

THE CHEMISTRY OF 4H-1,3-DITHIINS*

Fillmore Freeman

Department of Chemistry

University of California, Irvine

Irvine, CA 92717, U.S.A.

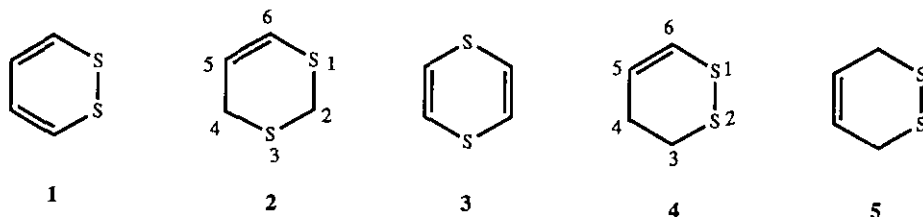
Abstract—1,2-Dithiins, 1,3-dithiins, 1,4-dithiins, and their derivatives continue to attract considerable attention owing to their bioactivity, to their unique structural features, to their potential superconducting properties, and to their chemical activity. This review describes the preparation, the chemistry, and the biological properties of 4H-1,3-dithiin and its derivatives.

CONTENTS

1. Introduction
2. 4H-1,3-Dithiins
 - 2.1 Structure
 - 2.2 Preparation
 - 2.3 Reactions
3. 4H-Benzo-1,3-dithiins
4. Naphtho[1,8-de]-1,3-dithiins
5. 1,3-Dithiino[5,4-b]indoles
6. [1,3]Dithiino[5,4-c]pyrazoles
7. 5H-[1,3]Dithiino[4,5-c]pyridazines
8. 4H-1,3-Dithiino[5,4-d]pyrimidines
9. 1,2-Dithiolo[4,3-d]-1,3-dithiins
10. Other Derivatives of 4H-1,3-Dithiin
11. Bioactivity

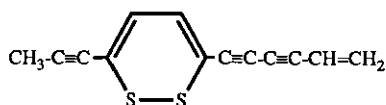
1. INTRODUCTION

1,2-Dithiin (*o*-dithiin, 1,2-dithia-3,5-cyclohexadiene, **1**),¹⁻³ 4H-1,3-dithiin (**2**),² 1,4-dithiin (*p*-dithiin, 1,4-dithia-2,5-cyclohexadiene, **3**),³⁻⁵ and their derivatives are found in natural products and are of considerable biological, experimental, and theoretical interest.⁶⁻²³ 1,2-Dithiin (**1**), 3,4-dihydro-1,2-dithiin (**4**),¹ and 3,6-dihydro-1,2-dithiin (**5**),¹ and their derivatives are of particular current interest owing to their antiviral properties and to their effectiveness against the acquired immunodeficiency virus (HIV, AIDS).^{24,25}

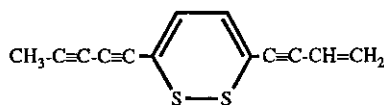


The major compounds in the young leaves of *Aspilia mossambicensis* and *Aspilia plurisetta* are 3-(5-hexene-1,3-diynyl)-6-(1-propynyl)-1,2-dithiin, thiarubrine A, **6**) and 3-(1,3-pentynyl)-6-(but-1-yn-3-ene)-1,2-dithiin, thiarubrine B, **7**).²⁶ Thiarubrine A (**6**), thiarubrine B (**7**), and the corresponding thiophene derivatives **8** and **9** are present in the roots of *Chaenactis douglasii* and *Eriophyllum lanatum*.²⁷⁻²⁹

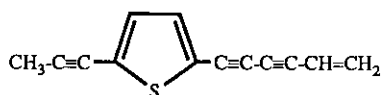
*This paper is dedicated to Professor Sir Derek H.R. Barton on the occasion of his 70th birthday.



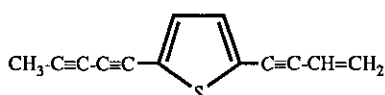
6



7

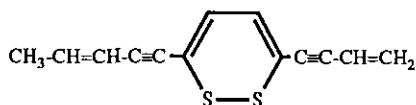


8

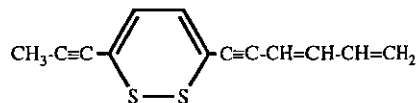


9

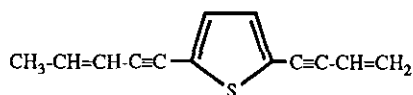
Several red-colored compounds [thiarubrine A (6), thiarubrine B (7), (*E*)-3-(3-buten-1-ynyl)-6-(3-penten-1-ynyl)-1,2-dithiin (10), (*E*)-3(3,5-hexadien-1-ynyl)-6-(1-propynyl)-1,2-dithiin (11)], and the corresponding thiophene derivatives (8, 9, 12, 13) have been isolated from several compositae.³⁰⁻⁴² The occurrence and structure of thiarubrine B (7) in *Eriophyllum caespitosum* have been discussed.^{37,43-45}



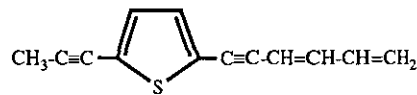
10



11



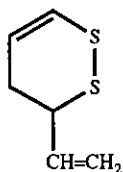
12



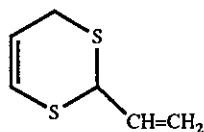
13

Thiarubrine A (6) and/or thiarubrine B (7) are also found in roots of *Ambrosia artemisiifolia*,³¹ in the aerial parts of *Pegolettia senegalensis*,³² in *Wedelia hookeriana*,³³ in *Schkuhria multiflora*,³⁴ in *Verbesina occidentalis*,³⁵ in roots and overground parts of other *Verbesina* species,³⁶ and in the roots of *Schkuhria senecioides*.⁴⁵ 3-(3-Buten-1-ynyl)-6-(3-penten-1-ynyl)-1,2-dithiin (10) is found in *Picradeniopsis woodhousei*,³⁸ in the *Lasthenia* species,³⁹ in *Oyedaea boliviana*,⁴⁰ and in *Verbesina*.⁴¹ 3-(3,5-Hexadien-1-ynyl)-6-(1-propynyl)-1,2-dithiin (11) has been found in the roots and aerial parts of *Melampodium divaricatum*.⁴²

3-Ethenyl-3,4-dihydro-1,2-dithiin (14) and 2-ethenyl-4H-1,3-dithiin (15) are found in the flavor components of cooked asparagus⁴⁶ and 1,2-dithiin (14) is a component of garlic.⁴⁷⁻⁵³ Volatile sulfur containing compounds which are enzymically produced from caucas (*A. victorialis*) have been identified.⁵³ The occurrence of 1-propenyl containing disulfides and 2-methyl-2-pentenal, one of the breakdown products of propanethial S-oxide in caucas, which is one of the garlic like *Allium* species, is chemotaxonomically interesting. 1,2-Dithiin (14) and 4H-1,3-dithiin (15), which have antithrombotic activity, were isolated from caucas and identified by ir, nmr (2D ¹H-¹H COSY), and mass spectrometry.⁵³

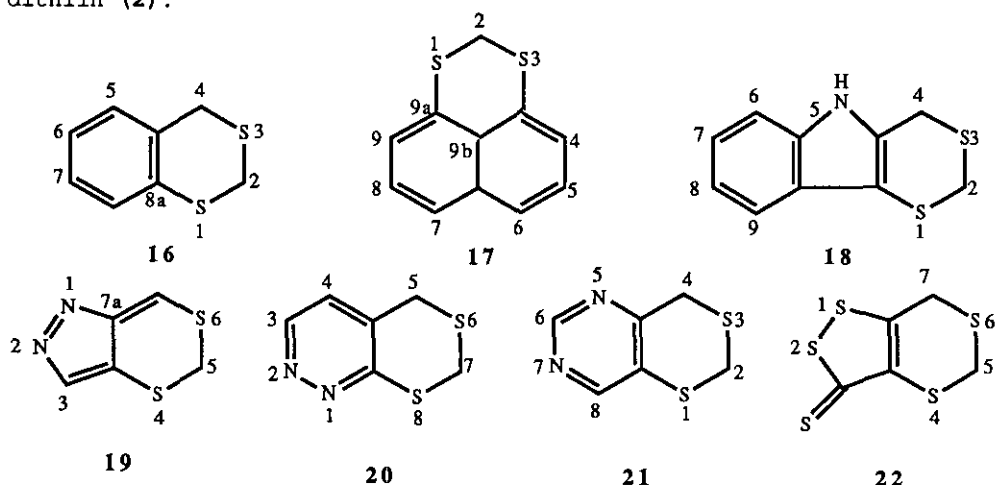


14



15

The chemistry of 1,2-dithiins (1),¹ 1,4-dithiins (3),⁴ 3,4-dihydro-1,2-dithiins (4),¹ and 3,6-dihydro-1,2-dithiins (5)¹ has been recently reviewed. This review, which covers the literature to 1988, will describe the chemistry of 4H-1,3-dithiins (2),² 4H-1,3-benzodithiins (16),⁵⁴ naphtho[1,8-de]-1,3-dithiins (17),⁵⁵ 1,3-dithiino[5,4-b]indoles (18),^{56,57} [1,3]dithiino[5,4-c]pyrazoles (19),^{57,59} 5H[1,3]dithiino[4,5-c]pyridazines (20),⁵⁸ 4H-1,3-dithiino[5,4-d]pyrimidines (21),^{57,59} 1,2-dithiolo[4,3-d]-1,3-dithiin (22),⁶⁰ and other derivatives of 4H-1,3-dithiin (2).



