno-thiazolium series. The N.M.R. spectrum of compound (53h) in dimethylsulphoxide solution shows non-equivalent N-methyl groups. By contrast, Vilsmeier salt (27c) has equivalent methyl groups in dimethylsulphoxide solution. This implies a considerable degree of double bond character in the carbon-nitrogen bond of the Vilsmeier salt (53h), which could arise by resonance of type (60) which is not possible in Vilsmeier salts derived from indeno-thiazolium salts. Because of this resonance the nitrogen atom carries a partial positive charge, and so the molecule will tend to take up a configuration (61A) or (61B) in which the nitrogen atom is directed away from the positively charged dithiolium ring.

The Vilsmeier salts (53) are solvolysed by aqueous methylamine in dimethylformamide solution, giving the aldimines (56). These compounds are of interest because of the similarity of their structures to the structures of the corresponding Vilsmeier salts. The structures of the aldimines are confirmed by their N.M.R. spectra in deutero-chloroform solution (table A 14). In trifluoroacetic acid the aldimines are protonated on nitrogen, giving the cations (57) which can be derived from the corresponding Vilsmeier salts by replacing one of the N-methyl groups by a hydrogen atom. The N.M.R. spectrum of the aldimine (56h) in trifluoroacetic acid is similar to that of the corresponding Vilsmeier salt (53h) in dimethylsulphoxide. The U.V. and visible spectra (table C 4) of the aldimines (56) in methanol containing 2% v/v perchloric acid are almost superimposable upon the

spectra of the corresponding Vilsmeier salts (53) in methanol. Addition of perchloric acid to trifluoroacetic acid solutions of the imines (56a) and (56h) leads to a further protonation, at C-4, giving the dications (58a) and (58h) which are analagous to the dications obtained by protonation of the corresponding Vilsmeier salts. In the N.M.R. spectra the N-methyl signal now appears as a doublet, indicating the presence of a mixture of the two geometrical isomers of the dications (58).

The Vilsmeier salts (53) are solvolysed by aqueous sodium hydrogen sulphide in dimethylformamide solution, giving 6a-thiathiophthenes in good yield. 2,5-Diethoxycarbonyl-6a-thiathiophthene was prepared by the reaction of phosphorus pentasulphide on diethyloxalylacetone. This thiathiophthene was observed by Arndt[153] as a coloured impurity in the reaction of diethyloxalylacetone with phosphorus pentasulphide, which gave as its major product the dipyrylene derivative (62). Successive hydrolysis and decarboxylation of this ester by prolonged heating in a solution of hydrobromic acid in glacial acetic acid gave a mixture of 2-ethoxycarbonyl-6a-thiathiophthene and the parent heterocycle, 6a-thiathiophthene, both of which could also be prepared by the Vilsmeier method. The monoester was readily hydrolysed to 6a-thiathiophthene-2-carboxylic acid when chromatographed on a column of high activity alumina.

The product from an attempted formylation of 2-methyl-6a-thiathiophthene, using dimethylthioformamide and phosphorus oxychloride as the Vilsmeier reagent, was shown to have the enamine structure(63).

This enamine is formed by condensation of dimethylthioformamide with the methyl group in the 2-position of 6a-thiathiophthene, which is known to be acidic[117].

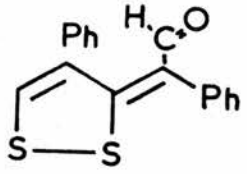
Hydrolysis of the Vilsmeier salts with aqueous sodium hydroxide in dimethylformamide solution gives the aldehydes (54). A by-product, formed in 3% yield during the preparation of the aldehyde (541), was shown to have the thione structure (64). Compound (64) is protonated in trifluoroacetic acid/perchloric acid solution to give the dication (65) whose N.M.R. spectrum is very similar to that of the dication (591) from protonation of the Vilsmeier salt (531). The mass spectrum of compound (64) shows prominent peaks corresponding to the loss of NMe_2 and S ($355 \xrightarrow{-44} 311 \xrightarrow{-32} 279 \xrightarrow{-32} 247$). Compound (64) gives an immediate red precipitate with mercuric chloride in ether solution, confirming the presence of a thione group in the molecule. The I.R. spectrum of compound (64) shows strong absorptions in the region 1100-1400 $cm.^{-1}$, similar to those observed for 4-phenyl-1,2-dithiole-3-thione[154]. This compound must be formed by nucleophilic attack by sulphide anion at the unsubstituted 5-position of the dithiolium ring of the Vilsmeier salt (531). The sulphide is presumably formed by decomposition of the Vilsmeier salt.

The U.V. and visible spectra of the 6a-thiathiophthenes and their oxygen analogues (54) conform to the general pattern which is characteristic for these pairs of compounds[67,69,70]. The visible absorption maxima for a series of mono and disubstituted 6a-thia-thiophthenes are given in table C 5. The effect of individual

be ca. δ9; the observed value is δ9.12.

An interesting feature of the 6a-thiathiophthene system is that the carbon-carbon bond distances and bond angles are almost identical to those in naphthalene, the 3- and 4-positions in 6a-thiathiophthene being equivalent to the 1- and 8- (peri) positions in naphthalene. The exocyclic bonds at the 3- and 4-positions in 6a-thiathiophthene are parallel and 2.41 $\mathring{A}$ apart (cf. 2.45 $\mathring{A}$ in naphthalene). Substituents located at the peri-positions in these two systems are in very close proximity to one another, and this is responsible for several unique properties of such peri-substituted derivatives.

The U.V. and visible spectra (table C 5) of 3-phenyl- and 3,4-diphenyl-6a-thiathiophthene closely resemble the spectrum of 6a-thiathiophthene itself, whereas the spectra of thiathiophthenes with a phenyl group in the 2- or 5-position are quite different, having an extra strong absorption at ca. 320 mμ. A phenyl group in the 2-position is able to conjugate strongly with the π-electron system of the thiathiophthene nucleus by resonance of the type (68), which is not possible with a phenyl group in the 3-position. Further, there is steric hindrance to coplanarity of a phenyl group in the 3-position. A similar effect is observed in the spectra of 1-phenyl- and 2-phenyl-naphthalene[156], but in the naphthalene system only the steric factor is operating. The difference in conjugating ability between phenyl substituents in the 2- and 3-positions of the 6a-thiathiophthene system are reflected in the N.M.R. spectra (table A 12), the 3-phenyl substituent appearing as a singlet and the 2-phenyl



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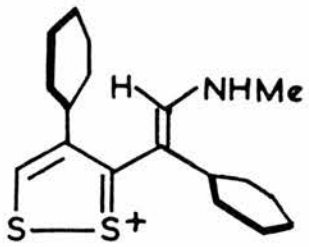

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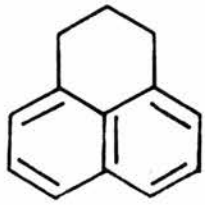

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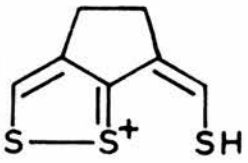

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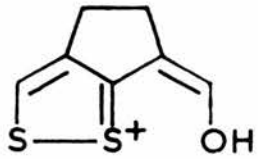

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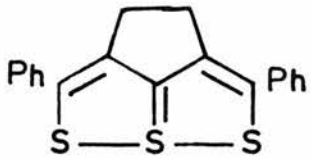

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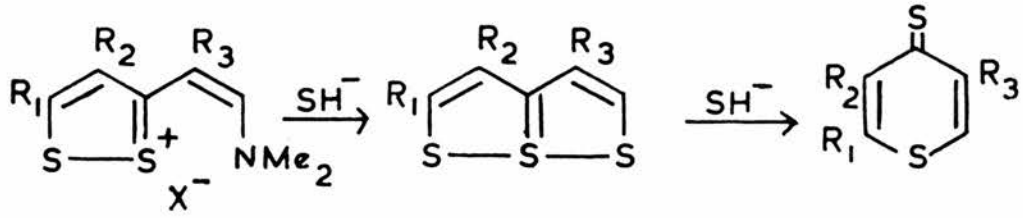
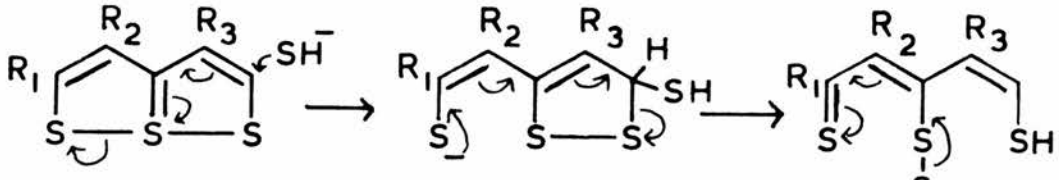


53 55 75



SCHEME 4

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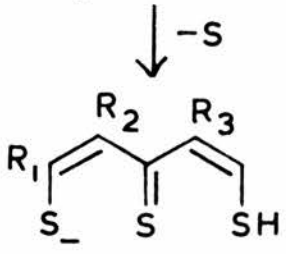

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PLATE 26

substituent as two groups of signals, one due to the ortho-protons and the other to the meta- and para-protons.

The N.M.R. spectrum of 3,4-diphenyl-6a-thiathiophthene shows a single peak at δ6.9 for the protons of the benzene rings. This should be compared with δ7.41 for the benzene protons in 3-phenyl-6a-thiathiophthene. As in 1,8-diphenylnaphthalene[156] the phenyl groups are parallel to each other and perpendicular to the plane of the 6a-thiathiophthene system. Calculations based on the data of Johnson and Bovey[157] predict that the shielding of the benzene protons when two benzene rings are arranged face to face at a distance of 2.41 Å is 0.36 p.p.m., which is of the correct order of magnitude. Even with this out of plane, parallel arrangement of the benzene rings there must be considerable strain in this molecule since the distance between the benzene rings (ca. 2.4 Å) is much less than twice the "van der Waals thickness" of a benzene ring (3.7 Å)[56]. This strain is reflected in the high reactivity of 3,4-diphenyl-6a-thiathiophthene toward nucleophiles (page 61).

It is of considerable interest to note that in the N.M.R. spectrum of the oxygen analogue (541) of 3,4-diphenyl-6a-thiathiophthene (table A 13) the phenyl protons appear as a slightly broadened singlet at δ6.91. This indicates that the carbonyl group is held in the cis-coplanar configuration (54), despite the strong steric interaction of the two phenyl groups. I.R. spectroscopy confirms this, the carbonyl stretching frequency being 1570 $cm.^{-1}$ compared with 1580 $cm.^{-1}$ for the aldehyde (54k), in which there is

little strain. The existence of this aldehyde in the strained cis-configuration, rather than in the trans-configuration (69) in which the bulky phenyl substituents are directed away from each other, is good evidence for a strong interaction between the carbonyl oxygen atom and the adjacent dithiole sulphur atom, whether this be by electrostatic attraction or by partial bonding.

Similarly, in the aldimine (561) the phenyl protons show up as a singlet at 6.84, indicating that the imine has the cis-configuration (56). In trifluoroacetic acid solution the imine is protonated on nitrogen, and the phenyl protons show a broad absorption in the normal aromatic region. In acid solution the nitrogen atom carries a partial positive charge and, because of electrostatic repulsions between the nitrogen atom and the dithiolium ring, the molecule will prefer to take up the trans-configuration (70). As a consequence of this geometry both the methyl group and the vinyl proton (H-5) show abnormal shielding, the signal for the latter being hidden by the aromatic signals. Both the methyl group and the vinyl proton lie above the plane of a benzene ring.

Another interesting strain effect, in the opposite sense, is observed in 3,4-ethano-6a-thiathiophthene (55f) which is the thia-thiophthene analogue of acenaphthene. The long wavelength absorption of 1,8-dimethylnaphthalene[158], acenaphthene[71] and 2,3-dihydrophenalene (71) all occur between 285 and 290 mμ. Assuming additivity of substituent effects, the visible maximum for 3,4-dimethyl-6a-thia-thiophthene should occur at 485 mμ, and the visible maximum for

3,4-propano-6a-thiathiophthene (55g) is close to this value (492 mμ). The anomalously large red shift observed for 3,4-ethano-6a-thiathiophthene (λ_{max} 524 mμ) can only be explained in terms of a strain effect. An X-ray crystallographic study[159] has shown that the dimethylene bridge in acenaphthene causes a significant distortion of the naphthalene nucleus by pulling together the peri-carbon atoms. In the case of acenaphthene this strain has no effect on the conjugated ΠΠ-system, since the U.V. spectra of acenaphthene and 2,3-dihydrophenalene, in which there is no strain, are virtually superimposable. However, in the thiathiophthene system an ethano-group bridging the peri-positions does have an effect on the conjugated ΠΠ-system. A possible explanation for this is that the strain is taken up by stretching the sulphur-sulphur bonds, rather than by a valence angle distortion as in acenaphthene, and that this causes a distortion of the ΠΠ-electron system.

A U.V. and visible spectroscopic study has shown that in acetonitrile containing 2% v/v perchloric acid the ethano-bridged thiathiophthene is protonated to the extent of 85%, whereas a maximum estimate for the protonation of the propano-bridged compound is 60%. The enhanced basicity of the ethano-bridged compound is probably due to the strain imposed by the ethano-bridge, which is relieved by protonation to give the mercaptovinyl-1,2-dithiolium structure (72). The U.V. spectrum of the protonated species (72) (λ_{max} 443 mμ) is similar to that of the isoconjugate Vilsmeier salt (53b) (λ_{max} 437 mμ). It is interesting to note that the peak at

443 mμ is slowly (over 15 min.) replaced by a peak at 380 mμ which could be due to the protonated form of the corresponding aldehyde (73) (λ_{max} for the aldehyde (54b) in acetonitrile/2% perchloric acid solution is 378 mμ). It would appear that the ethano-bridged thiathiophthene undergoes rapid protonation followed by a slower nucleophilic attack on the protonated form by water, giving the oxygen analogue (73).

Stavaux and Lozac'h[81] have reported that the 3,4-ethano-bridged thiathiophthene (74) is instantaneously desulphurised by mercuric acetate (100% excess) in boiling acetic acid to give a 99% yield of the corresponding ketone. Klingsberg[67] has reported that 2,5-diphenyl-6a-thiathiophthene is not attacked by mercuric acetate at room temperature. An exploratory experiment has shown that 2,5-diphenyl-6a-thiathiophthene is not completely desulphurised after five minutes reaction with a large excess of mercuric acetate in boiling acetic acid. The higher reactivity of the ethano-bridged thiathiophthene towards mercuric acetate could be a consequence of the strain imposed upon the molecule by the peri-bridge. A comparison with 2,5-diphenyl-3,4-propano-6a-thiathiophthene would be more conclusive since in the ethano- and propano-bridged compounds the electronic effects are the same.

The Rearrangement of 6a-Thiathiophthenes and Related Compounds by Nucleophiles.

Reaction of the Vilsmeier salts (53b) and (53h) with aqueous sodium hydrogen sulphide in dimethylformamide gives, in addition to the expected 6a-thiathiophthenes, 2-methyl- and 2-phenyl-4H-thiopyran-4-thiones in yields of 31 and 7% respectively. It has been established that 6a-thiathiophthenes (55) react with aqueous sodium hydrogen sulphide in dimethylformamide to give 4H-thiopyran-4-thiones (75). At room temperature the rates of formation and decomposition of the 6a-thiathiophthenes are sufficiently different in most cases to allow the thiathiophthenes to be isolated in good yield. When aqueous sodium sulphide is used in place of sodium hydrogen sulphide the thiathiophthenes are rearranged more rapidly and completely. For the preparation of 4H-thiopyran-4-thiones the reaction can be carried out in one stage by warming the Vilsmeier salts with aqueous sodium sulphide in dimethylformamide. The intermediate thiathiophthenes are at once rearranged by the excess of sodium sulphide. The sequence 1,2-dithiolium salt → Vilsmeier salt → 4H-thiopyran-4-thione thus provides a novel, flexible synthesis of 4H-thiopyran-4-thiones.

A probable precursor of the 4H-thiopyran-4-thiones is the anion (77) which could be formed either by reductive cleavage of a sulphur-sulphur bond in the 6a-thiathiophthenes by sulphide or hydrosulphide (mechanism A), or by disproportionation of the intermediate (76) resulting from nucleophilic attack on the 6a-thiathiophthenes (mechanism B) (scheme 4). These two mechanisms could be

TABLE A

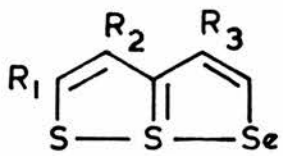
Reaction of 6a-thiathiophthenes with 2M-aqueous sodium hydrosulphide in dimethylformamide at 70° for 30 min.

6a Thiathiophthene	Yield of 4H-thiopyran-4-thione	Recovered starting material
2-Phenyl	65	3
2-Methyl [a]	42	27
2-t-Butyl	59	34
2,4-Diphenyl	44	40
2,5-Diphenyl [b]	8	79
3,4-Diphenyl [c]	99	
2-Phenyl-4-methyl	29	65

[a] Heated at 50° for 15 min.

[b] Sodium sulphide, 5min. at 60°

[c] Stood 5 min. at room temp. (reaction complete in < 5 sec.)