2. 4H-1,3-DITHIINS

2.1 Structure

Preliminary *ab initio* molecular orbital calculations show that the nonplanar conformational isomers of 4H-1,3-dithiin (2), 3,4-dihydro-1,2-dithiin (4), and 3,6-dihydro-1,2-dithiin (5) are more stable than the corresponding planar isomers (Tables 1, 2, 3)^{1,6,7} A comparison of Tables 1 and 2 shows that 3,4-dihydro-1,2-dithiin (4) is more stable than 4H-1,3-dithiin (2).

Table 1. *Ab Initio* Molecular Orbital Calculations for 4H-1,3-Dithiin (2)

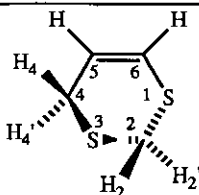
	conformation	
	planar C_s	nonplanar C_1
		
total energy (au) at RHF/3-21G(*)	-945.39667	-945.414241
energy difference (kJ mol ⁻¹)		41.34
total energy (au) at MP2/6-31G**/RHF/3-21G(*)		
energy difference (kJ mol ⁻¹)		
rS1C2 Å	1.820	1.812
rC2S3 Å	1.829	1.810
rS3C4 Å	1.828	1.816
rC4C5 Å	1.501	1.512
rC5C6 Å	1.313	1.318
rC6S1 Å	1.746	1.756
rC2H2 Å	1.079	1.080
rC2H2' Å	1.079	1.081
rC4H4 Å	1.083	1.084
rC4H4' Å	1.083	1.083
rC5H5 Å	1.075	1.075
rC6H6 Å	1.074	1.074
<S1C2S3	122.110	114.090
<C2S3C4	109.910	97.230
<S3C4C5	120.190	114.740
<C4C5C6	129.520	127.730
<C5C6S1	131.280	129.180
<C6S1C2	106.990	101.190
<H2C2H2'	108.580	108.430
<H4C4H4'	107.400	107.220
<H5C5C6	117.480	117.680
<H6C6C5	118.980	119.340
<S1C2S3C4	0	65.890
<C2S3C4C5	0	52.450
<S3C4C5C6	0	24.240
<C4C5C6S1	0	1.040
<C5C6S1C2	0	9.660
<C6S1C2S3	0	46.580

Table 2. *Ab Initio* Molecular Orbital Calculations for 3,4-Dihydro-1,2-dithiin (4)

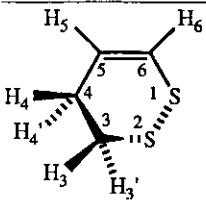
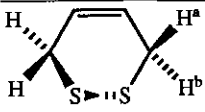
	conformation	
	planar C _s	nonplanar C ₁
total energy (au) at RHF/3-21G(*)	-945.39329	-945.4175
energy difference (kJ mol ⁻¹) at MP2/6-31G*//RHF/3-21G(*)	63.60	
rS1S2 Å	2.082	2.055
rS2C3 Å	1.840	1.822
rC3C4 Å	1.556	1.538
rC4C5 Å	1.505	1.515
rC5C6 Å	1.313	1.318
rC6S1 Å	1.744	1.766
rC3H3 Å	1.079	1.082
rC3H3' Å	1.079	1.081
rC4H4 Å	1.085	1.085
rC4H4' Å	1.085	1.087
rC5H5 Å	1.075	1.075
rC6H6 Å	1.075	1.073
<S1C2S3	109.470	97.440
<S2C3C4	122.450	111.130
<C3C4C5	121.050	115.250
<C4C5C6	130.320	128.210
<C5C6S1	130.770	127.450
<C6S1S2	105.940	100.740
<H3C3H3'	107.910	108.710
<H4C4H4'	106.030	107.040
<H5C5C6	116.750	117.300
<H6C6C5	119.410	120.120
<S1S2C3C4	0	69.350
<S2C3C4C5	0	52.330
<C3C4C5C6	0	12.100
<C4C5C6S1	0	0.220
<C5C6S1S2	0	23.200
<C6S1S2C3	0	50.050

Table 3. *Ab Initio* Molecular Orbital Calculations for 3,4-Dihydro-1,2-dithiin (4)

 7	conformation	
	planar C _{2v}	nonplanar C ₂
total energy (au) 3-21G*	-945.39189	-945.41604
energy difference between C _{2v} and C ₂ (kJ mol ⁻¹)	63.40	
(kJ mol ⁻¹)		-950.75680
total energy (au) MP2 6-31G*		
energy difference between C _{2v} and C ₂ (kJ mol ⁻¹)		
r _{S-S} Å	2.097	2.049
r _{C-S} Å	1.826	1.818
r _{C-C} Å	1.503	1.515
r _{C=C} Å	1.312	1.317
r _{C-H^a} Å	1.083	1.083
r _{C-H^b} Å	—	1.084
r _{C-H} Å	1.076	1.075
<H-C-H	107.610	107.920
<H-C=C	117.450	118.270
<C-S-S	108.830	97.890
<C-C=C	130.780	127.790
<C-C-S	120.390	114.140
dihedral angle CSSC	0	63.390
dihedral angle CCSS	0	52.570
dihedral angle CCCS	0	21.120
CCCC	0	0.710
twist angle ^a	0	36.860

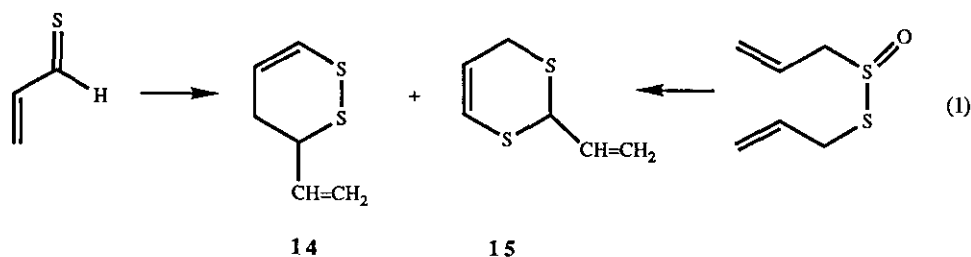
a) The twist angle between the S-S bond and the plane involving the four carbon atoms.

2.2 Preparation

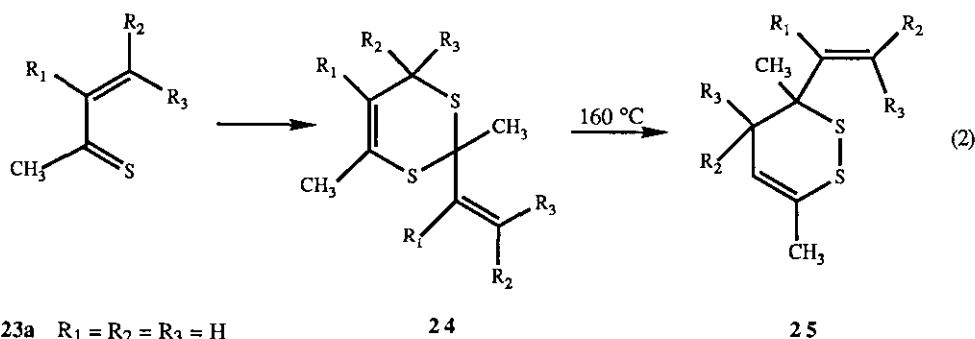
4H-1,3-Dithiin (2) has been reported as a product from the photoreduction of benzophenone by 1,3-dithiane.^{61a}

Thiocarbonyl compounds, with the carbon-sulfur double bond serving as the 2π dienophile component, have been employed in Diels-Alder reactions ($[4 + 2]$ cycloadditions) to prepare thiopyranyl systems.^{61b} However, dithioesters, thioaldehydes, and thioketones may participate as the diene partners of Diels-Alder reactions in which the thiocarbonyl group comprises a component of the 4π diene system.⁶¹⁻⁶⁸

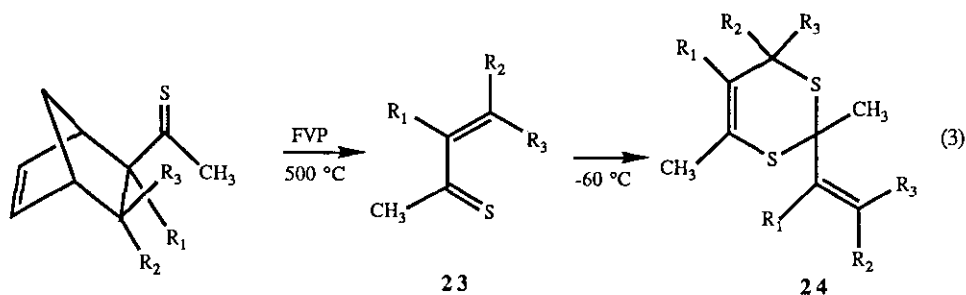
Diallyl disulfide decomposed quantitatively at 660 °K in the gas phase to give an equimolar mixture of propene and 2-propenethial.^{61c} On cool-trapping, 2-propenethial dimerized and the Diels-Adler adduct, predominantly the kinetic product 2-ethenyl-4H-1,3-dithiin (15), was isolated together with 3-ethenyl-3,4-dihydro-1,2-dithiin (14).^{61c,61d,62} Treating propenal with hydrogen sulfide and ethyl orthoformate in the presence of zinc chloride gave 1,2-dithiin 14 and 1,3-dithiin 15.⁶³ S-3-Propenyl 2-propenethiosulfinate (allicin), which undergoes β -elimination to afford 2-propenesulfinic acid and 2-propenethial, is a precursor of 1,2-dithiin (14) and 1,3-dithiin (15) (eq. 1).⁴⁷ The formation of 1,2-dithiin (14) in the aromatic components of cooked asparagus is assumed to involve reaction of hydrogen sulfide with 2-propenethial⁶³ which results from the thermal degradation of methionine.