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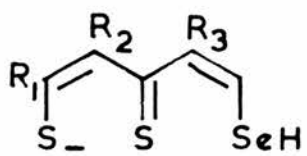

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PLATE 27

differentiated by labelling experiments. Until such evidence is available several factors favour the nucleophilic ring opening mechanism (B). (1) 2-Phenyl- and 2,4-diphenyl-6a-thiathiophthenes also react with aqueous sodium hydroxide in dimethylformamide to give the corresponding 4H-thiopyran-4-thiones as the major products. It is difficult to envisage any mechanism for this reaction other than one involving nucleophilic attack. (2) Although 6a-thiathiophthenes rearrange readily with nucleophiles in dimethylformamide solution, they appear to be stable in ethanolic solution. In particular, 2-phenyl-6a-thiathiophthene has completely reacted after treatment with aqueous sodium hydroxide in dimethylformamide at 70° for five minutes, but is unaffected after two hours by boiling methanolic potassium hydroxide[110]. While the acceleration of nucleophilic processes in dipolar aprotic solvents is well documented, it would seem unlikely that change of solvent would have such a drastic effect on the reducing ability of the sulphide and hydrogen sulphide anions, though this possibility cannot be entirely discounted. (3) The results of comparative studies which illustrate substituent effects on the rate of rearrangement are shown in table A opposite. 2,5-Diphenyl-6a-thiathiophthene is recovered in 80% yield under conditions where thiathiophthenes unsubstituted in the 5-position have completely reacted (page 110). One would expect reductive cleavage of a sulphur-sulphur bond in 6a-thiathiophthenes to occur more readily with electron withdrawing substituents in the nucleus. Therefore in terms of a reduction mechanism the 2,5-diphenyl

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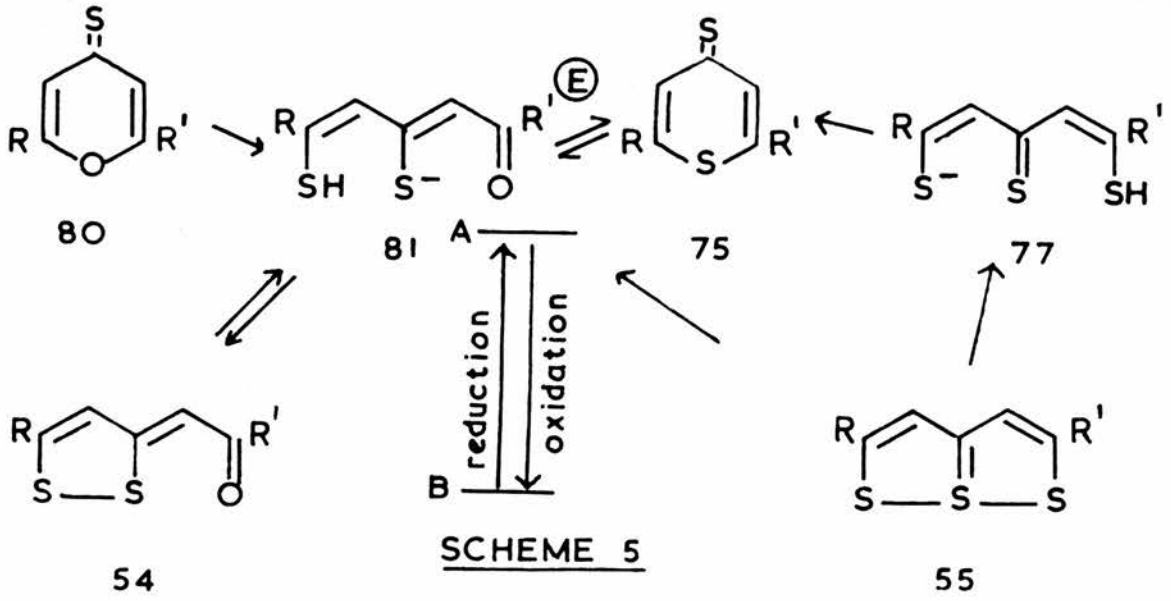
compound might be expected to be one of the most reactive thiathiophthenes. Of the thiathiophthenes unsubstituted in the 5-position which have been studied, the 2-phenyl-4-methyl- compound is the least reactive. This would again seem to be more consistent with a mechanism involving nucleophilic attack at the 5-position, which is less reactive towards nucleophiles because of the inductive effect of the methyl group in the 4-position. The decreased reactivity of the 2,4-diphenyl- compound compared with the 2-phenyl- compound could be explained by steric hindrance to nucleophilic attack at the 5-position.

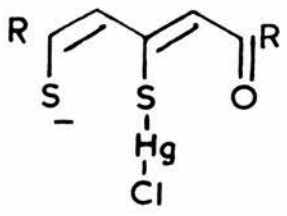
The unusually high reactivity of 3,4-diphenyl-6a-thiathiophthene towards nucleophiles must be due to the strain imposed on the molecule by the peri-phenyl substituents (page 55), the strain being relieved by rearrangement to the 4H-thiopyran-4-thione. Because of its high reactivity towards nucleophiles, 3,4-diphenyl-6a-thiathiophthene could not be isolated from the decomposition of the Vilsmeier salt precursor (531) in dimethylformamide solution, the rearrangement product being isolated instead in 94% yield. However, if the decomposition is carried out in methanol solution, 3,4-diphenyl-6a-thiathiophthene can be isolated in 50% yield along with a smaller amount (20%) of 3,5-diphenyl-4H-thiopyran-4-thione. This clearly illustrates the acceleration of the decomposition of 6a-thiathiophthenes when dipolar aprotic solvents are employed in place of protic solvents.

In the light of the foregoing discussion, the formation of 4H-thiopyran-4-thiones in the preparation of the selenium analogues(78)



SCHEME 5

	R	R′
u	H	H
v	Me	Me
w	Ph	Ph
x	Me	Ph
y	Ph	COOH
z	Ph	H



81*

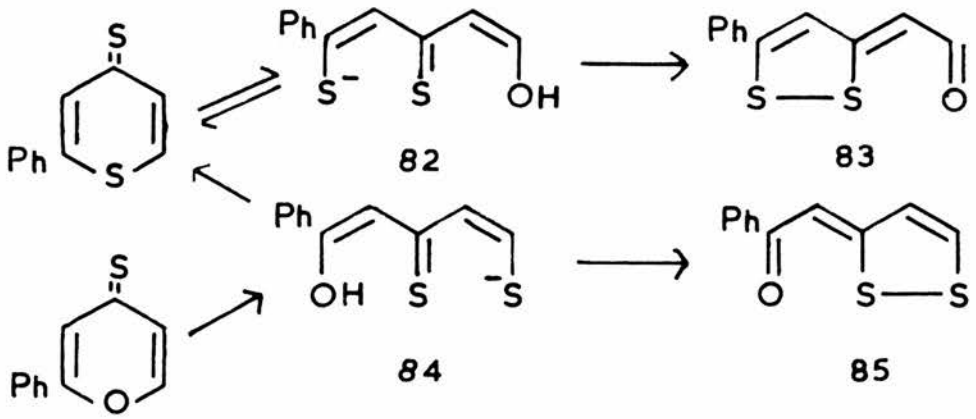


PLATE 28

by solvolysis of the appropriate Vilsmeier salts with aqueous sodium hydrogen selenide[162], can be readily understood. The thiopyran-4-thiones are formed by ring closure of an intermediate of type (79), with elimination of hydrogen selenide anion.

The rearrangement of 6a-thiathiophthenes by nucleophiles is a further addition to a unique series of heterocyclic rearrangements (scheme 5). Rearrangements between levels A and B of the diagram involve an oxidation (A→B) or a reduction (B→A). Traverso[99,100] has found that 4H-pyran-4-thiones (80), when treated with an excess of aqueous sodium (or potassium) sulphide or hydrogen sulphide in boiling ethanolic solution, give either 4H-thiopyran-4-thiones (75) or acylmethylenedithioles (54). The symmetrically substituted 4H-pyran-4-thiones (80,v and w) give 4H-thiopyran-4-thiones whereas the unsymmetrically substituted 4H-pyran-4-thiones (80,y and z) give acylmethylenedithioles. With 2-methyl-6-phenyl-4H-pyran-4-thione (80x) both products are formed, the acylmethylenedithiole (54x) being the major one. In a later paper[102] Traverso reported that the reaction of 2,6-dimethyl-4H-pyran-4-thione (80v) with one equivalent of aqueous sodium sulphide, at room temperature, gives the acylmethylenedithiole (54v). Since the acylmethylenedithioles (54,v and y) undergo further reaction with sodium sulphide to give the 4H-thiopyran-4-thiones (see below), Traverso suggested that the acylmethylenedithioles are intermediates in the formation of 4H-thiopyran-4-thiones from 4H-pyran-4-thiones. This would appear to be unlikely, since the conversion of a pyranthione to a thiopyranthione via an acylmethylenedithiole would

require an oxidation followed by a reduction.

Pfister-Guillouzo and Lozac'h[79] reinvestigated this reaction and confirmed Traverso's findings. Thus the symmetrically substituted 4H-pyran-4-thiones (80, u,v and w) give 4H-thiopyran-4-thiones and the unsymmetrically substituted compounds (80, x and z) give acylmethylenedithioles. Again, along with the acylmethylenedithiole (54x) a small amount of the 4H-thiopyran-4-thione is formed. Despite variations of temperature, concentration of potassium hydrogen sulphide and polysulphides, they were unable to obtain acylmethylenedithioles from symmetrically substituted 4H-pyran-4-thiones.

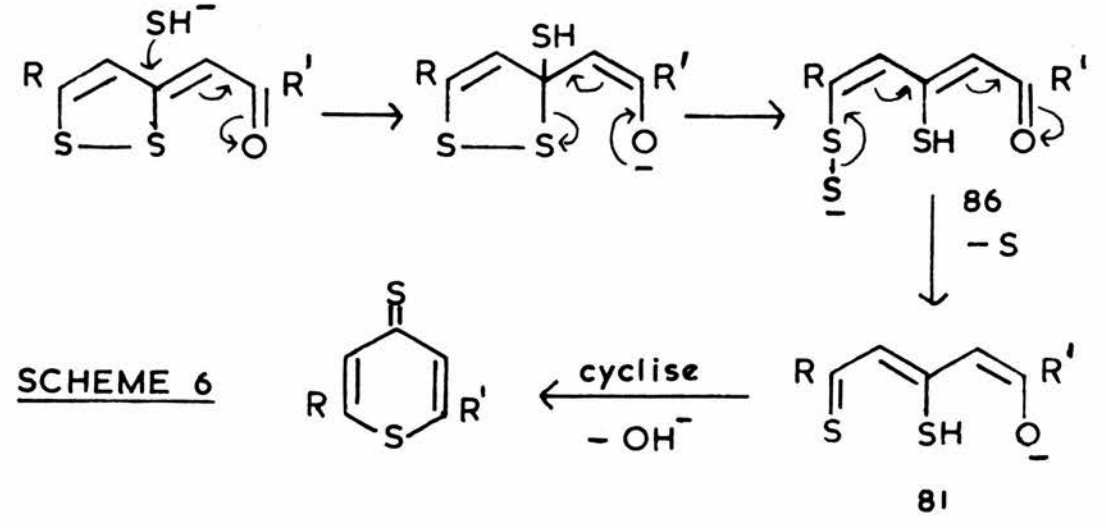
Nucleophilic ring opening of the 4H-pyran-4-thiones by sodium hydrogen sulphide gives intermediates of type (81) which then undergo one of two reactions: either recyclisation, with elimination of hydroxide, giving the 4H-thiopyran-4-thione, or oxidation to the acylmethylenedithiole. This oxidation is difficult to understand since there is no oxidising agent present. Possibly atmospheric oxidation is occurring. The rearrangement of 4H-thiopyran-4-thiones to acylmethylenedithioles[103,76], by treatment of their mercuric chloride complexes with aqueous sodium carbonate, proceeds in a similar manner, but in this case the mercuric ion probably acts as an oxidising agent. Ring opening of the mercuric chloride complex gives an intermediate (81*) which disproportionates, giving the acylmethylenedithiole.

In a preliminary investigation of these reactions in dipolar aprotic solvents, the rearrangements of 2-phenyl-4H-thiopyran-4-thione by sodium hydroxide and of 2-phenyl-4H-pyran-4-thione by sodium

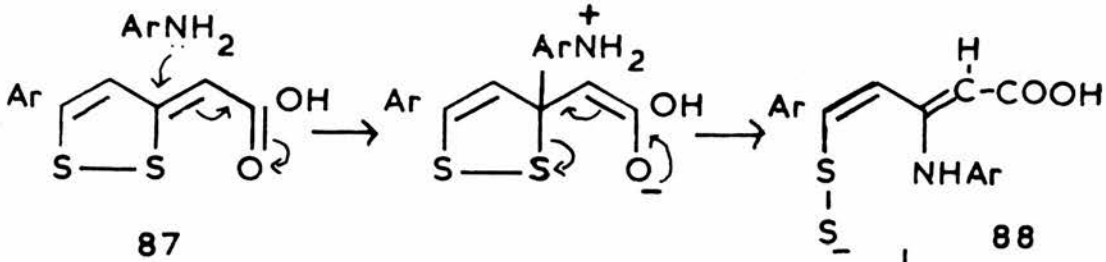
hydrogen sulphide were studied. Addition of aqueous sodium hydroxide to a solution of 2-phenyl-4H-thiopyran-4-thione gives a deep red solution of the intermediate (82) which is readily oxidised to the aldehyde (83) by aqueous potassium ferricyanide. Similarly, the reaction of 2-phenyl-4H-pyran-4-thione with aqueous sodium hydrogen sulphide gives a red solution of the intermediate (84) which is readily oxidised to the isomeric ketone (85). Intermediates (82) and (84) can also be oxidised by bubbling oxygen through the solutions. Dilution and acidification of the dimethylformamide solution of intermediate (82) regenerates the 4H-thiopyran-4-thione in 74% yield. Similar treatment of the dimethylformamide solution of intermediate (84) does not give the 4H-thiopyran-4-thione. However, when the dimethylformamide solution is treated with 70% perchloric acid, 2-phenyl-4H-thiopyran-4-thione is formed in $>$ 50% yield.

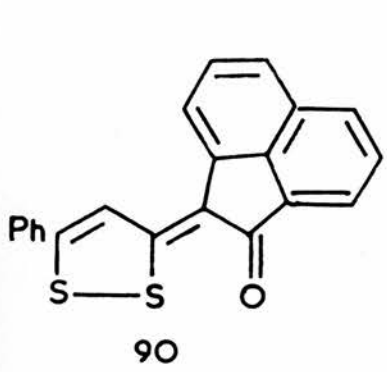
The observed "substituent effects" on the products of the reaction of 4H-pyran-4-thiones with sodium hydrogen sulphide must be a consequence of the balance between the position of the equilibrium (E, scheme 5) and the ease of atmospheric oxidation of the intermediate (81). The fact that 2-phenyl-4H-thiopyran-4-thione was not observed as a product of the reaction of 2-phenyl-4H-pyran-4-thione with sodium hydrogen sulphide is readily understood, since concentrated acid is required to cyclise the intermediate (84). This preliminary investigation would suggest that the course of these reactions could be controlled by using dimethylformamide as solvent.

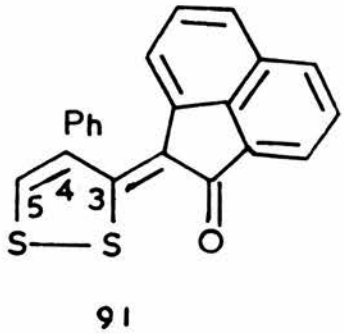
The rearrangement of acylmethylenedithioles to 4H-thiopyran-4-

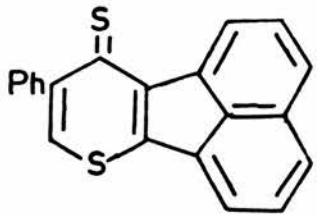


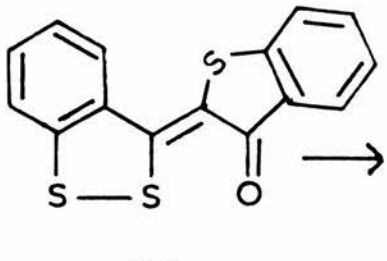
SCHEME 6











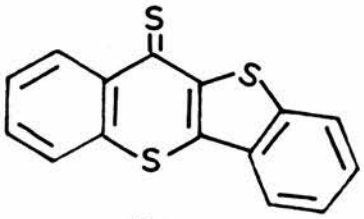


PLATE 29

thiones by sodium sulphide has been observed by Traverso[100,102], who proposed that the initial step in the reaction was a reductive cleavage of the sulphur-sulphur bond of the acylmethylenedithiole, giving an intermediate of the type (81, scheme 5), subsequent ring closure of this intermediate with elimination of hydroxide giving the 4H-thiopyran-4-thione. By analogy with the rearrangement of 6a-thiathiophthenes, the intermediate (81) could also be formed by disproportionation of the intermediate (86, scheme 6), arising from nucleophilic ring opening of the acylmethylenedithiole by attack at the 3-position of the dithiole ring. A precedent for nucleophilic attack at the 3-position exists in the reaction of the acids (87) with aniline[143], the products (89) being formed by disproportionation and decarboxylation of the anion (88) produced by nucleophilic attack at the 3-position of the dithiole ring and subsequent ring opening.

The rearrangement of acylmethylenedithioles by nucleophiles proceeds readily in dimethylformamide solution. The aldehyde (54k) is less reactive than the aldehyde (54h), presumably because of steric blocking of the 3-position of the dithiole ring by the phenyl group.

An interesting example of a rearrangement of an acylmethylene-dithiole to a 4H-thiopyran-4-thione has been reported by Mollier and Lozac'h[164]. The reaction of acenaphthenone with 5-phenyl-1,2-dithiole-3-thione in the presence of base gave the ketone (90). With 4-phenyl-1,2-dithiole-3-thione the product was not the ketone (91) but the 4H-thiopyran-4-thione derivative (92). A likely explanation for this difference is that the ketone (91) is formed initially but is

rearranged by nucleophilic attack at the 5-position by hydrosulphide anion formed in the initial condensation. This is not possible in the case of the compound (90) which carries a substituent in the 5-position. Admittedly nucleophilic attack at the 3-position of the dithiole ring is possible in both cases but, intuitively, one might expect reaction at the 3-position to be much slower than reaction at the 5-position because of steric blocking by the naphthalene portion of the molecule. The relative reactivities of the 3- and 5-positions of the dithiole ring in acylmethylenedithioles require further investigation.
The acylmethylenedithiole (93) is rearranged to the 4H-thiopyran-4-thione derivative (94) by both hydrosulphide and methylmercaptide anions[122]. The rearrangement by hydrosulphide anion can be explained in terms of a nucleophilic ring opening or a reduction mechanism whereas the rearrangement by methylmercaptide anion can only be explained in terms of a reduction mechanism.