Aliphatic α,β -unsaturated thioketones are unstable at 20 to 25 °C and exist in the dimeric 4H-1,3-dithiin structure (**24**) or the 1,2-dithiin structure (**25**) (eq. 2).⁶⁴⁻⁶⁸ Flash vacuum pyrolysis (FVP) preparation of α,β -unsaturated thioketones also led to regiospecific Diels-Alder dimerization with 4π and 2π thiocarbonyl participation (eq. 3). Molecular orbital calculations of the cyclodimerization have been reported.^{64b}

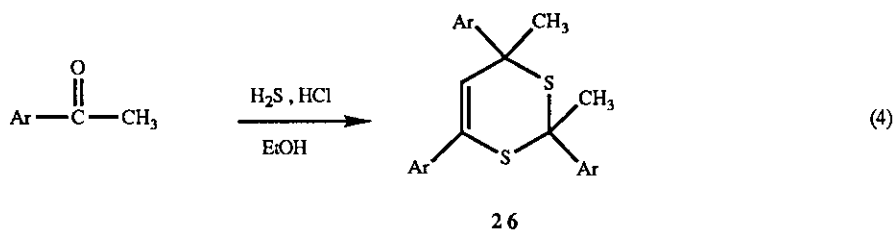


- 23a** $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{H}$
23b $\text{R}_1 = \text{R}_3 = \text{H}, \text{R}_2 = \text{CH}_3$
23c $\text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_3 = \text{H}$
23d $\text{R}_1 = \text{H}, \text{R}_2 = \text{R}_3 = \text{CH}_3$

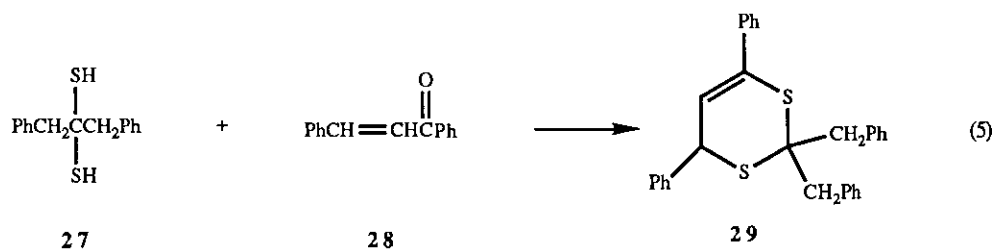


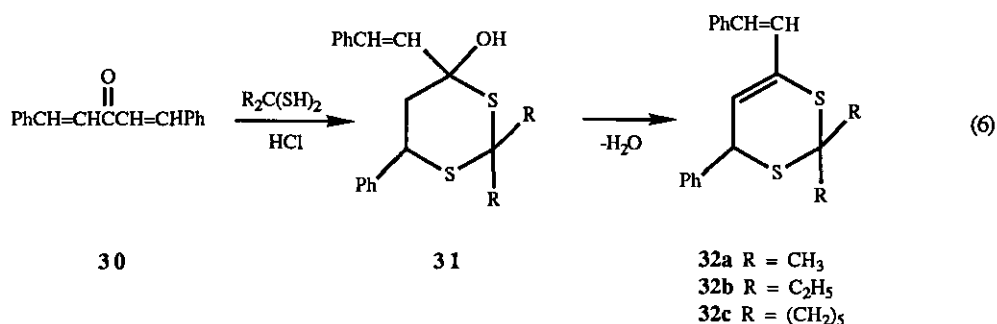
There is a need for careful investigations in order to accurately interpret the preferred kinetic mode and regioselectivity of the Diels-Alder dimerization reactions of α,β -unsaturated thioaldehydes and thio-ketones owing to the reversible nature of the cycloadditions and to the potential participation of the products in subsequent rearrangements.

Substituted aryl ethanones react with hydrochloric acid and hydrogen sulfide to give 2,4-dimethyl-2,4,6-triaryl-4H-1,3-dithiins (26) (eq. 4).⁶⁹⁻⁷² 1-(4-Methoxyphenyl)-1-propanone reacts similarly.⁷³

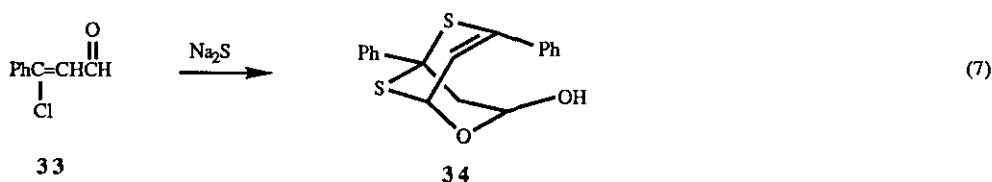


2,2-Dibenzyl-4,6-diphenyl-4H-1,3-dithiin (29) was isolated from the reaction of 1,3-diphenylpropane-2,2-dithiol (27) with benzalacetophenone (chalcone, 28) in ethanolic hydrogen chloride (eq. 5, 6).⁷⁴⁻⁷⁶ Other examples of 4H-1,3-dithiins from α,β -unsaturated carbonyl compounds are shown in equations 6 and 7.⁷¹

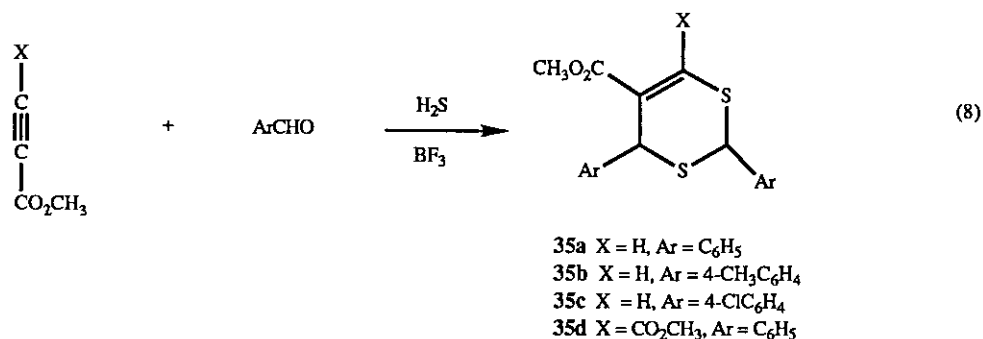




Attempts to prepare β -mercaptocinnamaldehyde from β -chlorocinnamaldehyde (33) and sodium sulfide led to a dimer (bicyclo[3.3.1]-5,7-diphenyl-3-hydroxy-2-oxa-6,9-dithia-7-nonene, 34).⁷⁷

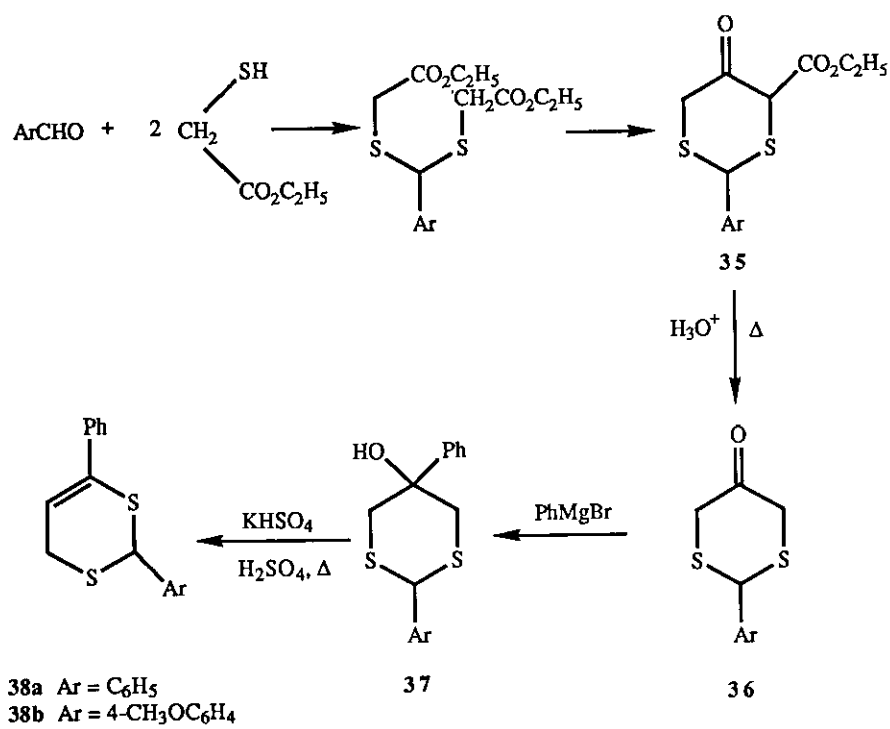


A series of 4H-1,3-dithiins (35) has been prepared by reaction of an alkynyl ester and an aromatic aldehyde with hydrogen sulfide in the presence of boron trifluoride.⁷⁸