In the rearrangement of the aldehyde (54k) to the corresponding 4H-thiopyran-4-thione by aqueous sodium hydrogen sulphide a small amount of 2,4-diphenyl-6a-thiathiophthene is formed, presumably by a simple carbonyl reaction. Both the aldehyde (54h) and 2-phenyl-6a-thiathiophthene undergo a carbonyl reaction with methylamine in dimethylformamide, giving the aldimine (56h). The thiathiophthene reacts much more rapidly than its oxygen analogue. The formation of the aldehydes (54h) and (54k) in the reaction of the corresponding thiathiophthenes with aqueous sodium hydroxide can be explained either by a simple carbonyl reaction or by oxidation of the intermediates (81)

during work-up of the reaction. Determination of the structures of the red products from the latter reactions may throw more light on the rearrangement of 6a-thiathiophthenes by hydroxide anion.

PART C

EXPERIMENTAL

I: Materials and Methods.

Melting points were determined on a Kofler hot-stage apparatus and are corrected.

Ultra-violet and visible spectra were measured with a Unicam S.P.800 spectrophotometer. Light absorption data refer to solutions in methanol, unless otherwise stated.

Infra-red spectra were measured with Perkin-Elmer 257 and 261 spectrophotometers. A Perkin-Elmer 137 instrument was also used for comparative studies.

N.M.R. spectra were measured at ca. 34° on a Perkin-Elmer R.10 spectrometer operating at 60 Mc. $sec.^{-1}$ at a sweep rate of 1.6 $c.sec.^{-2}$ and sweep width of 600 $c.sec.^{-1}$. Chemical shifts (δ) are expressed in parts per million downfield from tetramethylsilane as internal reference. Solutions were 0.5 M, otherwise saturated.

Microanalyses were carried out by Drs. Weiler and Strauss, Oxford, Dr. A. Bernhardt, Mulheim, Germany, and by Mr. J.R. Bews of this department.

Thin-layer chromatography was on 'Silica gel G' plates which were developed in iodine vapour. Alumina for column chromatography was Spence Type H 100/200 mesh, and silica was Whatman 'Chromedia' S.G. 31.

'Petrol' refers to 40/60 petroleum ether and 'ether' to diethyl ether.

Perchloric acid was 70% w/w Analar grade.

Acetonitrile was boiled over sodium hydride (dispersion in oil, 2 g. per litre) for 30 min. and distilled.

Dimethylformamide was allowed to stand over powdered calcium hydride for three days, filtered and then distilled at 15 mm.

Pyridine was distilled after standing over potassium hydroxide pellets for three days.

Diethyl ether was allowed to stand over calcium chloride for 48 hr., filtered, distilled and stored over sodium wire.

Benzene was pre-dried by azeotropic distillation, then boiled over sodium wire for 30 min., and distilled.

Acetic acid, acetic anhydride, chloroform, cyclohexane, ethanol, ethyl acetate, hexane, methanol, methylene chloride, nitromethane and 40/60 petroleum ether were all redistilled commercial materials.

2 M-Aqueous sodium hydrogen sulphide solutions were prepared by saturating a 2 M-aqueous solution of sodium sulphide nonahydrate (Analar grade) with hydrogen sulphide (2 hr.).

II: Preparation of 4H-Indeno[2,1-d]oxazolium Salts.

(i) Preparation of 1,2-indandione-2-oxime. To a stirred, ice-cold solution of indan-1-one (66 g., 0.5 mole) in a mixture of benzene (500 ml.) and ethanol (50 ml.) was added a solution of nitrosyl chloride (36 g., 0.55 mole) in benzene, over 1 hr. After the addition was completed the suspension was stirred for a further 30 min. The resulting white solid was filtered off, washed thoroughly with benzene

and dried. Recrystallisation from methanol gave 1,2-indandione-2-oxime (68.8 g., 86%) as long colourless needles, m.p. 205-207° (dec.) (lit.[130] 205-207°).

(ii) Modified preparation of 2-aminoindan-1-one hydrochloride. The following modification of the procedure of Ebel and Deuschel[130] gave a product of adequate purity while avoiding tedious H_2S 'detinning'. After completion of the reaction the sludge was evaporated to dryness and the residue dissolved in methanol. Addition of ether precipitated the amine hydrochloride which was used without further purification.

(iii) Acylation of 2-aminoindan-1-one hydrochloride.

a) Benzoylation. A solution of the amine hydrochloride (0.797 g., 5 m.moles) in water (10 ml.) was added dropwise to a vigorously stirred mixture of acetonitrile (10 ml.), 20% aqueous sodium hydroxide (10 ml.) and benzoyl chloride (1.15 ml., 10 m.moles). The mixture was stirred for a further 15 min. before being poured into water. The resulting precipitate was filtered off, washed well with water and crystallised from ethanol, giving 2-benzoylamino-3-benzoyloxy-indene (8) (0.3 g., 17%) as a felt of colourless needles, m.p. 173-174° (Found: C,77.5 ; H, 4.6; N, 3.7. $C_{23}H_{17}NO_3$ requires C, 77.8; H, 4.8; N, 3.9%), ν_{max} (Nujol) 3360 (NH), 1720 (C=O, ester), 1676 (C=C) and 1648 cm^{-1} (C=O, amide). The N.M.R. spectrum ($CDCl_3$) shows a singlet (2H) at δ4.27 (CH_2), a broad singlet (1H) at δ9.04 (NH) and a complex group of signals (14H) between δ7.2 and 8.5 (aromatic protons).

b) Benzoylation. Pyridine (100 ml.) was added dropwise over 1 hr. to a stirred, boiling suspension of the amine hydrochloride (18.35 g., 0.1 mole) and benzoyl chloride (17.31 ml., 0.15 mole) in acetonitrile (100 ml.) to which had been added 2 drops of conc. HCl. The mixture was stirred for a further 30 min. without heating, then poured into water (1.5 litres). The resulting white precipitate was filtered off, washed thoroughly with water, then with water/ethanol (1:1) (200 ml.) and finally recrystallised from ethanol. 2-Benzoylaminoindan-1-one (7, R=Ph) (12.93 g., 52%) formed colourless fibrous needles, m.p. 191-192° (lit.[133] 190°) (Found: C,76.3; H, 5.4; N, 5.8. $C_{16}H_{13}NO_2$ requires C, 76.5; H, 5.2; N, 5.6%), ν_{max} (Nujol) 3300 (NH), 1717 (C=O) and 1635 cm^{-1} (C=O, amide).

c) Trimethylacetylation. Pyridine (50 ml.) was added dropwise over 30 min. to a boiling suspension of the amine hydrochloride (9.17 g., 50 m. moles) and trimethylacetyl chloride (9.42 ml., 75 m. moles) in acetonitrile (50 ml.) to which had been added 1 drop of conc. HCl. The mixture was stirred for a further 30 min. without heating. The resulting solution was evaporated and saturated sodium bicarbonate solution (500 ml.) was added. After standing for 1 hr. the mixture was extracted with methylene chloride. The dried extracts were evaporated, and the residue was dissolved in ethanol and treated with charcoal. The ethanol solution was reduced in volume to ca. 25 ml. and benzene (100 ml.) was added. 2-Trimethylacetylaminoindan-1-one (7, R=Bu^t) (5.9 g., 51%) crystallised out as colourless needles. A sample recrystallised from benzene as colourless needles, m.p. 146-

147° (Found: C, 72.3; H, 7.3. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4%), ν_{max} (Nujol) 3385 (NH), 1728 (C=O) and 1632 cm^{-1} (C=O, amide).

(iv) Cyclisation of 2-acylaminoindan-1-ones.

a) 2-Benzoylaminoindan-1-one. The amide (12.55 g., 50 m. moles) was dissolved in freshly distilled phosphorus oxychloride (100 ml.) and the stirred mixture was boiled for 1 hr. After cooling, the solution was poured into water (1.5 litres) and was allowed to stand overnight before being extracted with methylene chloride. Evaporation of the dried extracts gave a brown crystalline residue which recrystallised from ethanol (charcoal) giving 2-phenyl-4H-indeno[2,1-d]oxazole (9, X=O, R=Ph) (8.07 g., 69%) as a mat of colourless needles, m.p. 171-172° (Found: C, 82.8; H, 5.0. $C_{16}H_{11}NO$ requires C, 82.4; H, 4.7%).

b) 2-Trimethylacetylaminoindan-1-one. A solution of the amide (3.47 g., 15 m.moles) in freshly distilled phosphorus oxychloride (20 ml.) was boiled for 1 hr. The cooled solution was poured into water (500 ml.) and allowed to stand overnight before being extracted with ether. The dried extracts were evaporated, and the dark oily residue was filtered through a column of alumina (2.5x20 cm.) with benzene as solvent. Evaporation of the benzene eluate (500 ml.) gave a colourless oily residue (1.92 g.) which was shown by T.L.C. to be a mixture of two compounds. A sample (1.4 g.) of this mixture was dissolved in ethanol (10 ml.) and perchloric acid (1.5 ml.) was added. Addition of ether precipitated the oxazolium perchlorate which was filtered off, washed with ether and dried. Work up of the filtrate to isolate the second component of the mixture gave no

tractable material. The perchlorate salt was basified with aqueous sodium bicarbonate solution and the base was extracted into benzene. Evaporation of the dried benzene extracts gave a yellow oily residue (737 mg.) which solidified on cooling. Block distillation (130°/ 0.1 mm.) gave 2-t-butyl-4H-indeno[2,1-d]oxazole (9, X=O, R=Bu^t) as a colourless solid, m.p. 52-53° (Found: C, 79.0; H, 7.3; N, 6.4. $C_{14}H_{15}NO$ requires C, 78.8; H, 7.1; N, 6.6%).

(v) Quaternisation of 4H-indeno[2,1-d]oxazoles.

a) 2-Phenyl-4H-indeno[2,1-d]oxazole. Methyl-p-toluenesulphonate (9.30 g., 50 m.moles) was heated to 130° in a 100 ml. R.B. flask and the oxazole (5.83 g., 25 m.moles) added portionwise over 10 min. The mixture was heated at this temperature for a further 45 min., cooled, and acetonitrile (50 ml.) and perchloric acid (2.1 ml.) were added. Ether was then added to precipitate the salt which was filtered off, washed with ethanol, then ether, and dried. Recrystallisation from acetonitrile (addition of ether) with charcoal screening gave 3-methyl-2-phenyl-4H-indeno[2,1-d]oxazolium perchlorate (10, X=O, R=Ph) (4.1 g., 47%). A sample recrystallised from methanol as colourless plates, m.p. 222-224° (Found: C, 58.9; H, 4.2. $C_{17}H_{14}ClNO_5$ requires C, 58.7; H, 4.1%).

b) 2-t-Butyl-4H-indeno[2,1-d]oxazole. A mixture of the oxazole (213 mg., 1 m.mole) and methyl-p-toluenesulphonate (279 mg., 1.5 m. mole) was heated at 130° for 10 min. The mixture was cooled and the resulting glass was dissolved in ethanol (5 ml.) and treated with perchloric acid (0.17 ml., 2 m.moles). Addition of ether precipitated

the salt which was filtered off, washed with ether, and dried, giving 3-methyl-2-t-butyl-4H-indeno[2,1-d]oxazolium perchlorate (10, X=O, R=Bu^t) (265 mg., 81%). A sample recrystallised from ethanol as colourless needles, m.p. 205-206° (Found: C, 55.0; H, 5.7; N, 4.5. $C_{15}H_{18}ClNO_5$ requires C, 55.0; H, 5.5; N, 4.3%).

III: Preparation of 3-Methyl-2-phenyl-4H-indeno[2,1-d]thiazolium perchlorate.

(i) Condensation of 1-bromoindan-2-one with thiobenzamide. A solution of 1-bromoindan-2-one[127] (21.10 g., 0.1 mole) in acetonitrile (60 ml.) was added to one of thiobenzamide (13.70 g., 0.1 mole) in acetonitrile (100 ml.). The product, which began to separate at once, was filtered off after 1 hr., washed thoroughly with ether, and dried, giving 1,2-dihydro-2-oxoinden-1-ylthiolbenzimidate hydrobromide (6, X=S, R=Ph) (33.6 g., 98%). A sample recrystallised from ethanol as colourless prisms, m.p. 174-175° (dec.>150°) (Found: C, 54.9; H, 4.3. $C_{16}H_{14}BrNOS$ requires C, 55.2; H, 4.1%).

(ii) Cyclisation of 1,2-dihydro-2-oxoinden-1-ylthiolbenzimidate hydrobromide. Thionyl chloride (5.4 ml., 75 m.moles) was added during 20 min. to a stirred suspension of the bromide (17.40 g., 50 m.moles) in dimethylformamide (100 ml.) at 0°. The solution was stirred at room temperature for 2 hr. then slowly poured into saturated sodium bicarbonate solution (500 ml.). The mixture was diluted with water (1 litre) and the resulting precipitate was filtered off, washed thoroughly with water, and dissolved in methylene chloride.

Evaporation of the dried methylene chloride solution yielded a crystalline residue which, after recrystallisation from benzene/ethanol (1:3) gave 2-phenyl-4H-indeno[2,1-d]thiazole (9, X=S, R=Ph) (10.88 g., 87%). A sample recrystallised from cyclohexane as colourless plates, m.p. 159-160° (Found: C, 77.1; H, 4.4; N, 5.6. $C_{16}H_{11}NS$ requires C, 77.1; H, 4.5; N, 5.6%).

(iii) Quaternisation of 2-phenyl-4H-indeno[2,1-d]thiazole. The thiazole (6.23 g., 25 m.moles) and methyl-p-toluenesulphonate (5.11 g., 27.5 m.moles) were heated together at 160° for 30 min. The cooled, semi-solid mass was dissolved in acetonitrile (40 ml.) and perchloric acid (2.7 ml.) was added. Addition of ether precipitated the product which was filtered off, washed with ether and dried, giving 3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium perchlorate (10, X=S, R=Ph) (8.08 g., 90%), identical with the product obtained by Reid and Salmond[127] from the cyclisation of 1,2-dihydro-2-oxoinden-1-yl N-methyl-thiolbenzimidate hydroperchlorate.

IV: Preparation of 4H-Indeno[2,1-d]selenazolium Salts.

(i) Condensation of 1-bromoindan-2-one with selenoamides.

a) With 2-selenopyridone. A solution of 2-selenopyridone[134] (7.9 g., 50 m.moles) in acetonitrile (200 ml.) was filtered into a cooled solution of 1-bromoindan-2-one (10.55 g., 50 m.moles) in acetonitrile (50 ml.). An oil formed initially but crystallised readily on being scratched. After 15 min. the white crystalline solid was filtered off, washed thoroughly with ether and dried, giving

2-(1,2-dihydro-2-oxoinden-1-ylseleno)pyridinium bromide (11) (16.18 g., 88%). A sample recrystallised from acetonitrile as colourless prisms, m.p. 155-158° (dec.>135°) (Found: C, 45.4; H, 3.2. $C_{14}H_{12}BrNOSe$ requires C, 45.6; H, 3.3%).

b) With selenobenzamide. A solution of 1-bromoindan-2-one (5.28 g., 25 m.moles) in acetonitrile (25 ml.) was added to an ice-cooled solution of selenobenzamide (4.6 g., 25 m.moles) in acetonitrile (30 ml.). The yellow salt which precipitated was filtered off, dissolved in hot ethanol (100 ml.) and filtered through a bed of celite to remove elementary selenium. Addition of ether to the cooled filtrate precipitated the salt which was filtered off, washed with ether and dried, giving 1,2-dihydro-2-oxoinden-1-ylselenolbenzimidate hydrobromide (6, X=Se, R=Ph) (6.34 g., 64%). A sample recrystallised from ethanol (addition of ether) as colourless prisms, m.p. 167-169° (dec.) (Found: C, 48.6; H, 3.7. $C_{16}H_{14}BrNOSe$ requires C, 48.6; H, 3.6%).

(ii) Cyclisation of selenolimidate salts.

a) 2-(1,2-dihydro-2-oxoinden-1-ylseleno)pyridinium bromide. The salt (9.23 g., 25 m.moles) was basified with aqueous sodium bicarbonate solution and the liberated base extracted into methylene chloride. The methylene chloride extracts were washed with water, dried (Na_2SO_4) and evaporated to dryness. The crystalline residue was dissolved in a mixture of methylene chloride (50 ml.) and nitromethane (50 ml.), and phosphorus pentachloride (20.8 g., 0.1 mole) was added portionwise to the stirred solution. A vigorous reaction ensued. The mixture was then boiled for 10 min., cooled, and methanol (20 ml.) was added

slowly to destroy the excess of phosphorus pentachloride. The solution was then reduced in volume to ca. 20 ml. and perchloric acid (2.1 ml., 25 m.moles) was added, followed by methanol (20 ml.). The product crystallised immediately and was filtered off, washed with methanol, then with ether, and dried giving 10H-indeno[2,1-d]pyrido[2,1-b]selenazolium perchlorate (12) (6.11 g., 66%). A sample recrystallised from acetonitrile as colourless needles, m.p. 264-267° (dec.) (Found: C, 45.1; H, 2.7. $C_{14}H_{10}ClNO_2Se$ requires C, 45.4; H, 2.7%).

b) 1,2-Dihydro-2-oxoinden-1-ylselenolbenzimidate hydrobromide. Thionyl chloride (1.62 ml., 22.5 m.moles) was added dropwise at 0° to a solution of the salt (5.94 g., 15 m.moles) in dimethylformamide (35 ml.), and the mixture was stirred for 2 hr. at room temperature. During this time elementary selenium was precipitated. The mixture was poured into aqueous sodium bicarbonate solution and extracted with ether. The dried ether extracts were evaporated and the residue was dissolved in ethanol, treated with charcoal, filtered and evaporated. The residue was extracted with boiling cyclohexane and the cyclohexane was evaporated leaving a crystalline residue. Recrystallisation from ethanol gave 2-phenyl-4H-indeno[2,1-d]selenazole (9, X=Se, R=Ph) (235 mg., 5%) as colourless prisms, m.p. 179-179.5° (Found: C, 64.7; H, 4.0. $C_{16}H_{11}NSe$ requires C, 64.9; H, 3.7%).

(iii) Quaternisation of 2-phenyl-4H-indeno 2,1-d selenazole. The selenazole (296 mg., 1 m.mole) and methyl-p-toluenesulphonate (205 mg., 1.1 m.moles) were heated together at 160° for 10 min. The cooled, semi-solid mass was dissolved in acetonitrile (2 ml.), and perchloric

acid (0.17 ml., 2 m.moles) was added. Addition of ether precipitated the salt which was filtered off, washed with ether and dried, giving 3-methyl-2-phenyl-4H-indeno[2,1-d]selenazolium perchlorate (10, X=Se, R=Ph) (352 mg., 86%). A sample recrystallised from acetonitrile as colourless needles, m.p. 250-251° (dec.>215°) (Found: C, 49.6; H, 3.4; N, 3.7. $C_{17}H_{14}ClNO_4Se$ requires C, 49.7; H, 3.4; N, 3.4%).

V: Preparation of Acyl Derivatives of 3-Methyl-2-phenyl-4H-indeno[2,1-d] thiazolium Anhydro-salt.

(i) The 4-acetyl derivative. Triethylamine (8.34 ml., 60 m.moles) was added all at once to a hot solution of the salt (5, X=S) (1.09 g., 3 m.moles) in acetic anhydride (50 ml.). The solution immediately became deep purple. After 5 min. the solution was poured into saturated potassium carbonate solution (1 litre). The mixture was allowed to stand for 2 hr. before being extracted with methylene chloride. Evaporation of the dried extracts left a purple-black residue which was chromatographed on a column of alumina (3x28 cm.) with a mixture of methylene chloride and acetonitrile (7:3) as eluant. An initial purple fraction (300 ml.) gave no useful material. Elution with methylene chloride/acetonitrile (6:4) gave an orange-red fraction (1 litre) which, on being evaporated, left a crystalline residue. Recrystallisation from benzene gave 4-acetyl-3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium anhydro-salt (15, R=COMe) (450 mg., 49%) as red needles, m.p. 191-196° (dec.) (Found: C, 75.0; H, 5.0; N, 4.9. $C_{19}H_{15}NOS$ requires C, 74.7; H, 5.0; N, 4.6%).

(ii) The 4-methoxycarbonyl derivative. Methyl chloroformate (3.12 ml., 40 m.moles) was added to a solution of the salt (5, X=S) (728 mg., 2 m.moles) in acetonitrile (30 ml.). Triethylamine (5.56 ml., 40 m.moles) was then added dropwise over 20 sec. A vigorous effervescence occurred and the solution became deep red. After standing for 5 min. the solution was poured into water and extracted with methylene chloride. Evaporation of the dried extracts gave a dark oily residue which was chromatographed on a column of alumina (2.5x22 cm.) with methylene chloride as eluant. Evaporation of the initial red fraction (1 litre) and recrystallisation of the residue from acetonitrile gave 4-methoxycarbonyl-3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium anhydro-salt (15, R=COOMe) (103 mg.,16%) as red plates, m.p. 225-227° (Found: C, 70.9; H, 4.9; N, 4.6. $C_{19}H_{15}NO_2S$ requires C, 71.0; H, 4.7; N, 4.4%).

(iii) The 4-formyl derivative. A solution of the Vilsmeier salt (17) (page82) (837 mg., 2 m.moles) in pyridine (20 ml.) was added to 2 N-aqueous sodium hydroxide (20 ml.) and the mixture kept at 50° with shaking for 5 min. The mixture was then diluted with water (500 ml.) and the resulting yellow suspension was extracted with benzene (4x500 ml.). The combined extracts were washed thoroughly with water and dried (Na_2SO_4) before being evaporated. Recrystallisation of the residue from nitromethane gave 4-formyl-3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium anhydro-salt (15, R=CHO) (80 mg., 14%) as orange needles, m.p. 272-274° (dec.>265°) (Found: C, 74.0; H, 4.5; N, 5.1. $C_{18}H_{13}NOS$ requires C, 74.2; H, 4.5; N, 4.8%).

VI: Preparation of Acyl Derivatives of 10H-Indeno[2,1-d]pyrido[2,1-b]selenazolium Anhydro-salt.

(i) The 10-acetyl derivative. Acetyl chloride (5.33 ml., 75 m. moles) was added dropwise, with swirling, to dry pyridine (75 ml.) at 0°. To the resulting white suspension was added the salt (12) (1.11 g., 3 m.moles), and the mixture boiled for 1 min. The solution became intensely red and all the solid dissolved. The reaction was quenched by pouring the mixture into cold water to give a dark orange-red suspension. Sodium carbonate (5 g.) was added and the mixture was extracted with methylene chloride. The dark red extracts were washed thoroughly with water and dried (Na_2SO_4), before being evaporated. The dark-red crystalline residue was chromatographed on a column of alumina made up with methylene chloride. Elution with methylene chloride/acetonitrile (6:4) gave a dark red eluate which when evaporated gave a red crystalline residue. Recrystallisation from acetonitrile (by displacement of methylene chloride) gave 10-acetyl-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium anhydro-salt (16, R=COMe) (520 mg., 55%). A sample recrystallised from acetonitrile as orange needles, m.p. 184-185 (dec.) (Found: C, 61.5; H, 3.4. $C_{16}H_{11}NOSe$ requires C, 61.6; H, 3.6%).

(ii) The 10-methoxycarbonyl derivative. Methyl chloroformate (1.94 ml., 25 m.moles) was added with swirling to a cooled mixture of pyridine (10 ml.) and acetonitrile (10 ml.), followed by triethylamine (2.47 ml., 25 m.moles). This mixture was added to the solid salt (12) (370 mg., 1 m.mole) and the resulting suspension

was heated to boiling for 1 min. The mixture was then poured into water, basified with sodium carbonate and extracted with methylene chloride. The dried extracts were evaporated and the residue was chromatographed on a column of alumina (3x22 cm.) made up with methylene chloride. Elution with methylene chloride/acetonitrile (6:4) gave a red eluate which was evaporated to a crystalline residue. Recrystallisation from acetonitrile (by displacement of methylene chloride) gave 10-methoxycarbonyl-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium anhydro-salt (16, R=COOMe) (27 mg., 8%) as red plates, m.p. 188-191° (Found: C, 58.7; H, 3.4; N, 4.3. $C_{16}H_{11}NO_2Se$ requires C, 58.6; H, 3.4; N, 4.3%).

(iii) The 10-formyl derivative.

a) Preparation of 10-dimethylaminomethylene-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium perchlorate. A mixture of the selenazolium salt (12) (3.70 g., 10 m.moles), dimethylformamide (7.8 ml., 0.1 mole) and acetic anhydride (80 ml.) was boiled for 2 hr. The cooled solution deposited a dark orange solid which was filtered off, washed with acetonitrile, then with ether and dried. Recrystallisation from nitromethane gave 10-dimethylaminomethylene-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium perchlorate (18) (1.38 g., 33%) as orange needles which decomposed > 295° (Found: C, 47.9; H, 3.6. $C_{17}H_{15}ClN_2O_4Se$ requires C, 47.9; H, 3.6%).

b) Hydrolysis of the Vilsmeier salt (18). Acetonitrile (40 ml.) and 1M-aqueous sodium hydroxide (40 ml.) when mixed form 2 layers. To this was added the Vilsmeier salt (18) (852 mg., 2 m.moles), and the

mixture was shaken for 20 min. The mixture was then poured into water and extracted with methylene chloride. Evaporation of the dried extracts afforded a dark, crystalline residue. Recrystallisation from acetonitrile (by displacement of methylene chloride) gave 10-formyl-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium anhydro-salt (16, R=CHO) (380 mg., 63%). A sample recrystallised from nitromethane as red rods, m.p. 241-244° (dec.) (Found: C, 60.4; H, 3.3. $C_{13}H_9NOSe$ requires C, 60.4; H, 3.0%).

VII: Preparation of Dimethylaminomethylene-indeno[2,1-d]thiazolium Salts.

The indenothiazolium salt and dimethylthioformamide were boiled in acetic anhydride for 10 min. The solution was cooled and the product crystallised out. Crystallisation was completed by addition of ether. The dimethylaminomethylene salt was filtered off, washed thoroughly with ether and dried.

(i) From 3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium perchlorate. The salt (1.82 g., 5 m.moles) and dimethylthioformamide (4.45 ml., 50 m.moles) in acetic anhydride (40 ml.) gave an orange crystalline product which, after recrystallisation from acetonitrile, gave 4-dimethylaminomethylene-3-methyl-2-phenyl-4H-indeno[2,1-d]thiazolium perchlorate (27c) (1.8 g., 86%) as orange needles, m.p. 251-253° (Found: C, 57.4; H, 4.8. $C_{20}H_{19}ClN_2O_4S$ requires C, 57.4; H, 4.6%).

(ii) From 2-t-butyl-3-phenyl-4H-indeno[2,1-d]thiazolium perchlorate. The salt (4.06 g., 10 m.moles) and dimethylthioformamide

(8.9 ml., 0.1 mole) in acetic anhydride (40 ml.) gave a yellow crystalline product which was recrystallised from acetonitrile. 4-Dimethylaminomethylene-2-t-butyl-3-phenyl-4H-indeno[2,1-d]thiazolium perchlorate (27b) (4 g., 87%) formed yellow prisms, m.p. 287-288° (dec.) (Found: C, 59.8; H, 5.6. $C_{23}H_{25}ClN_2O_4S$ requires C, 59.9; H, 5.5%).

(iii) From 2,3-diphenyl-4H-indeno[2,1-d]thiazolium perchlorate. The salt (4.26 g., 10 m.moles) and dimethylthioformamide (8.9 ml., 0.1 mole) in acetic anhydride (40 ml.) gave an orange crystalline product. Recrystallisation from acetonitrile gave 4-dimethylaminomethylene-2,3-diphenyl-4H-indeno[2,1-d]thiazolium perchlorate (27a) (4.1 g.,85%) as orange prisms, m.p. 282-285° (Found: C, 62.5; H, 4.6. $C_{25}H_{21}ClN_2O_4S$ requires C, 62.4; H, 4.4%).

(iv) From 10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate. The salt (1.62 g., 5 m.moles) and dimethylthioformamide (4.45 ml., 50 m.moles) in acetic anhydride (40 ml.) gave 10-dimethylaminomethylene-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate (24) (1.75 g., 93%) as orange needles.

(v) From 10H-indeno[2,1-d]pyrido[2,1-b]selenazolium perchlorate. The salt (370 mg., 1 m.mole) and dimethylthioformamide (0.89 ml., 10 m.moles) in acetic anhydride (8 ml.) gave 10-dimethylaminomethylene-10H-indeno[2,1-d]pyrido[2,1-b]selenazolium perchlorate (18) (362 mg., 85%).

VIII: Preparation of Thioformyl Derivatives of Indeno[2,1-d]thiazolium Anhydro-salts.

(i) From 2-t-butyl-3-methyl-4H-indeno[2,1-d]thiazolium perchlorate. The salt (1.6 g., 5 m.moles) in dimethylformamide (25 ml)was heated nearly to boiling with phosphorus oxychloride (1 ml.) for 2 min., during which time the solution became dark orange-brown. The cooled solution of the Vilsmeier complex was poured into 2 M-aqueous sodium hydrogen sulphide (25 ml.), and the yellow solid which precipitated was filtered off, washed well with water and dried in vacuo over phosphorus pentoxide. The dried material was chromatographed on a column of alumina (2.5x20 cm.) using benzene/acetonitrile (6:4) for elution. The initial brown fraction (300 ml.) was discarded. Elution with benzene/acetonitrile (4:6) gave an orange-brown fraction (400 ml.) which on evaporation gave 4-thioformyl-2-t-butyl-3-methyl-4H-indeno [2,1-d]thiazolium anhydro salt (34a) (0.73 g., 50%). A sample recrystallised from acetonitrile as yellow plates, m.p. 195-197° (dec.>185°) (Found: C, 66.8; H, 5.9. $C_{16}H_{17}NS_2$ requires C, 66.8; H, 6.0%).

(ii) From 10-dimethylaminomethylene-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate. Pyridine (25 ml.) and 2 M-aqueous sodium hydrogen sulphide (25 ml.) when mixed form 2 layers. To this was added the salt (1.89 g., 5 m.moles). The mixture was shaken for 20 min., during which time the salt dissolved and an orange precipitate of the product was formed. The mixture was then diluted with water and the precipitate was filtered off, washed thoroughly with water and dried in vacuo over phosphorus pentoxide. The crude, dry product

(1.07 g.) was then recrystallised from dimethylformamide giving 10-thioformyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium anhydro-salt (35) (712 mg., 44%) as orange needle clusters which decomposed $>215^{\circ}$ (Found: C, 67.0; H, 3.3; N, 5.5. $C_{15}H_{19}NS_2$ requires C, 67.4; H, 3.4; N, 5.2%).

(iii) From 6-dimethylaminomethylene-6H-indeno[1,2-d]pyrido[2,1-b] thiazolium perchlorate(25). The salt (1.895 g., 5 m.moles), acetonitrile (100 ml.) and 2 M-aqueous sodium hydrogen sulphide (25 ml.) were shaken together at ca. 40° for 5-10 min., after which time all the yellow salt had dissolved. The red thioaldehyde began to crystallise almost as soon as the salt had disappeared. Water (100 ml.) was added gradually, with swirling, to complete the precipitation. The red solid was filtered off, washed with water (100 ml.), then methanol (50 ml.) and finally ether (25 ml.) before being dried in vacuo. Recrystallisation of the product from dimethylformamide (addition of ethyl acetate) gave 6-thioformyl-6H-indeno[1,2-d]pyrido[2,1-b]thiazolium anhydro-salt (36) (920 mg., 69%) as fine orange needles which decomposed $>255^{\circ}$ (Found: C, 67.1; H,3.4; S, 23.7. $C_{15}H_9NS_2$ requires C, 67.4; H, 3.4; S, 24.0).

(iv) From 4-dimethylaminomethylene-2-t-butyl-3-phenyl-4H-indeno [2,1-d]thiazolium perchlorate. A mixture of dimethylformamide (25 ml.) and 2 M-aqueous sodium hydrogen sulphide (25 ml.) was added to a solution of the salt (2.305 g., 5 m.moles) in dimethylformamide (25 ml.) The mixture was cooled to 0°, and after 10 min. the crystalline product was filtered off, washed thoroughly with water and dried in vacuo

over phosphorus pentoxide. The crude, dry product was quickly recrystallised from nitromethane, giving 4-thioformyl-2-t-butyl-3-phenyl-4H-indeno[2,1-d]thiazolium anhydro-salt (34b) (759 mg., 43%). A sample recrystallised from acetonitrile as orange prisms which decompose $>215^{\circ}$ (Found: C, 72.0; H, 5.6. $C_{21}H_{19}NS_2$ requires C, 72.2 H, 5.5%).

In another run of this reaction in which the mixture was not cooled, no product had crystallised out after 30 min. The mixture was diluted with water and extracted with benzene. Evaporation of the dried benzene extracts yielded a crystalline residue which was filtered off with the aid of benzene, giving the thioaldehyde (34b) (283 mg., 16%). The benzene filtrate was evaporated and the oily residue was crystallised by addition of acetonitrile. The orange-brown crystalline compound was filtered off and recrystallised from acetonitrile, giving 2-anilino-3-thioformylindene (37) as brown needles which decompose slowly $>140^{\circ}$ and melt at 160° (Found: C, 76.4; H, 5.5; S, 12.5. $C_{16}H_{13}NS$ requires C, 76.4; H, 5.2; S, 12.8%). In the mass spectrum the molecular ion was at m/e=251 (high resolution 251.073, calculated for $C_{16}H_{13}NS$ is 251.077). The N.M.R. spectrum ($CDCl_3$) showed a singlet (2H) at δ3.81 (ring CH_2), a singlet (1H) at δ10.58 (CHS), a broad singlet (1H) at δ15.10 (NH, hydrogen bonded) and a complex group of signals (9H) between δ6.9 and 7.6 (aromatic protons). On shaking the deuterochloroform solution with D_2O the broad peak at δ15.10 disappeared, not immediately but after 2 hr., suggesting strong hydrogen bonding.

(v) Decomposition of 4-thioformyl-2-t-butyl-3-phenyl-4H-indeno [2,1-d] thiazolium anhydro-salt with sodium hydrogen sulphide. 2 M-Aqueous sodium hydrogen sulphide (10 ml.) was added to a solution of the thioaldehyde (349 mg., 1 m.mole) in dimethylformamide (35 ml.), and the mixture was allowed to stand at room temperature for 2 hr. The mixture was then diluted with water and extracted with benzene. Evaporation of the dried benzene extracts left a gummy residue which was chromatographed on a column of alumina (3x17 cm.) with benzene as eluant. An initial red fraction (100 ml.) was discarded. Evaporation of the orange-brown fraction (500 ml.) and recrystallisation of the residue from acetonitrile gave 2-anilino-3-thioformylindene (37) (45 mg., 13%).