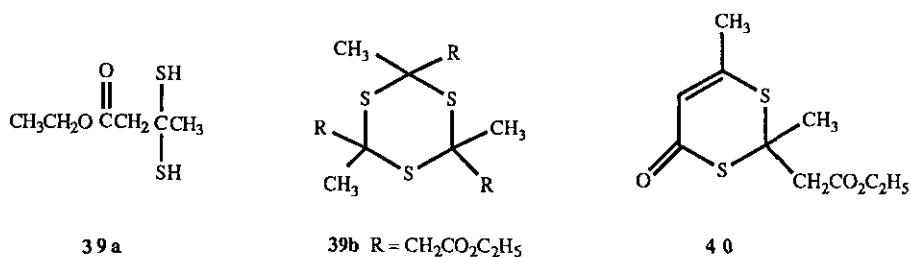


Scheme I shows the first general synthesis of 4H-1,3-dithiins (38).^{60,79}

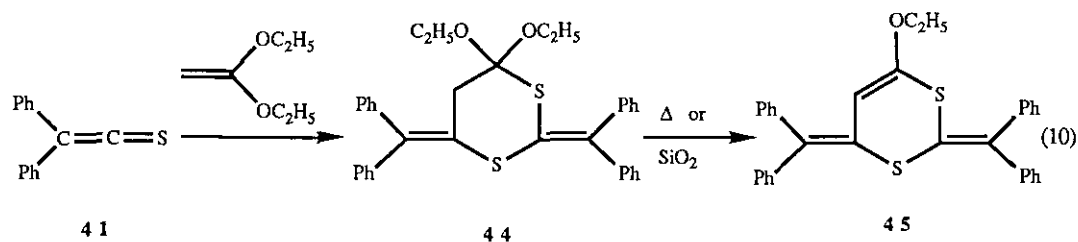
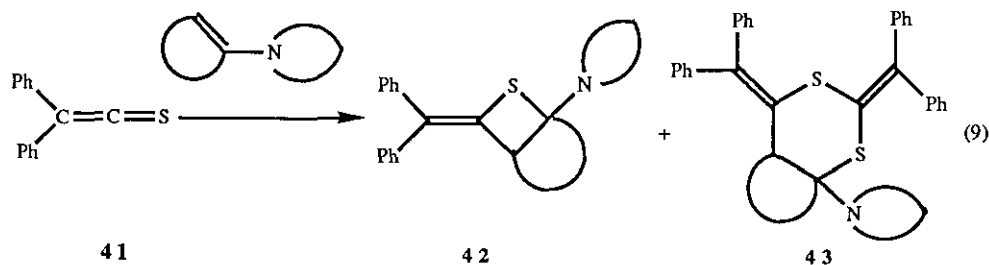
Scheme I



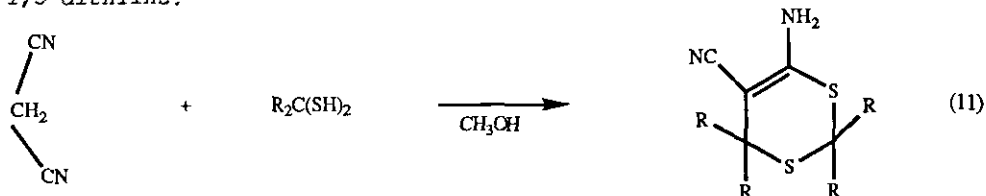
Ethyl 3-oxobutanoate reacts with hydrogen chloride and hydrogen sulfide to give products **39a**, **39b**, and 2,6-dimethyl-2-ethoxycarbonylmethyl-4-oxo-1,3-dithiin (**40**).⁸⁰ A mechanism for the formation of **40** via the dimerization of **39** and subsequent elimination of ethanol was proposed.⁸⁰



Diphenylthioketene (**41**)⁸¹ gives [2 + 2] cycloaddition products with electron rich unsaturated systems such as enamines and ketene acetals (eq. 9, 10).^{82,83} A mechanism via a zwitterionic intermediate is suggested by the formation of 2:1 cycloadducts.



Dicyanomethane (malononitrile)⁸⁴⁻⁸⁸ reacts with *gem*-dithiols in the presence of potassium hydroxide to give 4H-1,3-dithiins (**46**).⁸⁹ Benzylidenemalononitrile and cyclohexylidenemalononitrile gave analogous 4H-1,3-dithiins.

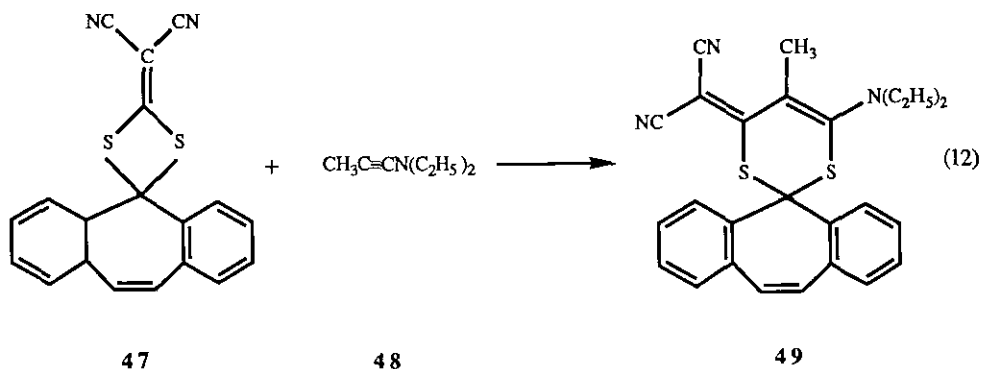


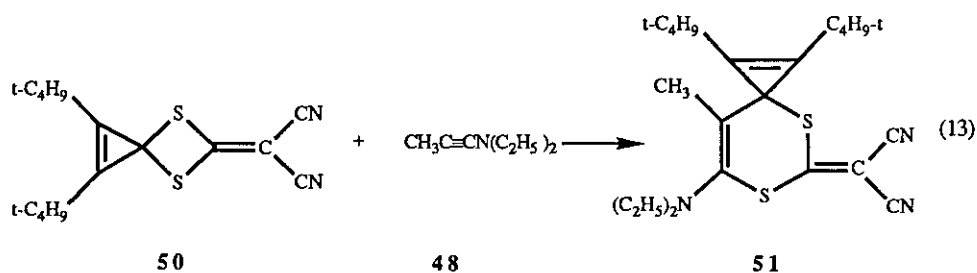
46a $R = CH_3$

46b $R = -(CH_2)_4-$

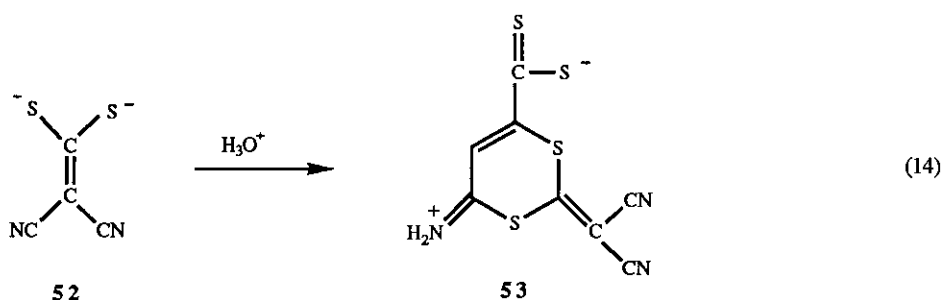
46c $R = -(CH_2)_5-$

The 2,4-bis(methylene)-1,3-dithietane (**47**) reacts with 1-(*N,N*-diethylamino)propyne (**48**) to yield **49**.⁹⁰ The reaction of spiro derivative **50** with **48** to give **51** may proceed via a cyclopropenium cation.¹⁰⁶

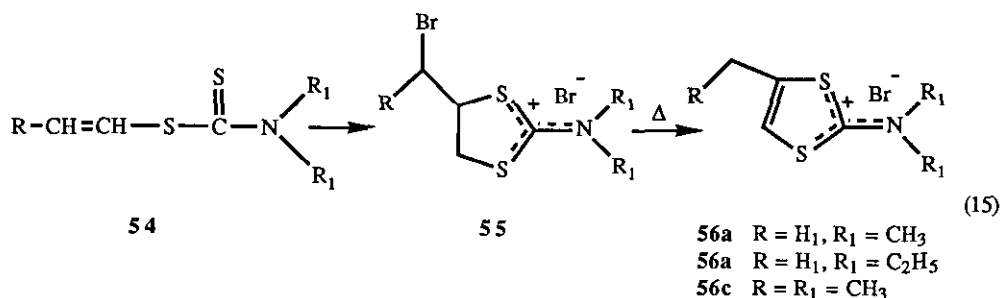




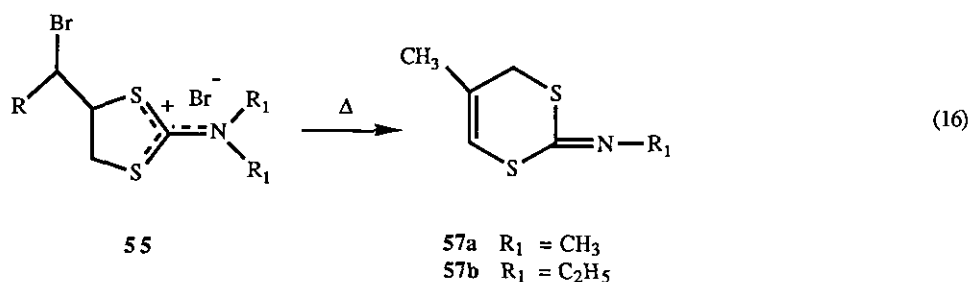
The substituted 4H-1,3-dithiin 53 is prepared from salt 52.⁹¹