(vi) Thionation of 1-phenylanilinomethylene-indan-2-one (38a). The ketone[128] (311 mg., 1 m.mole) was dissolved in hot pyridine (10 ml. phosphorus pentasulphide (111 mg., 0.5 m.mole) was added, and the mixture boiled for 20 sec. before being cooled and poured into water. The resulting yellow precipitate was extracted with benzene. The dried extracts were evaporated and the residue was chromatographed on a column of silica (3x11 cm.) with benzene as eluant. Evaporation of the red-brown benzene eluate left a crystalline residue. Recrystallisation from methylcyclohexane gave 1-phenylanilinomethylene-indan-2-thione (38b) (45 mg., 13%) as orange plates which decompose $> 160^{\circ}$ (Found: C, 80.5; H, 5.2; N, 4.0. $C_{22}H_{17}NS$ requires C, 80.7; H, 5.2; N, 4.3%). The N.M.R. spectrum ($CDCl_3$) showed a broad singlet (2H) at δ 4.05 (CH_2) and a complex group of signals (14H) between δ 6.7 and

8.6 (aromatic protons).

IX: Preparation of Derivatives of the Indeno[1,2,3-b,c]-1-thiacycl [2,3,3]azine System.

(i) Preparation of 6-methyl-2-(1,2-dihydro-2-oxoinden-1-ylthio) pyridine. 6-Methyl-2-(1,2-dihydro-2-oxoinden-1-ylthio)pyridinium bromide[128] (33.5 g., 0.1 mole) was added to a cold, saturated solution of potassium carbonate and the liberated base was extracted into methylene chloride. Evaporation of the dried extracts gave 6-methyl-2-(1,2-dihydro-2-oxoinden-1-ylthio)pyridine[128] (24.2 g., 95%) as cream-coloured granular prisms. This material was used without further purification.

(ii) Preparation of 1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate. Phosphorus pentachloride (83.4 g., 0.4 mole) was added portionwise over 2 min., with swirling, to a warm solution of the crude base (25.5 g., 0.1 mole) in nitromethane (150 ml.), and the resulting suspension was boiled for 2 min. The mixture was cooled to 0°, and methanol (100 ml.) was added dropwise to destroy the excess of phosphorus pentachloride. The resulting solution was evaporated to dryness, the solid residue was redissolved in ethanol (150 ml.), and perchloric acid (10.5 ml., 0.125 mole) was added. The product crystallised immediately. The precipitate was filtered off, washed thoroughly with ethanol, then ether, and dried, giving 1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate (43) (11.3 g., 35%). The product was identical (N.M.R. and I.R.) to a sample obtained by

cyclisation of the bromide salt[128].

(iii) 10-Acetyl-9-methylindeno[1,2,3-b,c]-1-thiacycl[2,3,3]azine.

a) Reaction of the salt (43) with acetic anhydride and triethylamine. Triethylamine (5.56 ml., 40 m.moles) was added dropwise over 2 min. to a boiling solution of the salt (676 mg., 2 m.moles) in acetic anhydride (40 ml.). The resulting dark red solution was boiled for a further 2 min., its colour changing to green. The green solution was cooled, poured into water and allowed to stand overnight before being basified with sodium carbonate. The resulting suspension was extracted with methylene chloride. The dried extracts were evaporated and the residue was chromatographed on a column of alumina (3x20 cm.) with methylene chloride/acetonitrile (5:1) as eluant. Evaporation of the green eluate yielded a dark green crystalline residue which, after recrystallisation from acetonitrile, gave 10-acetyl-9-methylindeno [1,2,3-b,c]-1-thiacycl[2,3,3]azine (42c) (176 mg., 29%) as dark green needles, m.p. 153-155° (Found: C, 74.9; H, 4.4; O, 4.4. $C_{19}H_{13}NOS$ requires C, 75.2; H, 4.3; O, 5.3%), γ_{max} (Nujol) 1633 cm^{-1} (C=O).

b) Reaction of the salt (43) with acetic anhydride and triethylamine in acetonitrile. Triethylamine (13.9 ml., 0.1 mole) was added to a boiling solution of the salt (1.69 g., 5 m.moles) and acetic anhydride (9.4 ml., 0.1 mole) in acetonitrile (100 ml.). The solution was boiled for a further minute then poured into water. The resulting yellow-green suspension was basified with sodium carbonate and then extracted with methylene chloride. The dried extracts were evaporated, leaving a semi-crystalline mass. Acetonitrile (30 ml.) was added and

the solid was filtered off. The filtrate was retained (see below). Recrystallisation of the solid from nitromethane gave 10-acetyl-1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium anhydro-salt (44) (632 mg., 46%). A sample recrystallised from acetonitrile as red prisms, m.p. 167-168° (dec.) (Found: C, 72.9; H, 4.5; N, 5.0. $C_{17}H_{13}NOS$ requires C, 73.1; H, 4.7; N, 5.0%). The acetonitrile filtrate was evaporated and chromatographed on a column of alumina (3x10 cm.) with methylene chloride as eluant. Evaporation of the green eluate followed by recrystallisation of the residue from acetonitrile gave the thiacyclazine (42c) (96 mg., 6%). When the reaction time was increased to 10 min. the solution changed colour from red to green and the only isolable product was the thiacyclazine derivative.

c) Cyclisation of 10-acetyl-1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium anhydro-salt. A solution of the acetyl compound (44) (279 mg., 1 m.mole) and triethylamine (1 ml.) in acetic anhydride (10 ml.) was boiled for 5 min., during which time the colour of the solution changed from red to green. The green solution was poured into water and the resulting suspension was basified with sodium carbonate before being extracted with methylene chloride. The dried extracts were evaporated and the residue was chromatographed on a column of alumina (3x10 cm.) with methylene chloride as eluant. Evaporation of the green eluate gave the thiacyclazine derivative (42c) (114 mg., 75%). When the above reaction was repeated in the absence of triethylamine the yield was 27%. Attempts to bring about cyclisation in the absence of acetic anhydride, e.g. with triethylamine or potassium

t-butoxide in dimethylformamide, were unsuccessful. Attempted thermal cyclisation in boiling nitrobenzene gave a green solution, but no product could be isolated from this.

(iv) Indeno[1,2,3-b,c]-1-thiacycl[2,3,3]azine.

a) Preparation of 10-dimethylaminomethylene-1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate. A mixture of the salt (43) (3.38 g., 10 m.moles), dimethylformamide (11.55 ml., 0.15 mole) and acetic anhydride (100 ml.) was boiled under reflux for 20 min. The resulting dark orange-brown solution was cooled and treated carefully with ether and the resulting brown precipitate was filtered off, washed with ether and dried (3.3 g.). This was shown, by integration of its N.M.R. spectrum, to be a mixture of the starting material and the required Vilsmeier salt in a molar ratio of 6:4. The mixture was dissolved in dimethylformamide (50 ml.), triethylamine (15 ml.) was added, and the mixture was allowed to stand in an ice bath for 1 min. Water (250 ml.) and methylene chloride (150 ml.) were added and the mixture was shaken thoroughly and then filtered. The brown residue was washed sparingly with methylene chloride, followed by ethanol, and finally with ether, and dried. Recrystallisation from methanol/acetonitrile (9:1, 100 ml.) with charcoal screening gave 10-dimethylaminomethylene-1-methyl-10H-indeno[2,1-d]pyrido[2,1-b]thiazolium perchlorate (48) (367 mg., 9%). A sample recrystallised from methanol as orange needles which decomposed $>198^{\circ}$ (Found: C, 55.2; H, 4.1; N, 7.4. $C_{18}H_{17}ClN_2O_4S$ requires C, 55.0; H, 4.4; N, 7.1%).

b) Cyclisation of the Vilsmeier salt (48). Triethylamine (16 ml.) was added to a solution of the crude mixture from the previous reaction (10 m.moles scale) in dimethylformamide (50 ml.), and the mixture was boiled for 2 min. The resulting dark green solution was diluted with water and extracted with methylene chloride. The extracts were washed 6 times with water, dried (Na_2SO_4) and evaporated. The resulting solid residue was chromatographed on a column of alumina (3x22 cm.) with methylene chloride as eluant. Evaporation of the dark green eluate gave a crystalline residue which was dissolved in boiling benzene (25 ml.). Boiling cyclohexane (50 ml.) was then added. After filtration and cooling the product crystallised as dark green needle clusters (525 mg.). The mother liquors were rechromatographed on a short column of alumina, the green eluate was evaporated and the residue recrystallised from cyclohexane (by displacement of methylene chloride) to give a further 200 mg. of product. The total yield of indeno[1,2,3-b,c]-1-thiacycl[2,3,3]azine (42b) was 725 mg.(29%). A sample recrystallised from cyclohexane as bronze plates which started to decompose $>140^{\circ}$ and melted at 150-152° (Found: C, 77.3; H, 3.9; S, 12.9. $C_{16}H_9NS$ requires C, 77.7; H, 3.7; S, 13.0%), molecular weight (mass spectrometry) 247. The mass spectrum showed the presence of an impurity containing chlorine (molecular weight 281).

When the above reaction was repeated using the purified Vilsmeier salt (48) (197 mg., 0.5 m.mole) and triethylamine (2 ml.) in dimethylformamide (10 ml.) the yield of thiacyclazine was 103 mg. (83%).

X: Preparation of 1,2-Dithiolium Salts.

The 1,3-diketone was dissolved in glacial acetic acid (50 ml. per 25 m.moles of diketone). Perchloric acid or hydrobromic acid (40% w/v solution in acetic acid) was then added, immediately followed by hydrogen disulphide, and the mixture was heated to the appropriate temperature for 5 min. The hot acetic acid solution was decanted from any sulphur that remained, then cooled, and ether was added to precipitate the dithiolium salt. The salt was filtered off, washed with carbon disulphide to remove traces of sulphur, then washed thoroughly with ether and dried.

(i) 3-Benzyl-5-phenyl-1,2-dithiolium perchlorate. Phenylacetyl acetophenone (11.9 g., 50 m.moles), perchloric acid (6.3 ml.), and hydrogen disulphide (2.4 ml.), at 70-75°, gave 3-benzyl-5-phenyl-1,2-dithiolium perchlorate (9.25 g., 50%). A sample recrystallised from acetic acid (addition of ethyl acetate) as colourless leaflets, m.p. 135° (Found: C, 52.0; H, 3.6. $C_{16}H_{13}ClO_4S_2$ requires C, 52.1; H, 3.5%).

(ii) 3-Benzyl-4-phenyl-1,2-dithiolium bromide. Hydroxymethylene dibenzyl ketone[161] (5.97 g., 25 m.moles), hydrobromic acid (6.75 ml.), and hydrogen disulphide (1.2 ml.), at 70-75°, gave 3-benzyl-4-phenyl-1,2-dithiolium bromide (6.7 g., 77%). A sample recrystallised from acetic acid (addition of ethyl acetate) as yellow plates, m.p. 164-174° (dec.) (Found: C, 54.7; H, 4.0. $C_{16}H_{13}BrS_2$ requires C, 55.0; H, 3.7%).

(iii) 3,5-Dimethyl-1,2-dithiolium bromide. Acetylacetone (10 g., 50 m.moles), hydrobromic acid (13.5 ml.), and hydrogen disulphide (2.4 ml.), at 70-75°, gave, on addition of ether, a colourless oil which solidified when triturated with ethanol. The crystalline solid was filtered off with the aid of ethanol, giving 3,5-dimethyl-1,2-dithiolium bromide (9.5 g., 78%). A sample recrystallised from acetic acid (addition of ethyl acetate) as colourless prisms which decomposed 150° (Found: C, 28.5; H, 3.6. $C_5H_7BrS_2$ requires C, 28.4; H, 3.3%).

(iv) 3,4-Dimethyl-1,2-dithiolium perchlorate. 3-Hydroxymethylenebutan-2-one (from acidification of 6.1 g., 50 m.moles, of its sodium enolate), perchloric acid (6.3 ml.), and hydrogen disulphide (2.4 ml.), at 70-75°, gave a brown-purple solid. Repeated recrystallisation from acetic acid (addition of ether), with charcoal screening, gave 3,4-dimethyl-1,2-dithiolium perchlorate (2.6 g., 22%) as dark prisms which decomposed $>$ 150° (Found: C, 28.0; H, 3.3. $C_5H_7ClO_4S_2$ requires C, 26.0; H, 3.1%).

(v) 3,4-Cyclopenteno-1,2-dithiolium perchlorate. 2-Hydroxymethylenecyclopentanone (2.8 g., 25 m.moles), perchloric acid (3.15 ml.), and hydrogen disulphide (1.2 ml.), at 60°, gave 3,4-cyclopenteno-1,2-dithiolium perchlorate (2.47 g., 40%). A sample recrystallised from acetic acid (addition of ether) as colourless prisms, m.p. 147-148° (Found: C, 29.6; H, 3.0. $C_6H_7ClO_4S_2$ requires C, 29.7; H, 2.9%).

(vi) 3,4-Cyclohexeno-1,2-dithiolium perchlorate. 2-Hydroxymethylenecyclohexanone (6.3 g., 50 m.moles), perchloric acid (6.3 ml.), and hydrogen disulphide (3 ml.), at 60°, gave 3,4-cyclohexeno-1,2-

dithiolium perchlorate (5.51 g., 42%). A sample recrystallised from acetic acid as colourless needles, m.p. 111-112° (Found: C, 32.9; H, 3.6. $C_7H_9ClO_4S_2$ requires C, 32.8; H, 3.5%).

XI: Preparation of 3-Dimethylaminovinyl-1,2-dithiolium Salts.

Dimethylthioformamide (4.25 ml., 50 m.moles) was added to a suspension of the dithiolium salt (10 m.moles) in acetic anhydride and the mixture was boiled for 5 min. The mixture was then cooled and ether was added to induce crystallisation. The crystalline product was filtered off, washed thoroughly with ether, and dried.

(i) From 3-benzyl-5-phenyl-1,2-dithiolium perchlorate. The salt (3.68 g.) in acetic anhydride (40 ml.) gave 3-(2-dimethylamino-1-phenylvinyl)-5-phenyl-1,2-dithiolium perchlorate (3.89 g., 92%). A sample recrystallised from acetonitrile (addition of ethyl acetate) as red prisms, m.p. 180-181° (Found: C, 53.8; H, 4.3. $C_{19}H_{18}ClNO_4S_2$ requires C, 53.8; H, 4.3%).

(ii) From 3-benzyl-4-phenyl-1,2-dithiolium bromide. The salt (3.48 g.) in acetic anhydride (40 ml.) gave 3-(2-dimethylamino-1-phenylvinyl)-4-phenyl-1,2-dithiolium bromide (3.20 g., 80%). A sample recrystallised from acetonitrile as red prisms, m.p. 189-190° (Found: C, 56.3; H, 4.6. $C_{19}H_{18}BrNS_2$ requires C, 56.4; H, 4.5%).

(iii) From 3,5-dimethyl-1,2-dithiolium bromide. The salt (2.11 g.) in acetic anhydride (30 ml.) gave, on addition of ether, a dark oil which was washed with ether and dissolved in hot ethanol (30 ml.). Addition of perchloric acid (1.0 ml.) precipitated a dark brown

crystalline material which was filtered off, washed thoroughly with ether and dried, giving 3-dimethylaminovinyl-5-methyl-1,2-dithiolium perchlorate (2.04 g., 71%). A sample recrystallised from acetonitrile (addition of ethyl acetate) as brown granular prisms, m.p. 168-169° (Found: C, 33.9; H, 4.4. $C_8H_{12}ClNO_4S_2$ requires C, 33.6; H, 4.2%).

XII: Preparation of 6a-Thiathiophthenes.

(i) 2-Phenyl-6a-thiathiophthene from 3-dimethylaminovinyl-5-phenyl-1,2-dithiolium perchlorate[162]. 2 M-Aqueous sodium hydrogen sulphide (25 ml.) was added to a solution of the Vilsmeier salt (1.74 g., 5 m.moles) in dimethylformamide (25 ml.). The mixture was poured into water and extracted with benzene. Evaporation of the dried benzene extracts gave a crystalline residue which was chromatographed on a column of alumina (3x26 cm.) with benzene as eluant. Evaporation of the red benzene eluate gave a crystalline residue which recrystallised from cyclohexane giving 2-phenyl-6a-thiathiophthene (980 mg.,83%) as red needles, m.p. 134-135° (lit.[99] 135-136°). Continued elution with benzene/ether (3:1) gave a red-brown fraction which on evaporation gave a crystalline residue. Recrystallisation from petrol afforded 2-phenyl-4H-thiopyran-4-thione (77 mg., 7%) as brown plates, m.p. 79-80° (lit.[100] 79-80°).

(ii) 2,4-Diphenyl-6a-thiathiophthene from 3-(2-dimethylamino-1-phenylvinyl)-5-phenyl-1,2-dithiolium perchlorate. 2 M-Aqueous sodium hydrogen sulphide (25 ml.) was added to a solution of the Vilsmeier salt (2.12 g., 5 m.moles) in dimethylformamide (25 ml.). The mixture was diluted with water and extracted with benzene. The red extracts

were washed with water, dried (Na_2SO_4) and evaporated. The crystalline residue was chromatographed on a column of alumina (2.5x10 cm.) with benzene as eluant. Evaporation of the red eluate gave a crystalline residue which was recrystallised from hexane. 2,4-Diphenyl-6a-thia-thiophthene (1.26 g., 81%) was obtained as red needles, m.p. 128-129° (lit.[67] 129-131°).

(iii) 3,4-Diphenyl-6a-thiathiophthene.

a) From 3-(2-dimethylamino-1-phenylvinyl)-4-phenyl-1,2-dithiolium bromide. 1M-Aqueous sodium hydrogen sulphide (10 ml.) was added to a solution of the Vilsmeier salt (2.02 g., 5 m.moles) in methanol (30 ml.) at 0° and the mixture swirled for 30 sec. The mixture was then diluted with water and extracted with benzene. The red benzene extracts were washed with water, dried (Na_2SO_4) and evaporated. The crystalline residue was dissolved in a mixture of benzene and petrol (6:4) and adsorbed on a column of alumina (3x25 cm.). Initial elution with benzene/petrol (6:4) gave a purple fraction which, after evaporation and recrystallisation of the residue from cyclohexane, gave 3,4-diphenyl-6a-thiathiophthene (782 mg., 50%), identical with a sample prepared by reaction of 3,5-epidithio-2,5-diphenyl-2,4-pentadienal with phosphorus pentasulphide (see below). Continued elution with benzene gave a yellow-green fraction which was shown by T.L.C. to be impure. The benzene fraction was evaporated and rechromatographed on a column of alumina (2.5x30 cm.) with benzene/petrol (6:4) as eluant. Evaporation of the green fraction gave a crystalline residue which, when recrystallised from cyclohexane, gave 3,5-diphenyl-4H-thiopyran-4-thione

(280 mg., 20%) as green needles, m.p. 170-171° (Found: C, 73.0; H, 4.4. $C_{17}H_{12}S_2$ requires C, 72.8; H, 4.3%).

b) From 3,5-epidithio-2,5-diphenyl-2,4-pentadienal (page 104). A stirred mixture of the aldehyde (296 mg., 1 m.mole) and phosphorus pentasulphide (250 mg.) in toluene (20 ml.) was boiled for 1 hr. The hot mixture was filtered, and the gummy residue was washed with hot benzene (2x50 ml. portions). The combined extracts were evaporated, and the residue was chromatographed on a column of alumina (2.5x15 cm.) with benzene as eluant. Evaporation of the red eluate and recrystallisation of the residual solid from hexane gave 3,4-diphenyl-6a-thiathiophthene (48 mg., 15%) as red needles, m.p. 189-190° (Found: C, 65.0; H, 3.8. $C_{17}H_{12}S_3$ requires C, 65.3; H, 3.9%).

(iv) 2-Methyl-6a-thiathiophthene from 3-dimethylaminovinyl-5-methyl-1,2-dithiolium perchlorate. 2 M-Aqueous sodium hydrogen sulphide (25 ml.) was added to a solution of the Vilsmeier salt (1.43 g., 5 m. moles) in dimethylformamide (25 ml.). The mixture was then diluted with water and extracted with benzene. The benzene extracts were washed with water, dried (Na_2SO_4) and evaporated. The residue was dissolved in a mixture of benzene and petrol (4:1) and adsorbed on a column of alumina (3x20 cm.). Elution with benzene/petrol (4:1) gave an orange fraction which, after evaporation and recrystallisation from cyclohexane, afforded 2-methyl-6a-thiathiophthene (252 mg., 29%) as orange plates, m.p. 136-137° (Found: C, 41.6; H, 3.4; S, 55.1. $C_6H_6S_3$ requires C, 41.4; H, 3.5; S, 55.2%). Further elution with benzene gave a pale red-brown (dichroism) solution which, after evaporation and recryst-

allisation of the residue from cyclohexane, gave 2-methyl-4H-thiopyran-4-thione (222 mg., 31%) as yellow brown plates, m.p. 56-56.5° (Found: C, 50.8; H, 4.2. $C_6H_6S_2$ requires C, 50.6; H, 4.3%).

Attempted formylation of 2-methyl-6a-thiathiophthene. 2-Methyl-6a-thiathiophthene (174 mg., 1 m.mole) was added portionwise, over 5 min., to a stirred mixture of dimethylthioformamide (5 ml.) and phosphorus oxychloride (0.38 g., 2.5 m.moles) at 75°. The mixture was then cooled and 2 M-aqueous sodium hydroxide (10 ml.) was added. The mixture was then poured into water and extracted with benzene. The red benzene extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of alumina (2.5x15 cm.) with benzene/petrol (3:2) as eluant. The red eluate contained a mixture of starting material, dimethylthioformamide and product. The red solution was evaporated, and the residue was dissolved in acetone (10 ml.). Perchloric acid (0.084 ml., 1 m.mole) was then added. Addition of ether precipitated brown crystals of a perchlorate salt which were filtered off, washed with ether and dried. The salt was basified with aqueous triethylamine, and the liberated base was extracted into benzene. Evaporation of the dried extracts afforded a crystalline residue which, after recrystallisation from acetonitrile, gave 2-dimethylaminovinyl-6a-thiathiophthene (63) (42 mg., 18%). A sample recrystallised from cyclohexane as red needles which decomposed $>140°$ (Found: C, 47.2; H, 4.9; N, 6.1. $C_9H_{11}NS_3$ requires C, 47.1; H, 4.8; N, 6.1%), ν_{max} (Nujol) 1613 cm^{-1} (C=C). The N.M.R. spectrum showed a singlet (6H) at δ 2.98 (NMe_2), a singlet

(1H) at δ7.41 (H-3), an AB quartet at δ5.57, 7.49 (J=12.9 c/s) ($CH=CH-NMe_2$) and an AB quartet at δ7.34, 8.53 (J=6.6 c/s) (H-4, H-5).

(v) 3,4-Ethano-6a-thiathiophthene from 3,4-cyclopenteno-1,2-dithiolium perchlorate. A mixture of dimethylthioformamide (10 ml.) and phosphorus oxychloride (0.912 g., 6 m.moles) was added to the salt (486 mg., 2 m.moles), and the resulting solution warmed for 10 min. at 60°. The solution was cooled to 0° and dimethylformamide (20 ml.) was added, followed by 2 M-aqueous sodium hydrogen sulphide (25 ml.). The mixture was then diluted with water and extracted with benzene. The deep red benzene extracts were washed thoroughly with water and dried (Na_2SO_4). The extracts were evaporated and the residual dimethylthioformamide was distilled off at 0.1 mm. The residue was chromatographed on a column of silica (3x25 cm.) with benzene/petrol (2:3) as eluant. Evaporation of the red fraction gave a crystalline residue which, after recrystallisation from cyclohexane, afforded 3,4-ethano-6a-thiathiophthene (221 mg., 59%) as red needles, m.p. 109-110° (Found: C, 45.2; H, 3.3. $C_7H_6S_3$ requires C, 45.1; H, 3.3%).

(vi) 3,4-Propano-6a-thiathiophthene from 3,4-cyclohexeno-1,2-dithiolium perchlorate. A mixture of dimethylthioformamide (10 ml.) and phosphorus oxychloride (1.52 g., 10 m.moles) was added to the salt (1.29 g., 5 m.moles) and the mixture treated as described in (v) above. Evaporation of the red eluate from the chromatography gave a red oil which solidified on cooling. Recrystallisation from cyclohexane gave 3,4-propano-6a-thiathiophthene (700 mg., 70%) as red plates, m.p. 80° (Found: C, 48.0; H, 4.1. $C_8H_8S_3$ requires C, 48.0; H, 4.0%).

(vii) 3-Methyl-6a-thiathiophthene from 3,4-dimethyl-1,2-dithiolium perchlorate. A mixture of dimethylthioformamide (10 ml.) and phosphorus oxychloride (1.52 g., 10 m.moles) was added to the salt (1.16 g., 5 m. moles) and the mixture treated as described in (v) above. Evaporation of the orange eluate from the chromatography gave an oil which would not crystallise. The oil was extracted thoroughly with petrol, leaving a black insoluble tar behind. The petrol extracts were reduced in volume to 20 ml., and then cooled to 0°. 3-Methyl-6a-thiathiophthene (82 mg., 9%) crystallised as red needles. A sample recrystallised from methanol as red needles, m.p. 58-59° (Found: C, 41.3; H, 3.4. $C_6H_6S_3$ requires C, 41.4; H, 3.5%).

(viii) 2,5-Diethoxycarbonyl-6a-thiathiophthene from diethyloxalyl acetone. Phosphorus pentasulphide (115.2 g.) was added portionwise to a boiling solution of diethyloxalyl acetone (57.6 g., 0.2 mole) in benzene (1.5 litres), and the mixture was boiled for 1 hr. The hot benzene solution was decanted off, and the remaining solid was extracted with boiling benzene (2x500 ml. portions). The combined benzene extracts were washed with water and dried (Na_2SO_4). The extracts were evaporated and the oily residue was chromatographed on a column of alumina (6x29 cm.) with benzene/petrol (7:3) as eluant. Evaporation of the purple fraction (2 litres) gave a crystalline residue which, after recrystallisation from cyclohexane, afforded 2,5-diethoxycarbonyl-6a-thiathiophthene (2.64 g., 4%) as purple needles, m.p. 140° (Found: C, 43.5; H, 4.3. $C_{11}H_{12}O_4S_3$ requires C, 43.4; H, 4.0%).

(ix) 2-Ethoxycarbonyl-6a-thiathiophthene and 6a-thiathiophthene from 2,5-diethoxycarbonyl-6a-thiathiophthene. The diester (304 mg., 1 m. mole) was dissolved in a solution of hydrobromic acid in acetic acid (50 ml.) and the mixture was boiled for 96 hr. The solution was then poured into water and the resulting suspension extracted with ether. The ether extracts were washed twice with water, twice with sodium bicarbonate solution, and again twice with water before being dried (Na_2SO_4). Evaporation of the ether extracts gave a dark residue which was dissolved in a mixture of benzene and petrol (1:1) and adsorbed on a column of alumina (2x24 cm.). Initial elution with benzene/petrol (1:1) gave an orange fraction which, after evaporation and recrystallisation from hexane, afforded 6a-thiathiophthene (40 mg., 25%) as pink plates, m.p. 112-112.5° (lit.[75] 112.5-113.5°) (Found: C, 37.7; H, 2.3; S, 60.0. Calc.for $C_5H_4S_3$: C, 37.5; H, 2.5; S, 60.0%). Further elution with benzene/petrol (4:1) gave a red-purple fraction which, after evaporation and recrystallisation from hexane, afforded 2-ethoxycarbonyl-6a-thiathiophthene (18 mg., 8%) as red prismatic needles, m.p. 96° (Found: C, 41.4; H, 3.3. $C_8H_8O_2S_3$ requires C, 41.4; H, 3.5%).

(x) 2-Ethoxycarbonyl-6a-thiathiophthene from 5-ethoxycarbonyl-3-methyl-1,2-dithiolium perchlorate. To a solution of ethylacetylpyruvate (3.95 g., 25 m.moles) in acetic acid (25 ml.) was added perchloric acid (3.15 ml.), followed by hydrogen disulphide (1.5 ml.), and the mixture was heated for 5 min. at 60°. The hot acetic acid solution was decanted from the remaining sulphur and cooled. Dry ether (200 ml.) was added and the solution stood in a refrigerator for 1 hr. The ether

was decanted, leaving 5-ethoxycarbonyl-3-methyl-1,2-dithiolium perchlorate (1.7 g.) as a brown oil which darkened rapidly. To this oil was added a mixture of dimethylthioformamide (5 ml.) and phosphorus oxychloride (1 g.) and the mixture was warmed for 10 min. at 60°. The solution was cooled and 2 M-aqueous sodium hydrogen sulphide (20 ml.) was added. The mixture was then diluted with water and extracted with benzene. The extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated and the residual dimethylthioformamide was distilled off at 0.1 mm. The residue was chromatographed on a column of silica (3x24 cm.) with benzene/petrol (4:1) as eluant. An initial dark brown fraction was rejected. The purple fraction (1.5 litres) was evaporated and the residue recrystallised from cyclohexane, giving 2-ethoxycarbonyl-6a-thiathiophthene (202 mg., 3.5% based on diketone) as red needles.

The ester (232 mg., 1 m.mole) was dissolved in benzene (30 ml.) and adsorbed on a column of "CAMAG" alumina (Brockmann activity 1) (2.5x27 cm.), and benzene (200 ml.) was run through the column. The column was then allowed to stand 'wet' for 10 min. Elution with methanol gave a red fraction containing unreacted starting material. Elution with water gave a red solution of the acid. The unreacted ester was recycled through a fresh column of alumina. The combined aqueous eluates were washed thoroughly with ether, acidified with dilute hydrochloric acid and extracted with ether. The dried ether extracts were reduced in volume to ca. 200 ml. and benzene (20 ml.) was added. The remainder of the ether was then evaporated, the product crystallising from the remaining benzene. 2-Carboxy-6a-thiathiophthene (122 mg., 60%) formed

red needles which shrivelled and decomposed $> 205^{\circ}$ (Found: C, 35.6; H, 2.0. $C_6H_4O_2S_3$ requires C, 35.3; H, 2.0%).

XIII: Preparation of Acylmethylenedithioles.

(i) From 3-dimethylaminovinyl-5-phenyl-1,2-dithiolium perchlorate[162]. 2 M-Aqueous sodium hydroxide (10 ml.) was added to a solution of the Vilsmeier salt (696 mg., 2 m.moles) in dimethylformamide (12 ml.). The mixture was then poured into water and extracted with ether. Evaporation of the dried ether extracts yielded a yellow crystalline solid which, after recrystallisation from hexane, gave 3,5-epidithio-5-phenyl-2,4-pentadienal (54h) (390 mg., 89%) as yellow plates, m.p. 93-93.5° (Found: C, 59.8; H, 3.7. $C_{11}H_8OS_2$ requires C, 60.0; H, 3.7%).

(ii) From 3-(2-dimethylamino-1-phenylvinyl)-5-phenyl-1,2-dithiolium perchlorate. The Vilsmeier salt (848 mg., 2 m.moles), treated as in (i) above, gave 3,5-epidithio-2,5-diphenyl-2,4-pentadienal (54k) (338 mg., 57%) as orange plates from hexane, m.p. 118-119° (lit.[67] 119-120°).

(iii) From 3-(2-dimethylamino-1-phenylvinyl)-4-phenyl-1,2-dithiolium bromide. 2 M-Aqueous sodium hydroxide (50 ml.) was added to a solution of the Vilsmeier salt (4.04 g., 10 m.moles) in dimethylformamide (150 ml.). The mixture was poured into water and the resulting suspension was extracted with ether (2x1 litre portions). The dried extracts were evaporated and the oily residue was chromatographed on a column of alumina (2x26 cm.) with benzene/petrol (7:3) as eluant.

Evaporation of the initial yellow fraction (750 ml.) gave a crystalline residue which, after recrystallisation from hexane, afforded 3,5-epidithio-2,4-diphenyl-2,4-pentadienal (541) (330 mg., 11%) as orange needles, m.p. 188° (Found: C, 69.0; H, 4.1. $C_{17}H_{12}OS_2$ requires C, 68.9; H, 4.1%), ν_{max} 1570 $cm.^{-1}$ (CHO).

Further elution with benzene gave an orange fraction (500 ml.) which, after evaporation and recrystallisation of the residue from cyclohexane, afforded 5-(2-dimethylamino-1-phenylvinyl)-4-phenyl-1,2-dithiole-3-thione (64) (106 mg., 3%) as orange needles, m.p. 126-128° (molecular formula $C_{19}H_{17}NS_3$ by mass spectrometry). The N.M.R. spectrum ($CDCl_3$) showed a singlet (6H) at δ2.40 (NMe_2), a singlet (1H) at δ6.57 (=CH-NMe_2), a singlet at δ7.18 (phenyl group in 4-position of dithiole ring) and a broad signal at ca. δ7.25 for the second phenyl group. In trifluoroacetic/perchloric acid solution the N.M.R. spectrum showed two singlets (3H, 3H) at δ3.36 and 3.54 (NMe_2, non-equivalent), a doublet (1H) at δ5.89 (J=9 c/s) (PhCH) and two signals at δ7.66 and δ7.85 (broad) (phenyl protons). The I.R. spectrum (Nujol) showed medium to strong absorptions at 1134, 1168, 1270, 1291, 1301, 1320 and 1365 $cm.^{-1}$

Further elution with benzene/ether (4:1) gave a yellow fraction (200 ml.) which, after evaporation and recrystallisation of the residue from cyclohexane, afforded a yellow compound (20 mg.), m.p. 194-196°, whose structure is unknown. In a repeat run of the above reaction the two by-products were not formed. When the reaction was repeated using methanol as solvent, the yield of aldehyde (541) was 37%.

(iv) From 3-dimethylaminovinyl-5-methyl-1,2-dithiolium perchlorate. 2 M-Aqueous sodium hydroxide (25 ml.) was added to a solution of the Vilsmeier salt (1.43 g., 5 m.moles) in dimethylformamide (25 ml.). The mixture was then diluted with water and extracted with benzene. The dried extracts were evaporated and the residue chromatographed on a column of alumina (3x20 cm.) with benzene as eluant. The yellow fraction was evaporated and the residue recrystallised from hexane, giving 3,5-epidithio-2,4-hexadienal (54b) (266 mg., 34%) as yellow plates, m.p. 80° (Found: C, 45.9; H, 3.5. $C_6H_6OS_2$ requires C, 45.5; H, 3.8%).

(v) From 3-methyl-4-phenyl-1,2-dithiolium perchlorate[162]. Oxalyl chloride (2.15 ml., 25 m. moles) was added dropwise over two minutes to a mixture of the salt (2.92 g., 10 m.moles) and dimethylthioformamide (2.25 ml.) in chloroform (10 ml.). Brisk effervescence took place. The supernatant liquid was then poured off, the gummy residue was washed several times with ether, then dissolved in dimethylformamide (50 ml.) and added portionwise to 2 M-aqueous sodium hydroxide (50 ml.). The mixture was then diluted with water and extracted with benzene. Evaporation of the dried extracts left a dark brown residue which was chromatographed on a column of alumina (2x32 cm.) with benzene/petrol (4:6) for elution. Evaporation of the yellow fraction gave 3,5-epidithio-4-phenyl-2,4-pentadienal (54i) (211 mg., 9%). A sample, recrystallised from hexane, melted at 115-117° (lit.[69] 115.5-117°).

XIV: Preparation of N-Methylaldimines of Acylmethyleredithioles.