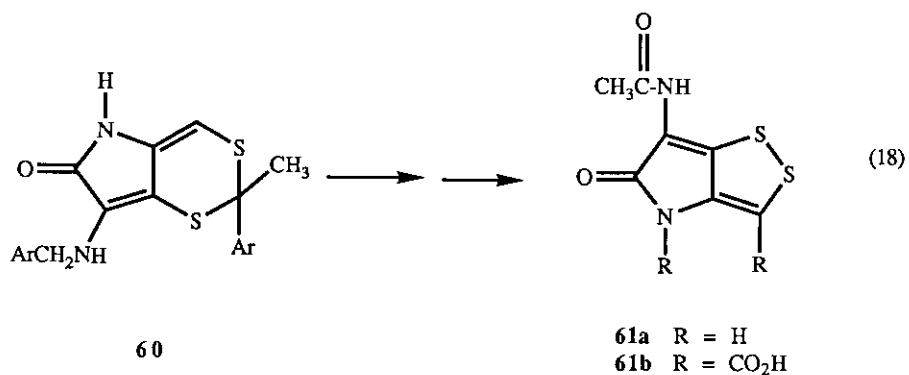
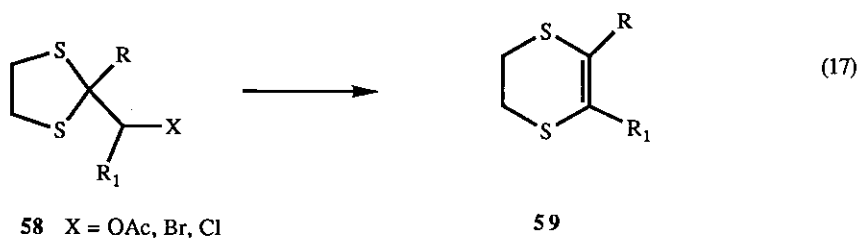


Bromination of β,γ -unsaturated dithiocarbamates (54) leads to the quantitative formation of the corresponding 2-dialkylamino-4-(α -bromoalkyl)-1,3-dithioanylium bromides (55) via regiospecific (S-5) participation by the dithiocarbamate function.⁹² Thermal transformation of 55 into 2-dialkylamino-4-alkyl-1,3-dithiolium salts (56) occurs in good yields.⁹³ The dithiolium salts (56) are an important class of synthetic intermediates⁹⁴ for the preparation of tetrathiofuvalene derivatives which possess interesting electroconductivity properties.⁹⁵ This new synthetic route to 4-alkyl-1,3-dithiolium salts is more advantageous than other methods^{96,97} owing to its operational simplicity and to the accessibility of starting materials.

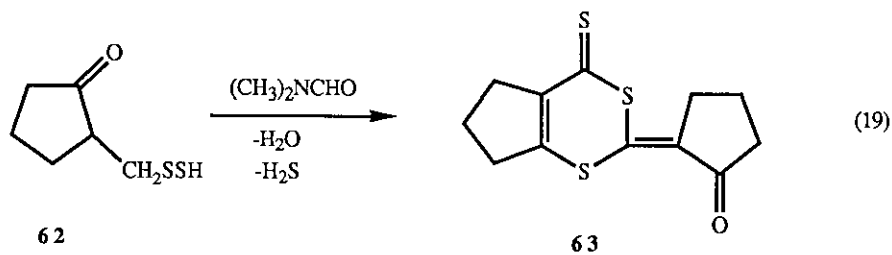


Pyrolysis of 2-dialkylamino-4-bromomethyl-4-methyl-1,3-dithioanylium bromides (**55**, $\text{R} = \text{R}_1 = \text{CH}_3$; $\text{R} = \text{CH}_3$; $\text{R} = \text{CH}_3$, $\text{R}_1 = \text{C}_2\text{H}_5$) gives the six-membered 2-alkyl-imino-5-methyl-1,3-dithia-4-cyclohexenes (2-alkylimino-5-methyl-1,3-dithiins, **57**).⁹⁸ This novel ring transformation may be the first example of a ring expansion of 1,3-dithiolane derivatives into a 1,3-dithiin system, although ring expansions of 1,3-dithiolane derivatives such as **58** into dihydro-1,4-dithiin systems (**59**) is well precedented.⁹⁹⁻¹⁰³ A crucial step in the synthesis of the antibiotic holomycin (**61**) is the ring contraction of a 1,3-dithiin (**60**) to a 1,2-dithiole (eq. 18).^{104,105}

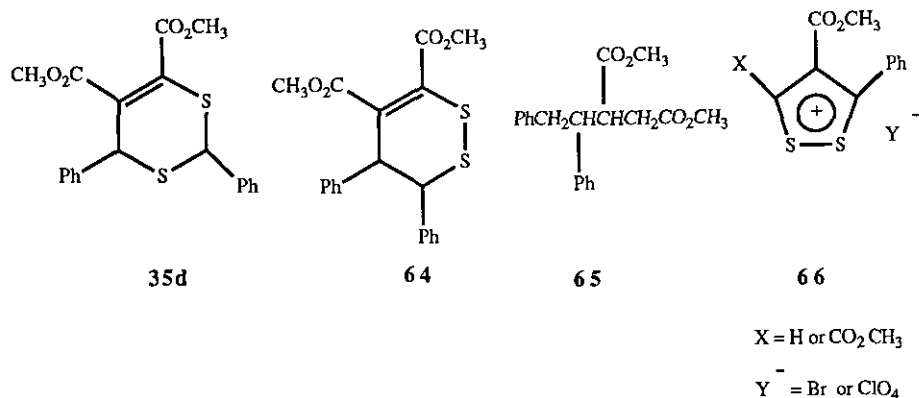




In dipolar aprotic solvents, 2-oxocyclopentanedithiocarboxylic acid (**62**) is converted into 6,7-dihydro-2-(2-oxocyclopentylidene)cyclopenta-[d][1,3] dithiin-4(5H)-thione **63** or into its positional isomer.¹⁰⁶



Thermolysis (185 °C) of dimethyl 2,4-diphenyl-1,3-dithiin-5,6-dicarboxylate (**35d**) affords isomeric dimethyl 3,4-dihydro-3,4-diphenyl-1,2-dithiin-5,6-dicarboxylate (**64**).⁷⁸ Desulfurization of **64** with Raney nickel gave diester (**65**). The mechanism of this unusual rearrangement might involve fission of a C-S bond with formation of intermediate allylic (and benzylic) diradicals (Scheme II). The structures of the 1,3-dithiins **35** were further supported by their spectral properties and oxidative rearrangement to the dithiolium salts (**66**).⁷⁸



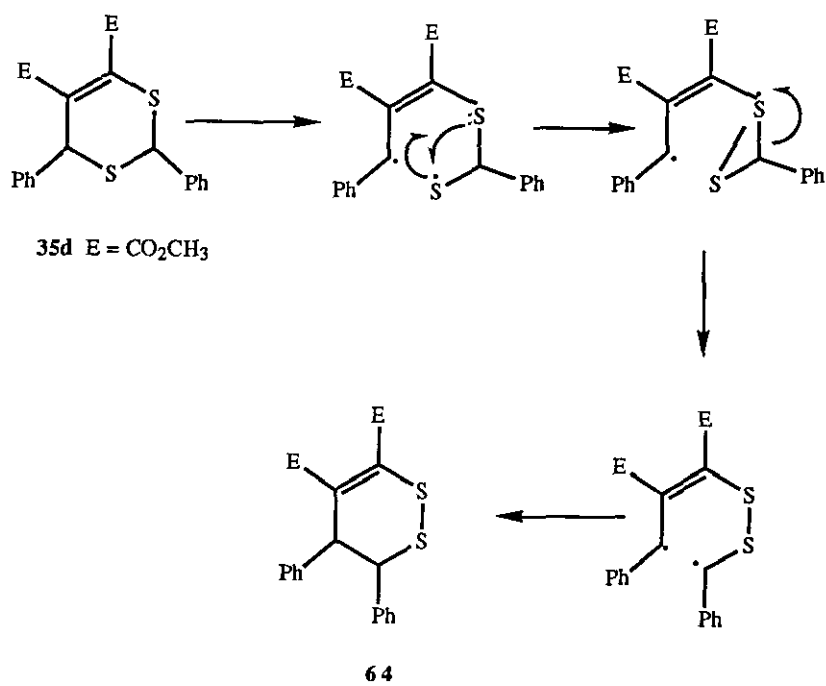
2.3 REACTIONS

The unexplored chemistry of 4H-1,3-dithiin (**2**) and its derivatives remains a fertile area for future study.