(i) From 3-dimethylaminovinyl-5-phenyl-1,2-dithiolium perchlorate. Aqueous methylamine (25-30%, 10 ml.) was added to a solution of the

Vilsmeier salt (696 mg., 2 m.moles) in dimethylformamide (12 ml.) The mixture was then poured into water and extracted with ether. Evaporation of the dried extracts gave a yellow crystalline solid which was recrystallised from acetonitrile, giving N-methyl-3,5-epidithio-5-phenyl-2,4-pentadienaldimine (56h) (385 mg., 82%) as yellow needles, m.p. 155-157° (Found: C, 61.9; H, 4.4. $C_{12}H_{11}NS_2$ requires C, 61.8; H, 4.8%).

(ii) From 3-(2-dimethylamino-1-phenylvinyl)-5-phenyl-1,2-dithiolium perchlorate. The Vilsmeier salt (848 mg., 2 m.moles), treated as in (i) above, gave N-methyl-3,5-epidithio-2,5-diphenyl-2,4-pentadienaldimine (56k) (494 mg., 80%) as orange plates from acetonitrile, m.p. 173-173.5° (Found: C, 69.5; H, 4.8. $C_{18}H_{15}NS_2$ requires C, 69.9; H, 4.9%).

(iii) From 3-(2-dimethylamino-1-phenylvinyl)-4-phenyl-1,2-dithiolium bromide. Aqueous methylamine (25-30%, 5 ml.) was added to a solution of the Vilsmeier salt (404 mg., 1 m.mole) in dimethylformamide (10 ml.). The mixture was then poured into water and extracted with ether. Evaporation of the dried extracts left a yellow crystalline residue which, after recrystallisation from benzene/cyclohexane (1:1), gave N-methyl-3,5-epidithio-2,4-diphenyl-2,4-pentadienaldimine (56l) (180 mg., 58%) as yellow needles, m.p. 185-190° (Found: C, 70.2; H, 5.1. $C_{18}H_{15}NS_2$ requires C, 69.9; H, 4.9%).

(iv) From 3-dimethylaminovinyl-5-methyl-1,2-dithiolium perchlorate. Aqueous methylamine (25-30%, 25 ml.) was added to a solution of the Vilsmeier salt (1.43 g., 5 m.moles) in dimethylformamide (25 ml.). The mixture was then diluted with water and extracted with benzene.

The dried benzene extracts were evaporated and the residue was chromatographed on a column of alumina (3x20 cm.) with benzene for elution. Evaporation of the yellow fraction (250 ml.) gave a yellow crystalline residue which was recrystallised from hexane, giving N-methyl-3,5-epidithio-2,4-hexadienaldimine (56b) (510 mg., 60%) as yellow plates, m.p. 136-137° (Found: C, 49.0; H, 5.0. $C_7H_9NS_2$ requires C, 49.1; H, 5.3%).

(v) From 3-methyl-1,2-dithiolium perchlorate[162]. A mixture of the salt (4.34 g., 20 m.moles) and dimethylthioformamide (8.4 ml., 0.1 mole) in acetic anhydride (80 ml.) was boiled for 5 min. The acetic anhydride was distilled off at 15 mm. and the remaining black oil was washed several times with ether. The oil was then dissolved in dimethylformamide and aqueous methylamine (25-30%, 50 ml.) was added. the mixture was poured into water and extracted with ether. The extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of alumina (3x20 cm.) with benzene as eluant. Evaporation of the yellow fraction gave a crystalline residue which, after recrystallisation from hexane, afforded N-methyl-3,5-epidithio-2,4-pentadienaldimine (56a) (255 mg., 8%) as yellow needles, m.p. 107-108° (Found: C, 45.7; H, 3.9. $C_6H_7NS_2$ requires C, 46.1; H, 3.9%).

XV: The Rearrangement of 6a-Thiathiophthenes and Related Compounds by Nucleophiles.

4-Methyl-2-phenyl-6a-thiathiophthene and 2-t-butyl-6a-thiathiophthene were prepared following the methods outlined above, by Drs. S. McKenzie and K.O.Wade respectively. 2,5-Diphenyl-6a-thiathiophthene was prepared by Dr.D.H. Reid[162].

The 4H-thiopyran-4-thiones described in this section are: 2-methyl- (m.p. 56-56.5°); 2-t-butyl- (m.p. 97°)[a]; 2-phenyl- (m.p. 79-80°)[100]; 5-methyl-2-phenyl- (m.p. 113-114°)[b]; 2,5-diphenyl- (m.p. 135-136°)[b]; 2,6-diphenyl- (m.p. 129°)[99]; 3,5-diphenyl- (m.p. 170-171°).

[a] Characterised by Dr.K.O.Wade. [b] Characterised by Dr.S. McKenzie.)

The yields quoted in this section are of T.L.C. pure, crystalline material (before recrystallisation). Products were identified by T.L.C., melting points, and comparative infra-red spectroscopy.

(i) Rearrangement of 6a-thiathiophthenes by sodium sulphide.

2 M-Aqueous sodium sulphide (5 ml.)was added to a solution of the 6a-thiathiophthene (1 m.mole) in dimethylformamide (20 ml.) and the mixture warmed at 60° for 5 min. The mixture was then poured into water and extracted with benzene. The benzene extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of alumina with benzene as eluant. The 4H-thiopyran-4-thione eluted slowly with benzene.

6a-Thiathiophthene	4H-Thiopyran-4-thione	Yield (%)
2-t-Butyl-	2-t-Butyl-	76
2-Phenyl-	2-Phenyl-	69
4-Methyl-2-phenyl-	5-Methyl-2-phenyl-	77
2,4-Diphenyl-	2,5-Diphenyl-	80
2,5-Diphenyl-[c]	2,6-Diphenyl-	8

([c] Starting material recovered in 79% yield)

(ii) Rearrangement of 6a-thiathiophthenes by sodium hydrogen sulphide. 2 M-Aqueous sodium hydrogen sulphide (5 ml.) was added to a solution of the 6a-thiathiophthene (1 m.mole) in dimethylformamide (20 ml.) and the mixture warmed at 70° for 30 min. The mixture was then diluted with water and extracted with benzene. The benzene extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of alumina with benzene/petrol (4:1) as eluant. The initial fractions contained the unreacted starting material. Further elution with benzene gave the 4H-thiopyran-4-thione.

6a-Thiathiophthene	4H-Thiopyran-4-thione	Yield (%)	Yield of recovered starting material (%)
2-Methyl-[d]	2-Methyl-	42	27
2-t-Butyl-	2-t-Butyl-	59	34
2-Phenyl-	2-Phenyl-	65	3
4-Methyl-2-phenyl-	5-Methyl-2-phenyl-	29	65
2,4-Diphenyl-	2,5-Diphenyl-	44	40
3,4-Diphenyl-[e]	3,5-Diphenyl-	99	-

([d] Heated 15 min. at 50°. [e] Stood 5 min. at room temperature; the reaction was complete in < 5 sec.)

(iii) Reaction of 3-dimethylaminovinyl-1,2-dithiolium salts with sodium sulphide. 2 M-Aqueous sodium sulphide (10 ml.) was added to a solution of the Vilsmeier salt (2 m.moles) in dimethylformamide (40 ml.) and the mixture heated at 60° for 5 min. The mixture was then worked up as described in (i) above.

Vilsmeier salt	4H-Thiopyran-4-thione	Yield (%)
53d	2-t-Butyl-	64
53h	2-Phenyl-	85
53j	5-Methyl-2-phenyl-	80
53k	2,5-Diphenyl-	80
53l [f]	3,5-Diphenyl-	92

([f] Stood 1 min. at room temperature. The mixture was then diluted with water, the crystalline product filtered off, dried, and recrystallised from cyclohexane.)

(iv) Rearrangement of 6a-thiathiophthenes by sodium hydroxide.

a) 2-Phenyl-6a-thiathiophthene. Degassed 2 M-aqueous sodium hydroxide (5 ml.) was added to a solution of 2-phenyl-6a-thiathiophthene (236 mg., 1 m.mole) in degassed dimethylformamide (20 ml.), under nitrogen, and the mixture was heated at 70° for 5 min. The mixture was then diluted with water and extracted with benzene, retaining the aqueous layer (see below). The benzene extracts were washed thoroughly with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of alumina with benzene as eluant. Initial elution with benzene gave 2-phenyl-4H-thiopyran-4-thione (62 mg., 30%). Further elution with benzene/ether (3:1) gave 3,5-epidithio-5-phenyl-

2,4-pentadienal (54h) (25 mg., 11%). The red aqueous layer was acidified with dilute hydrochloric acid and extracted with ether. The dried ether extracts were evaporated and the residual red oil was dissolved in the minimum volume of dimethylformamide, and acetonitrile was added. The solid which precipitated was filtered off and recrystallised from chloroform, giving red needles (35 mg.), m.p. 204-205° (Found: C, 40.6; H, 2.1; S, 45·6%). This red compound (A) was insoluble in alkali. When the above reaction was repeated with non-degassed solutions, in a flask open to the atmosphere, the yields were as follows: 4H-thiopyran-4-thione (35%), aldehyde (12%) and compound A (57 mg., residue recrystallised directly from chloroform).

b) 2,4-Diphenyl-6a-thiathiophthene. Degassed 2 M-aqueous sodium hydroxide (5 ml.) was added to a solution of 2,4-diphenyl-6a-thiathiophthene (312 mg., 1 m.mole) in degassed dimethylformamide (20 ml.), under nitrogen, and the mixture heated to 70° for 15 min. Work-up as in (a) above gave 2,5-diphenyl-4H-thiopyran-4-thione (79 mg., 28%), 3,5-epidithio-2,5-diphenyl-2,4-pentadienal (54k) (26 mg., 8%) and a red compound (79 mg.) from the aqueous layer. This red compound was highly insoluble and could not be recrystallised.

(v) Reaction of 2-phenyl-6a-thiathiophthene with methylamine. Aqueous methylamine (40%, 2 ml.) was added to a solution of 2-phenyl-6a-thiathiophthene (236 mg., 1 m.mole) in dimethylformamide (20 ml.) and the mixture stood at room temperature for 5 min. The red solution very quickly became yellow. The mixture was poured into water and extracted with ether. The aqueous layer was retained (see below). The

dried extracts were evaporated and the residue was chromatographed on a column of alumina with benzene as eluant. Evaporation of the yellow fraction gave N-methyl-3,5-epidithio-5-phenyl-2,4-pentadienaldimine (56h) (221 mg., 94%). The aqueous layer was made up to 250 ml. and the sulphide estimated with iodine (back titration with thiosulphate). The aqueous layer contained 31.4 mg. (98%) of sulphide ions.

(vi) Rearrangement of acylmethylenedithioles by sodium sulphide and sodium hydrogen sulphide.

a) 3,5-Epidithio-5-phenyl-2,4-pentadienal. 2 M-Aqueous sodium hydrogen sulphide (5 ml.) was added to a solution of the aldehyde (220 mg., 1 m.mole) in dimethylformamide (20 ml.) and the mixture heated at 70° for 5 min. The mixture was then cooled, poured into water, the solution acidified with dilute hydrochloric acid and extracted with benzene. The dried benzene extracts were evaporated and the residue was chromatographed on a column of alumina with benzene for elution. Evaporation of the red-brown eluate gave 2-phenyl-4H-thiopyran-4-thione (103 mg., 50%). When the above reaction was repeated using 2 M-aqueous sodium sulphide and heating at 50°, the yield of 2-phenyl-4H-thiopyran-4-thione was 165 mg. (80%).

b) 3,5-Epidithio-2,5-diphenyl-2,4-pentadienal. 2 M-Aqueous sodium hydrogen sulphide (5 ml.) was added to a solution of the aldehyde (296 mg., 1 m.mole) in dimethylformamide (20 ml.) and the mixture heated at 90° for 10 min. After cooling the mixture was poured into water, the solution acidified with dilute hydrochloric acid and extracted with benzene. The dried benzene extracts were evaporated

and the residue chromatographed on a column of alumina with benzene as eluant. An initial red-brown fraction was followed by a green fraction which was evaporated, giving 2,5-diphenyl-4H-thiopyran-4-thione (174 mg., 62%). The first fraction was evaporated and the residue rechromatographed on a column of alumina with benzene/petrol (1:9) for elution. Evaporation of the red eluate gave 2,4-diphenyl-6a-thiathiophthene (17 mg., 5%). When the above reaction was repeated using 2 M-aqueous sodium sulphide the only isolable product was 2,5-diphenyl-4H-thiopyran-4-thione (170 mg., 61%).

(vii) Reaction of 3,5-epidithio-5-phenyl-2,4-pentadienal with methylamine. Aqueous methylamine (40%, 2 ml.) was added to a solution of the aldehyde (220 mg., 1 m.mole) in dimethylformamide (20 ml.) and the mixture was allowed to stand at room temperature for 3 hr. The mixture was poured into water and extracted with benzene. The dried benzene extracts were evaporated and the residue was chromatographed on a column of alumina with benzene for elution. Evaporation of the yellow fraction gave N-methyl-3,5-epidithio-5-phenyl-2,4-pentadienaldimine (56h) (218 mg., 93%).

(viii) Reaction of 2-phenyl-4H-thiopyran-4-thione with sodium hydroxide. 2 M-Aqueous sodium hydroxide (10 ml.) was added to a solution of the thione (204 mg., 1 m.mole) in dimethylformamide (20 ml.) and the mixture swirled for 2 min. The resulting red solution was diluted with water. When this aqueous solution was shaken with benzene no coloured material extracted into the benzene layer. The aqueous solution was acidified with dilute hydrochloric acid and extracted with

benzene. The benzene extracts were worked up as described in (i) above, giving 2-phenyl-4H-thiopyran-4-thione (151 mg., 74% recovery). In a similar experiment the red solution* was diluted with water (20 ml.) and 1M-aqueous potassium ferricyanide (5 ml.) was added and the mixture swirled for 1 min. The solution was then poured into water and extracted with ether. The dried extracts were evaporated and the residue was chromatographed on a column of alumina with benzene/ether (3:1) as eluant. Evaporation of the yellow fraction gave 3,5-epidithio-5-phenyl-2,4-pentadienal (54h) (171 mg., 77%). In a further experiment oxygen was bubbled through the red solution* for 8 hr., after which the solution was diluted with water and extracted with benzene. The dried benzene extracts were evaporated and the residue was chromatographed on a column of alumina with benzene as eluant. An initial brown fraction gave 2-phenyl-4H-thiopyran-4-thione (10 mg., 5% recovery). Further elution with benzene/ether (3:1) gave a yellow fraction which, after evaporation, afforded 3,5-epidithio-5-phenyl-2,4-pentadienal (69 mg., 33%).

(ix) Reaction of 2-phenyl-4H-pyran-4-thione with sodium hydrogen sulphide. 2 M-Aqueous sodium hydrogen sulphide (2 ml.) was added to a solution of the thione (188 mg., 1 m.mole) in dimethylformamide (20 ml.) and the solution allowed to stand at room temperature, under nitrogen, for 15 min. The resulting deep red solution* was poured into water and the resulting solution acidified with dilute hydrochloric acid and extracted with ether. Normal work-up of the ether extracts gave only 20 mg. of mixed products. In a similar experiment 70% perchloric acid

(5 ml.) was added to the red solution* and the mixture was then diluted with water and extracted with benzene. The dried benzene extracts were evaporated and the residue was chromatographed on a column of alumina with benzene/petrol (4:1) for elution. Evaporation of the red-brown eluate gave an impure crystalline residue (185 mg.). Recrystallisation from cyclohexane gave 2-phenyl-4H-thiopyran-4-thione (110 mg., 54%), m.p. 79-80°. A second crop melted at 55-60° and was discarded.

In a further experiment the deep red solution* was diluted with water (20 ml) and 1M-aqueous potassium ferricyanide (10 ml.) was added. The resulting yellow solution was poured into water and extracted with ether. Evaporation of the dried ether extracts gave an oily residue which was chromatographed on a column of alumina with benzene/ether (4:1). Evaporation of the yellow eluate gave 3,5-epidithio-1-phenyl-2,4-pentadien-1-one (85) (148 mg., 67%). A sample recrystallised from cyclohexane as yellow needles, m.p. 128-129° (lit.[79] 130°). When oxygen was bubbled through the red solution for 4 hr. the yield of the ketone was 52 mg.(23%).

APPENDIX A : N.M.R. SPECTRAL DATA

Signals are singlets unless otherwise stated; b = broad, d = doublet, t = triplet, q = quartet, m = multiplet, AB = AB quartet. J values are in cycles per second (c/s).

Table A 1 : Thiol- and selenolimidate salts in trifluoroacetic acid solution.

Compound	Absorption
6 X=S, R=Ph	3.90, 4.23 (AB, J=17.6, CH_2); 5.72 (CH); complex 7.2-7.8.
6 X=Se, R=Ph	3.90, 4.19 (AB, J=17.3, CH_2); 5.93 (CH); complex 7.2-8.2.
11	3.86 (CH_2); 6.02 (CH); 8.97d (J=6.4)(H_α); complex 7.3-8.4.

Table A 2 : Azoles in deuterochloroform solution.

Compound	Absorption
9 X=O, R=Bu^t	1.47 (Bu^t); 3.46 (CH_2); complex 7.0-7.6.
9 X=O, R=Ph	3.59 (CH_2); 8.16q (ortho-protons); complex 7.1-7.7.
9 X=S, R=Ph	3.86 (CH_2); 7.96q (ortho-protons); complex 7.1-7.7.
9 X=Se, R=Ph	3.83 (CH_2); 7.89q (ortho-protons); complex 7.0-7.6.

Table A 3 : Azolium salts in trifluoroacetic acid solution.

Compound	Absorption
10 X=O, R=Bu^t	1.77 (Bu^t); 3.96 (CH_2); 4.30 (Me); complex 7.4-7.9.
10 X=O, R=Ph	4.06 (CH_2); 4.31 (CH_3); complex 7.4-8.3.
10 X=S, R=Ph	4.23 (CH_2); 4.32 (CH_3); complex 7.4-7.9.
	‡ 4.29 (CH_2); 4.17 (CH_3); complex 7.4-8.3.
10 X=Se, R=Ph	4.12 (CH_2); 4.20 (CH_3); complex 7.3-7.9.
12	4.27 (CH_2); complex 7.4-9.3.

‡ deuterodimethylsulphoxide solution

Table A 4 : Amides (7)

Compound	Absorption
7 R=Ph (in deutero-dimethylsulphoxide solution)	3.17 (H_B), 3.54 (H_A), 4.57 (H_X) (ABX, J_{AB}= 16.6, J_{AX}=7.9, J_{BX}=5.6); 9.08d (H_M, J_{MX}= 7.4). On shaking with D_2O the doublet at 9.08 disappears and the multiplet at 4.57 is simplified to a quartet.
7 R=Bu^t (in deutero-chloroform solution)	1.22 (Bu^t); 2.95 (H_B), 3.58 (H_A), 4.32 (H_X) ABX, J_{AB}=16, J_{AX}=7.9, J_{BX}=5.5); 6.80d (H_M, J_{MX}=6.3). On shaking with D_2O the doublet at 6.80 disappears and the multiplet at 4.32 is simplified to a quartet.

Table A 5 : Acyl derivatives (15), (16) and (44) in deuterochloroform solution.

Compound	Absorption
15 R=CHO	compound insoluble
15 R=COMe	2.75 (Me); 4.59 (NMe); 7.59 (Ph); complex 6.9-8.1.
	‡ 2.57 (Me); 4.54 (NMe).
15 R=COOMe	3.91 (Me); 4.53 (NMe); 7.59 (Ph); complex 6.9-8.4.
16 R=CHO	‡complex 7.0-9.0; 9.83 (CHO); 11.85b (H_α).
16 R=COMe	2.80 (Me); complex 7.0-8.2; 12.13b (H_α).
16 R=COOMe	3.93 (Me); complex 7.0-8.4; 11.64b (H_α).
44	2.70 (COMe); 3.28 (Me); complex 7.1-8.2.

‡ deuterodimethylsulphoxide solution

Table A 6 : Acyl derivatives (15), (16) and (44) in trifluoroacetic acid solution.

Compound	Absorption
15 R=CHO	4.25 (Me); complex 7.3-8.3.
15 R=COMe	2.66 (Me); 4.24 (NMe); 5.59 (CH); 7.82 (Ph); complex 7.5-8.1.
15 R=COOMe	4.07 (Me); 4.32 (NMe); 5.44 (CH); 7.82 (Ph); complex 7.5-8.1.
16 R=CHO	complex 7.1-8.7; 10.59d (J=6, H_α).
16 R=COMe	2.54 (Me); 5.62 (CH); complex 7.6-8.9; 9.14d (J=6, H_α)
16 R=COOMe	3.97 (Me); 5.48 (CH); complex 7.5-8.8; 9.14d (J=6, H_α)
44	2.52 (COMe); 3.15 (Me); 6.01 (CH); complex 7.6-8.7.

Table A 7 : Vilsmeier salts in trifluoroacetic acid solution.

Compound	H_A	H_B	J_{AB}	NMe_2	
27c	++ 8.26d	5.96d	9.7	4.04, 4.30	4.26 (NMe); complex 7.6-8.1.
	‡ 8.45			3.49	4.32 (NMe)
27b	++	5.43d	10.0	3.31, 3.77	1.56 (Bu^t); complex 7.4-8.1.
27a		5.75d	10.0	3.51, 3.72	complex 7.2-8.2.
18		6.14d	9.3	4.04, 4.40	9.04d (J=5.7, H_α); complex 7.7-8.9.
24		6.22d	9.0	4.08, 4.42	9.12d (J=6.0, H_α); complex 7.7-8.9.
25		6.03d	9.0	4.04, 4.28	9.90d (J=6.0, H_α); complex 7.7-8.9.
48		6.46d	9.7	3.99, 4.31	3.16 (Me); complex 7.7-8.7.

‡ deuterodimethylsulphoxide solution

++ When these spectra were run in deuterotrifluoroacetic acid solution the doublet due to H_B disappeared and the doublet due to H_A collapsed to a singlet.

Table A 8 : Thioaldehydes.

Compound.	Absorption.
36 (part spectrum in dimethyl-acetamide)	10.2 (CHS)
34a (deuterodimethyl-sulphoxide)	1.67 (Bu^t); 4.44 (Me); 10.20 (CHS).

Table A 9 : Thiacyclazines

Compound	Absorption
42b	+ complex 6.4-8.5
	++ 4.8b, 5.8b (integrate to ca. ½H); complex 6.8-8.8.
42c	+ ca. 2.45b (Me + COMe); complex 7.0-8.3.
	+++ 2.22 (Me); 2.46 (COMe).
	++ 2.62 (Me); 2.70 (Me); 5.66 (CH); complex 7.4-8.6.

\+ deuterochloroform solution

++ trifluoroacetic acid solution

+++ benzene solution

Table A 10 : 1,2-Dithiolium salts in trifluoroacetic acid solution.

Compound	H-5	H-4	$CH_{2(3)}$	R_1	R_2	R_3
52a	10.26d (J=4.9)	8.56d	3.29			
b		8.27	3.16	3.16		
c	9.98		3.07		2.70	
d		8.39	3.18	1.72		
f	9.72		3.59t		(2.8-3.8)	
g	9.90		3.5		(2.0-2.4 and 3.1-3.7)	
h		8.62	3,21	7.5-8.2		
i	10.03		3.10		7.4-7.8	
j		8.62	3.56q	7.5-8.2		1.70t
k		8.68	4.77	7.6-8.2		7.51
l	10.13		4.59		7.4-8.2	7.64

(In tables 11 to 15 the numbering of hydrogen atoms and substituents is related to the diagram shown below).

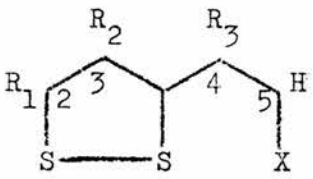


Table A 11 : Dimethylaminomethylene dithiolium salts in trifluoroacetic acid/perchloric acid solution.

Cpd.	H-2	H-3	H-4*	H-5	NMe_2	R_1	R_2	R_3
53b		8.62	5.03	ca.8.6	3.90, 4.01	3.28		
d		8.75	5.07	ca.8.7	3.89, 4.00	1.77		
h		8.97	5.08	ca.8.8	3.89, 3.99	7.6-8.3		
j		9.01	5.73m		3.97, 3.99	7.5-8.3		2.12d J=7.3
k		9.03	6.32d J=6.0		3.78, 4.10	7.5-8.3		7.72
l	10.32		6.18d J=8.6		3.51b		7.85	7.73
‡ h		7.71	6.64d (J=12.2)	8.48d	3.22, 3.43	7.5-8.1		

* When R_3=H, H-4 is a methylene group.

‡ deuterodimethylsulphoxide solution

Table A 12 : 6a-Thiathiophthenes in deuterochloroform solution.

Cpd.	H-2	H-3	H-4	H-5	R_1	R_2	R_3
55a	9.12d (J=6.3)	7.91d	7.91d	9.12d			
b		7.72	7.77d (J=6.3)	9.13d	2.67		
c	8.58		7.83d (J=6.6)	9.43d		2.53	
d		7.86	7.87d (J=6.4)	9.32d	1.43		
e		8.55	8.07d (J=6.2)	9.26d	1.41t 4.39q		
f	8.59			8.59			(3.34)
g	8.78			8.78		(1.99q, 3.00t)	
h		8.16	7.84d (J=6.4)	9.06d			
i	8.84		7.79d (J=6.4)	9.14d		7.41	
j		8.12		8.60	7.2-8.0		2.44
k		8.09		8.82	7.2-7.8		7.42
l	9.04			9.04			(6.90)
‡		8.72	8.72	(COOEt 1.43t, 4.43q)			

‡ 2,5-diethoxycarbonyl-6a-thiathiophthene

Table A 13 : Furothiophthenes in deuterochloroform solution.

Cpd.,	H-2	H-3	H-4	H-5	R_1	R_2	R_3
54a *	7.70d (J=5.5)	6.78d	6.41d (J=1.5)	8.97d			
b		6.98	6.70d (J=1.6)	9.36d	2.49		
h		7.49	6.82d (J=1.6)	9.41d	7.2-7.8		
i	7.88		6.72d (J=1.6)	9.39d		7.43	
j		7.49		9.23	7.3-7.9	2.25	
l	8.01			9.37			(6.91b)

* taken from reference 76

Table A 14 : Aldimines in deuterochloroform solution.

Cpd.	H-2	H-3	H-4	H-5	R_1	R_2	R_3	NMe
56a	8.89d (J=7.0)	7.47d	7.06d (J=3.2)	7.93d				3.61
b		7.24	6.91d (J=3.3)	7.89d	2.61			3.58
h		7.80	7.08d (J=3.5)	7.89d	7.2-8.0			3.60
j		7.62		7.62	7.2-8.0		2.28	3.52
k		7.88		7.95	7.2-8.0		7.44	3.63
l	8.76			7.88		(6.84)		3.67

Table A 15 : Aldimines in trifluoroacetic acid solution.

Cpd.	H-2	H-3	H-4	H-5	R_1	R_2	R_3	NMe
56a	8.56d (J=5.9)	7.60d	6.46d (J=12.3)	8.19d				3.23
b		7.38b	6.31d (J=12.6)	8.14d	2.69d J=0.8			3.20
h		7.79	6.41d (J=12.4)	8.19d	7.5-8.0			
j		7.94		8.32	7.4-7.9		2.13	3.42
k		8.00		8.47	7.3-7.9		7.63	3.32
l	8.28					(7.2-7.9)		

56a and 56h in trifluoroacetic acid/perchloric acid solution.

56a 5.25b (CH_2); 3.82, 3.88 (NMe).

56h 5.16b (CH_2); 3.82, 3.92 (NMe).

Table A 16 : 4H-Thiopyran-4-thiones in deuterochloroform solution.

Cpd.	H-2	H-3	H-5	H-6	R_1	R_2	R_3
75b *		7.80	7.81d (J=10.0)	7.54d	2.37		
d		8.05	7.89d (J=10.0)	7.61d	1.40		
h *		8.17	7.92d (J=9.8)	7.58d	7.4-7.9		
j		8.29		7.48	7.3-7.8		2.47
k		8.39		7.51	7.3-7.8		7.38
l	7.50			7.50		(7.35)	

(* J_{H3-H5} = 1.2 observed)

Table A 17 : 4H-Thiopyran-4-thiones in trifluoroacetic acid solution.

Cpd.	H-2	H-3	H-5	H-6	R_1	R_2	R_3
75b		8.49	8.50d (J=9.7)	9.22d	3.04		
d *		8.71	8.53d (J=9.4)	9.30d	1.68		
h *		8.82	8.53d (J=9.5)	9.29d	7.5-8.0		
j		8.88		9.07	7.6-8.0		2.79
k		8.99		9.11	7.4-8.1		7.4-8.1
l	9.22			9.22			(7.4-7.9)

(* J_{H3-H5} = 1.4 observed)

APPENDIX B : I.R. SPECTRAL DATA

Solvent shift data for acyl derivatives (21) and (15).

Solutions were 0.01M or saturated (*) when this concentration could not be achieved.

Compound		Tetrachloro-ethylene	Tetrahydro-furan	Chloroform.	Tetrabromo-ethane
21 X=S,	R=CHO	1591*	1592	1578	1577
	R=COMe	1571*	1569	1550	1550
	R=COOMe	1637*	1637	1625	1618
X=Se,	R=CHO			1583	
	R=COMe			1545	
	R=COOMe			1629	
15	R=CHO		1619*	1588	1583*
	R=COMe	1587*	1587	1562	1562
	R=COOMe	1652*	1651	1640	1634

APPENDIX C : U.V. AND VISIBLE SPECTRAL DATA

Table C 1 : Azoles and azolium salts in methanol.

Compound.	Absorption λ_{max}, mμ (log ε)
9 X=O, R=Bu^t	281, 222sh. (4.48, 4.07).
X=O, R=Ph	326, 246, 224 (4.46, 3.18, 4.07).
X=S, R=Ph	343, 260, 223sh. (4.41, 3.40, 3.96).
X=Se, R=Ph	352, 272, 230 (4.42, 3.72, 3.95).
10 X=O, R=Bu^t	296, 288, 282, 276sh. (4.13, 4.18, 4.22, 4.18).
X=O, R=Ph	325, 247 (4.15, 3.94).
X=S, R=Ph	337, 255sh., 235sh. (4.29, 3.70, 3.81).
X=Se, R=Ph	346, 260 (4.29, 3.81)
12	355, 343sh., 324sh., 274, 235, 217sh. (4.34, 4.30, 4.09, 3.76, 4.09, 4.26).

Table C 2 : Acyl derivatives in methanol.

15 R=CHO	450, 335, 265, 232sh., 210 (3.42, 4.42, 4.24, 4.20, 4.61).
R=COMe	470, 340, 300, 268, 232sh., 209 (3.26, 4.30, 4.00, 4.26, 4.23, 4.55).
R=COOMe	476, 374, 319, 294, 261, 230 (3.34, 4.23, 4.27, 4.19, 4.36, 4.33).
16 R=CHO	466, 382, 336, 285sh., 228 (3.48, 4.21, 4.32, 3.99, 4.58).
R=COMe	480, 387, 340, 310sh., 285sh., 229 (3.45, 4.17, 4.27, 4.15, 4.07, 4.52).

Compound.	Absorption.
16 R=COOMe	510, 392, 324sh., 311sh., 299, 235, 215 (3.40, 4.23 4.15, 4.21, 4.23, 4.51, 4.31).

Visible solvent shifts for acyl derivatives.

	Methanol	Cyclohexane
15 R=CHO	450	526*
COMe	470	548
COOMe	476	546
16 R=CHO	466	565*
COMe	480	584
COOMe	510	593

* Tetrachloroethylene

Table C 3 : Thiacyclazines

42b	(methanol) 754, 685, 626, 487, 370, 292, 242 (3.09, 3.13, 2.98, 3.79, 4.23, 4.08, 4.36). (1% v/v perchloric acid in methanol) 327, 270sh., 245, 214 (3.72, 4.07, 4.25, 4.43).
42c	(methanol) 630, 482, 348, 281, 241, 214 (3.25, 4.49, 4.40, 4.13, 4.41, 4.42). (1% v/v perchloric acid in methanol) 323, 278, 238, 213 (3.76, 4.06, 4.28, 4.42).
50 (ref. 148)	(tetrahydrofuran) 723, 655, 602 (2.44, 2.71, 2.65) (ethanol) 467, 366, 342, 285, 262 (4.03, 4.23, 4.14, 4.70, 4.68).

Table C 4 : Vilsmeier salts and aldimines in 2% v/v perchloric acid in methanol.

Compound	Absorption
53b	437, 420sh., 269, 246 (4.58, 4.50, 3.79, 3.91).
h	457, 313, 235sh. (4.48, 4.22, 3.90).
j	456, 363, 315, 230 (4.27, 3.98, 4.00, 3.93).
k	460, 318, 225 (4.47, 4.26, 4.25).
l	458, 295, 265, 223 (4.09, 3.59, 3.84, 4.25)
56b	432, 414sh., 270, 244 (4.58, 4.49, 3.77, 3.91).
h	451, 312, 235 (4.44, 4.18, 3.93).
j	447, 313, 230sh. (4.46, 4.17, 3.89).
k	452, 316, 224 (4.47, 4.26, 4.23).
l	453, 300, 264, 221 (4.43, 3.64, 3.90, 4.30).

Table C 5 : 6a-Thiathiophthenes in cyclohexane.

55a	472, 254, 230 (3.68, 4.69, 4.20).
b	470, 262, 235 (3.72, 4.68, 4.18).
c	476, 258, 232 (3.64, 4.63, 4.18).
e	501, 257, 232 (3.70, 4.49, 4.25).
f	524, 260, 238 (3.66, 4.66, 4.30).
g	492, 260, 233 (3.72, 4.72, 4.33).
h	487, 322, 270sh., 249 (3.94, 4.11, 4.56, 4.61).
i	480, 259, 230
j	493, 320, 265, 251 (3.95, 4.01, 4.50, 4.50).
k/	

Compound	Absorption.
55k	497, 322, 265sh., 252 (3.94, 4.09, 4.54, 4.58).
1	495, 272, 240 (3.69, 4.64, 4.40).
‡	519, 262, 235sh., 222 (4.04, 4.51, 4.57, 4.62).
63	527, 410, 330sh., 264 (4.54, 4.10, 3.86, 4.71).

‡ 2,5-diethoxycarbonyl-6a-thiathiophthene

Visible absorptions of 6a-thiathiophthenes in methanol.

6a-thiathiophthene	475
2-methyl-	471
2,5-dimethyl-	469
3-methyl-	480
3,4-propano-	492
3,4-ethano-	524
2-phenyl-	490
2,5-diphenyl-	510
3-phenyl-	483
3,4-diphenyl-	497
2,4-diphenyl-	497
2-phenyl-4-methyl-	494

Table C 6 : Aldehydes (cyclohexane) and aldimines (methanol).

Compound	Absorption
54b	423, 406, 231 (4.08, 4.09, 4.24).
h	432, 293, 232, 215sh., (4.05, 4.11, 4.25, 4.17).
i	436, 415, 286, 245, 221 (3.95, 3.99, 3.43, 4.04, 4.30).
j	449, 295, 236, 225sh., (4.03, 4.08, 4.24, 4.20).
k	452, 296, 275, 235 (4.14, 4.11, 4.10, 4.33).
l‡	445, 288sh., 227 (4.16, 3.67, 4.32).
56 a	415, 263sh., 235 (4.08, 3.89, 4.46).
b	414, 265sh., 234 (4.14, 3.82, 4.46).
h	435, 289, 234 (4.19, 4.02, 4.50).
j	442, 284, 236 (4.19, 4.02, 4.52).
k	447, 280, 236 (4.24, 4.18, 4.52).
l	435, 298, 256, 236 (4.05, 3.99, 4.33, 4.43).

‡ methanol

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