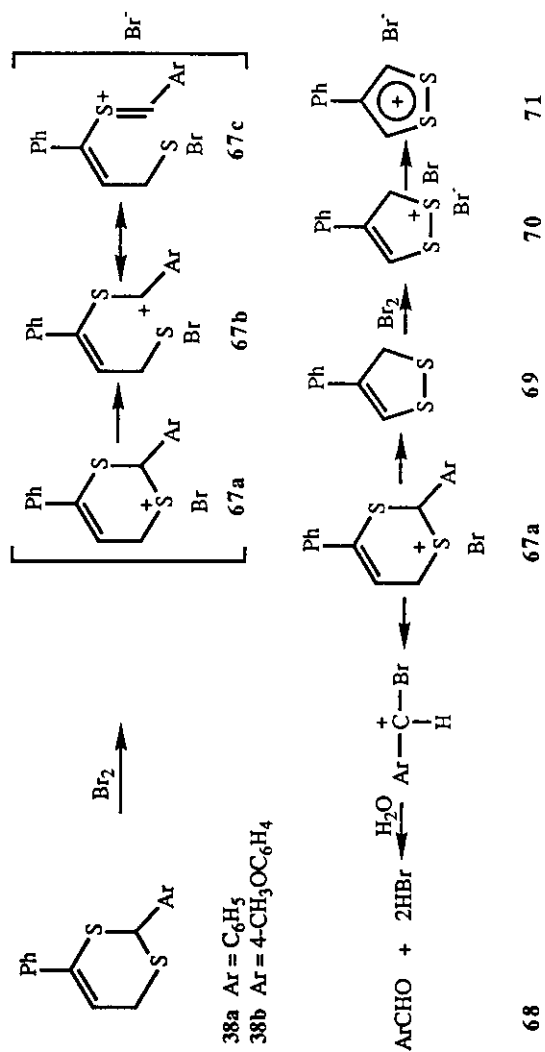
The isomerization of 2-ethenyl-4H-1,3-dithiin (**15**) to 3-ethenyl-3,4-dihydro-1,2-dithiin (**14**) has been observed (eq. 1).⁶¹⁻⁶³

4H-1,3-Dithiins (**38**, Scheme I) react with dibromine in ethanoic acid to give aldehydes (**68**, 55-60%) and 4-phenyl-1,2-dithiolium bromide (**71**, Scheme III).⁷⁹ Sulfuryl chloride reacts similarly with **38**.

Scheme II

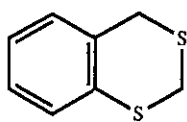


Scheme III



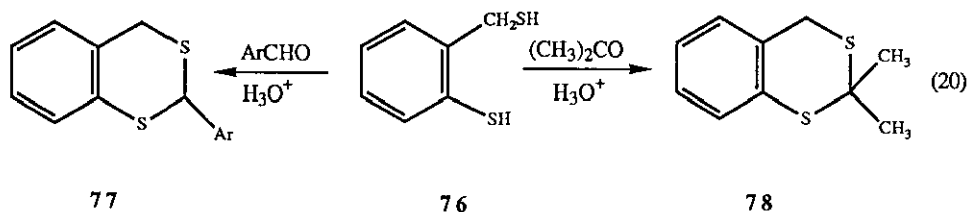
Some of the versatile chemical reactivity of the labile 4H-1,3-dithiin 53 (eq. 13) is shown in Scheme IV.⁹¹ It is seen that a 1,2-dithiolethione (72), an isothiazole (73), and open chain products (74, 75) are formed.

3. 4H-BENZO-1,3-DITHIINS

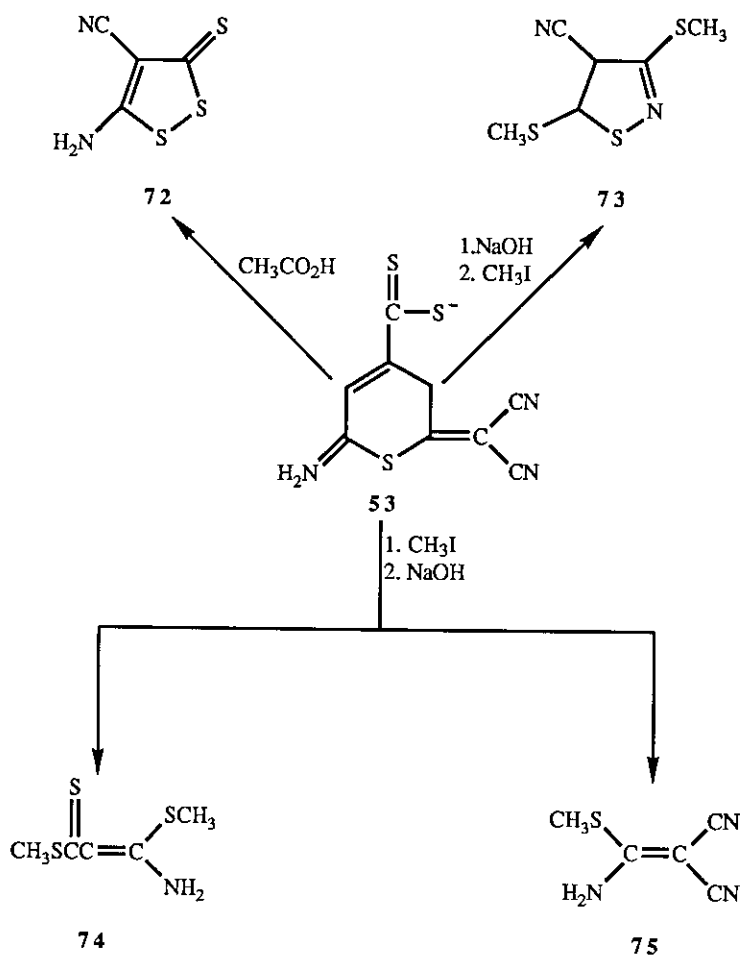


16

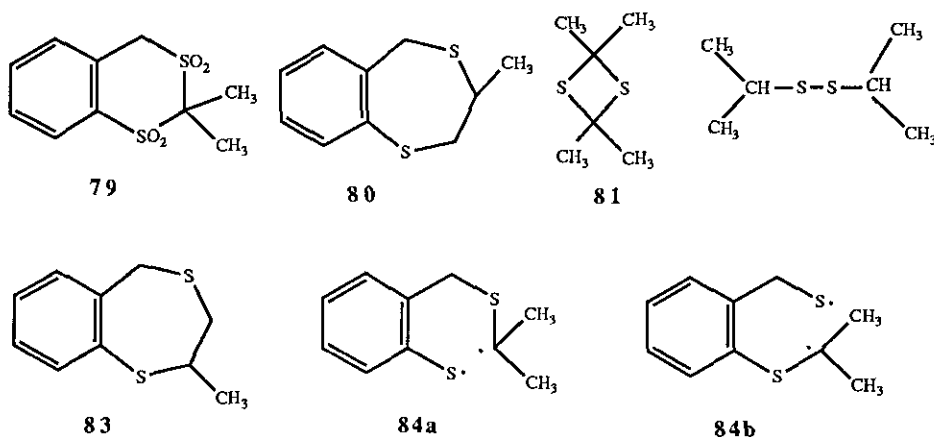
Although the parent compound (4H-benzo-1,3-dithiin, 16) is not known, 2-aryl-4H-1,3-benzodithiins (77) and 2,2-dimethyl-4H-1,3-benzodithiin (78) have been prepared from 1-mercapto-2-thiomethylbenzene (76).^{54,79} Permanganate ion oxidizes the 1,3-dithiin (78) to the corresponding disulfone (79).



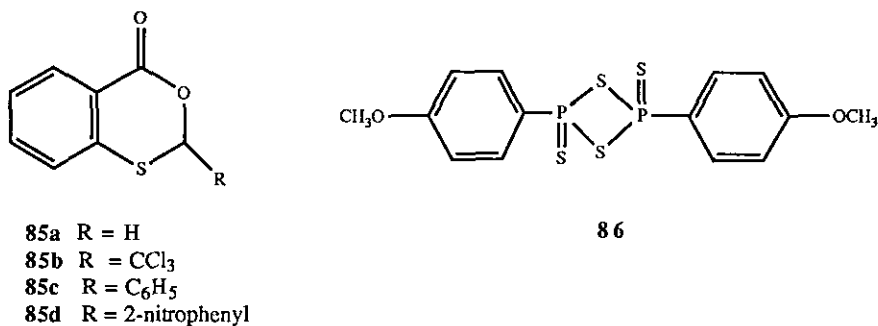
Scheme IV

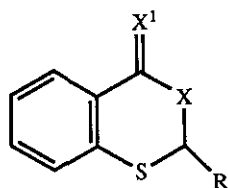


Photolysis of the 1,3-dithiin (78) gave the rearranged product (80) (15%) in addition to compound (81) (4%) and disulfide (82) (3%).¹⁰⁷ The absence of compound (83) suggests that initial carbon-sulfur bond cleavage occurs only in the direction to give the more stable thiyl radical 84a.



3,1-Benzoxathian-4-ones (85), when heated with 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson reagent, 86) or with P_4S_{10} gave one or more of the following products: 3,1-benzoxathian-4-thione (87), 1,3-benzothian-4-one (88), 1,3-benzodithian-4-thione (89), and 3H-1,2-benzodithiole-3-thione (90).¹⁰⁸ Lithium aluminum hydride reduces thione (90) to dithiol (76).⁷³

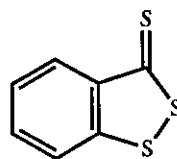




87 $X^1 = S, X = O$

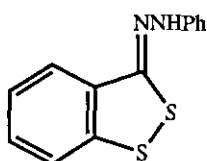
88 $X^1 = O, X = S$

89 $X^1 = S, X = S$

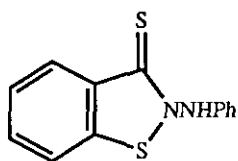


90

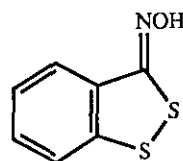
Compound **89** ($R = Ph$) reacted with phenylhydrazine or hydroxylamine to give known compounds **91** and **92**, respectively.¹⁰⁸ 4-Phenylhydrazono-2-phenyl-1,3-benzodithian (**93**) was isolated as a byproduct from the phenylhydrazine reaction. The 3H-1,2-benzodithiol-3-imines (eg. **91a**) are in equilibrium (Dimroth rearrangement) with 1,2-benzisothiazole-3(2H)-thiones (eg. **91b**).¹⁰⁸



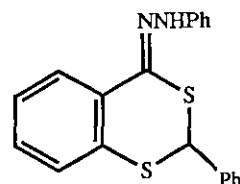
91a



91b

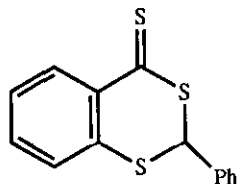


92

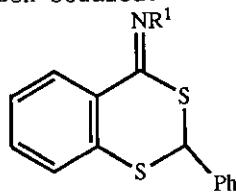


93

Another report¹⁰⁹ describes the reaction of 3,1-benzoxathian-4-ones (**85**, $R = (CH_2)_{10}CH_3, CH_3, Ph$) with Lawesson reagent (**86**) or with P_4S_{10} to give a mixture of **87**, **89**, and 1,2-benzodithiolethione (**90**). Compound **89** ($X = X^1 = S; R = Ph$) reacts with primary amines and hydrazines to give **94** ($X = S; X^1 = NR^1; R^1 = alkyl, aryl$). The reactions of **89** with Ph_2CN_2 , diazofluorene, and Cu-bronze have also been studied.¹⁰⁹

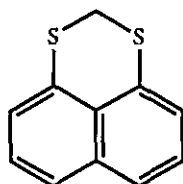


89



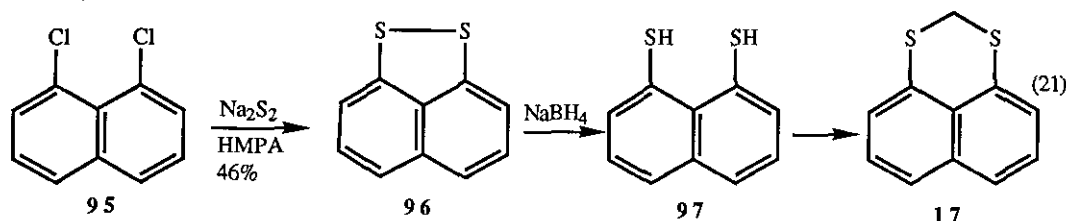
94

4. NAPHTHO[1,8-de]-1,3-DITHIINS

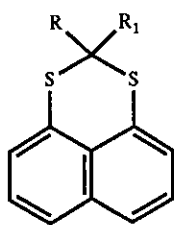


17

Naphtho[1,8-de]-1,3-dithiin (17)^{55,110} was prepared in 26% yield by treatment of 1,8-dimercaptonaphthalene (naphtho[1,8-cd]-1,2-dithiole, 97) with sodium hydride and diiodomethane at 22-24 °C in tetrahydrofuran.

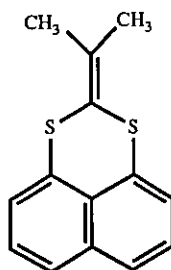


The reaction of dithiol (97) with propanone afforded the 1,3-dithiin (98).¹¹¹ 2-Phenylnaphtho[1,8-de]-1,3-dithiin (99) was prepared from the reaction of the dithiol (97) and phenylmethanal.¹¹² Naphtho[1,8-de]-2-isopropylidene-1,3-dithiin (100) was prepared (95%) from the Wadsworth-Emmons reaction of diethyl [naphtho[1,8-de]-1,3-dithiin-2-yl]phosphonate (101) and propanone.⁵⁵ Compound 101 was prepared from naphtho[1,8-de]-1,3-dithiin-2-thione (102) (eq. 22).⁵⁵

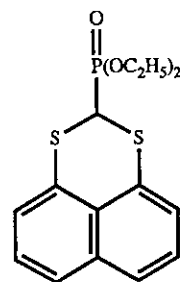


98 $R = R^1 = \text{CH}_3$

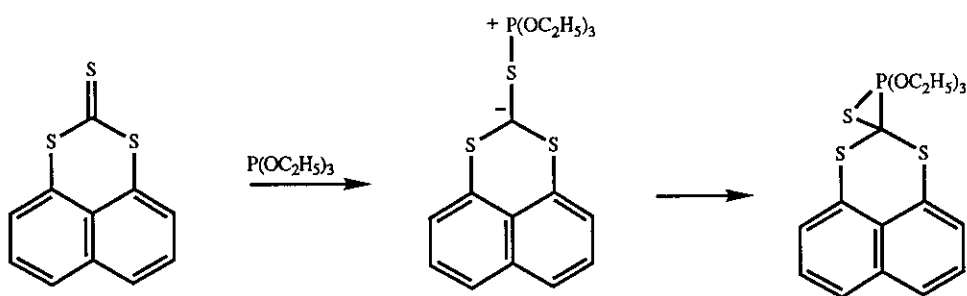
99 $R = \text{H}, R^1 = \text{C}_6\text{H}_5$



100



101

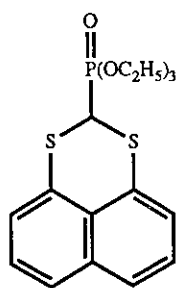


102

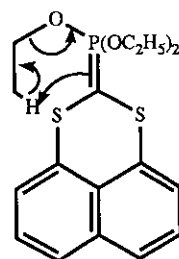
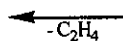
103

104

(22)

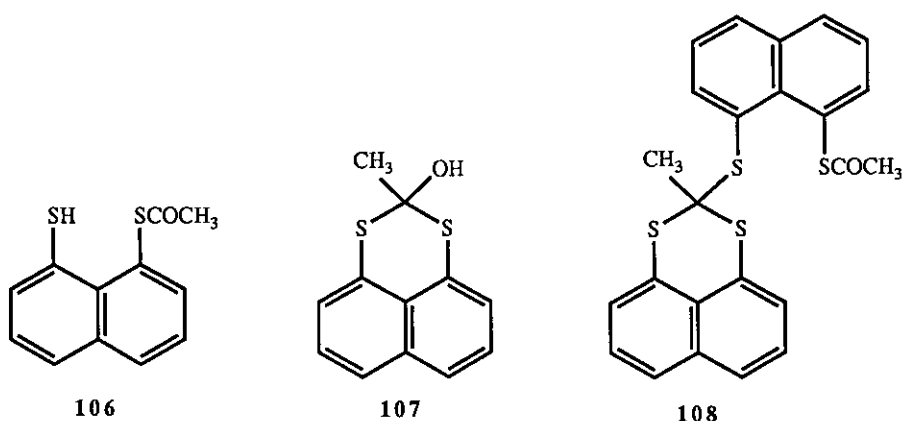


101

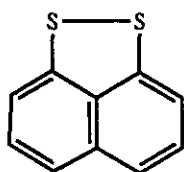


105

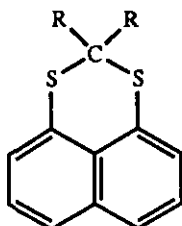
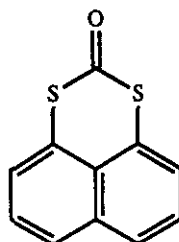
The tetrahedral intermediate (107) in the intramolecular acyl transfer reaction of mono-S-acylated 1,8-naphthalenedithiol (106) was found to be sufficiently stable to allow isolation or direct characterization by spectroscopy.¹¹³ Compound 107 (106) dissolves in 96% sulfuric acid to give an intense blush-violet solution showing a single methyl signal at δ 2.75 (ppm from external TMS) and a multiplet at δ 7.0 - 8.0. Dilution of the solution with cold water gave a trace of 107 (106) and compound 108. A carbenium ion intermediate was proposed.¹¹³



Refluxing 1,2-dithaacenenaphthene (96) and bis(toluenesulfonyl)diazomethane with copper acetylacetonate in benzene gave the insertion product (109) (88%).¹¹⁴ The pyrolysis of 109 or 110 at 148 °C gave carbonyl compound (111). Similar reactions were observed with 111 and diphenyldiazomethane in the presence of copper salts. The fact that diphenyl disulfide did not react with these carbenes implied that the five membered ring disulfide was more reactive to electrophilic reagents than ordinary sulfides.¹¹⁴

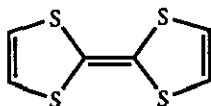


96

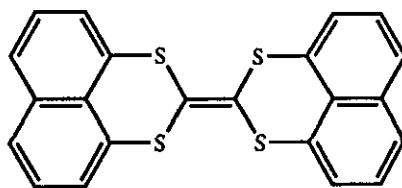
109 R = 4-CH₃C₆H₄110 R = C₆H₅

111

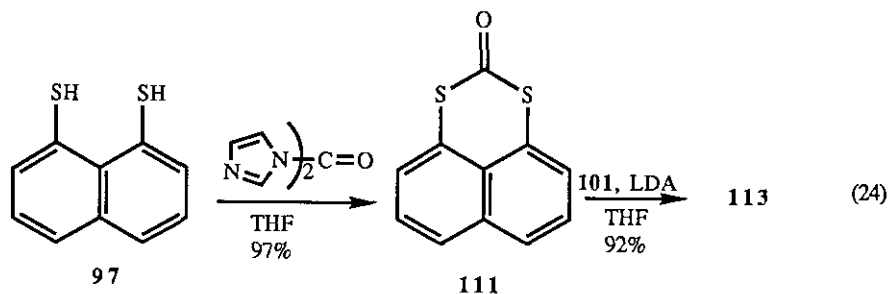
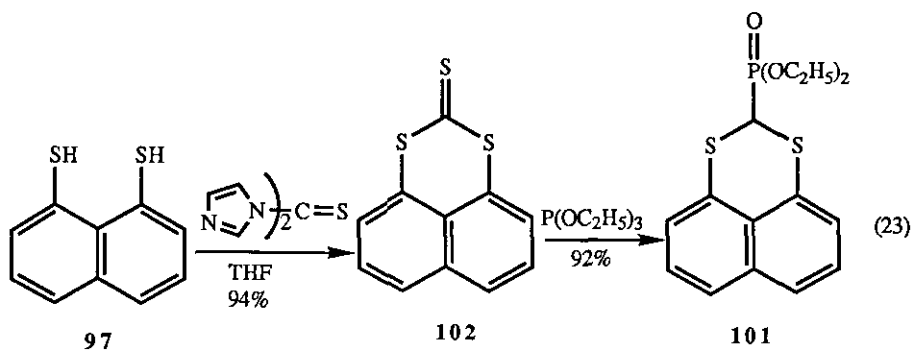
The discovery of tetrathiafulvalene (TTF, **112**) forming charge-transfer salts with low-dimensionally metallic properties has generated considerable interest in other electron donors which exhibit similar conductivity.⁵⁵ Binaphtho[1,8-*de*]-1,3-dithiin-2-ylidene (**113**), which belongs to the same tetrathiaethylene class, but differs structurally from TTF (**112**) in the fused heterocyclic member, was prepared and its donor character was examined by cyclic voltammetry.^{55,110}



112

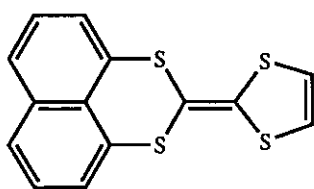


113

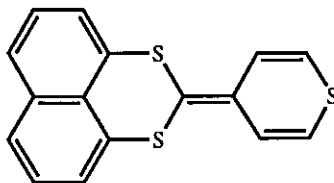


The cyclic voltammetry of 113 exhibited a reversible redox wave, whose half-wave oxidation potential was situated at 1.14 V vs. a Ag/AgCl reference electrode in cyanobenzene (0.1 M $(\text{C}_4\text{H}_9)_4\text{NClO}_4$, Pt electrode, $100 \text{ mV}\cdot\text{s}^{-1}$ scan rate).⁵⁵ In contrast, the cyclic voltammetry of 17 and 105 showed irreversible oxidations with somewhat higher peak potentials. The easier oxidation of 113 and the greater stability of the resulting radical cation may be attributed to the extended conjugation of π electrons through the central olefin.⁵⁵

Although cyclic voltammetry indicated that symmetrical 2,2'-binaphtho[1,8-de]-1,3-dithiinylidene (113) and its selenium analog were poor donors, unsymmetrical 2-(1,3-dithio-2-ylidene)naphtho[1,8-de]-1,3-dithiin (114) and 2-(4H-thiopyran-4-ylidene)naphtho[1,8-de]1,3-dithiin (115) possess considerable donor abilities.¹¹¹ These compounds (114, 115) are capable of forming crystalline charge transfer complexes with strong acceptors as TCNQ, TCNQF₄, and DDQ, which are semiconducting.⁵⁵

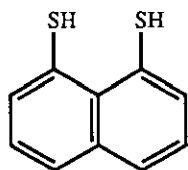


114

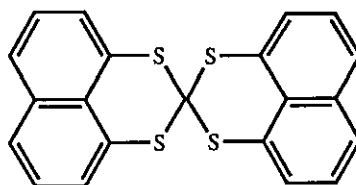
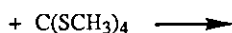


115

Nonplanar 2,2'-spirobinaphtho[1,8-de]-1,3-dithiin (111) has been prepared from the dithiol (97) and tetramethyl orthothiocarbonate (116).¹¹¹ The He(I) PE spectra of 98 and 117 have been measured.¹¹¹



116

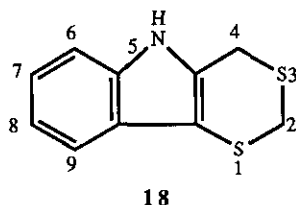


117

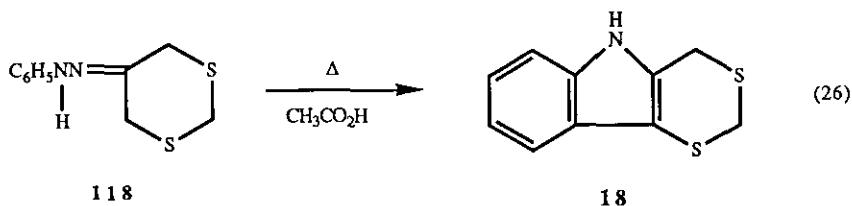
(25)

The He(I) photoelectron spectra of naphtho[1,8-*de*]-1,3-dithiin (17) has also been measured.¹¹⁵ Oxidation of 17 gives the radical cation. The PES ionization energies and the esr coupling in the radical cation were satisfactorily reproduced by a molecular state parameterized HMO model.¹¹⁵

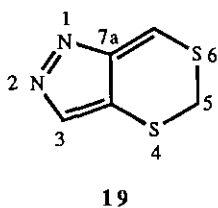
5. 1,3-DITHIINO[5,4-*b*]INDOLES



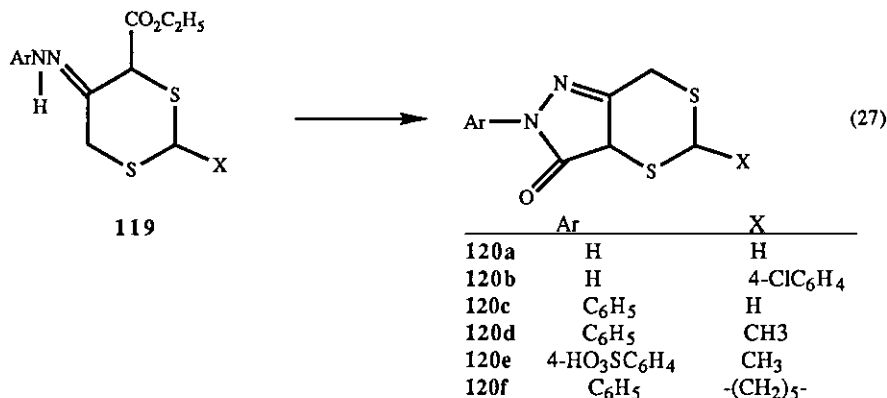
The 4,5-dihydro derivative 18 was obtained from 1,3-dithiane-5-phenylhydrazone (118).^{56,57}



6. [1,3]DITHIINO[5,4-*c*]PYRAZOLES

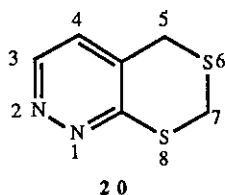


The hydrazones of 2,7-dihydro-1,3-dithiino[5,4-c]-pyrazol-3(3aH)-ones were prepared from ethyl 5-oxo-1,3-dithiane-4-carboxylates (**119**).^{57,59}

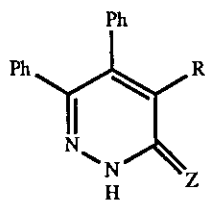


The acetamide derivative of [1,3]dithiino[5,4-c]pyrazole (**19**) and 2,7-dihydro-5-phenyl[1,3]dithiino[5,4-c]pyrazole-(3aH)-one were prepared and tested as sensitive silver halide photothermographic materials for producing dye images.¹¹⁶

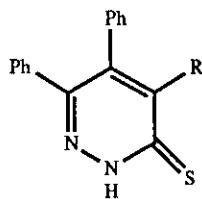
7. 5H-[1,3]DITHIINO[4,5-c]PYRIDAZINE



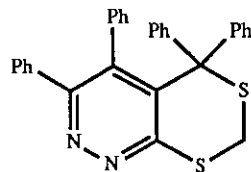
Reaction of **121** (R = CPh₂OH; Z = O, S) with P₄S₁₀ gave **122** (R = CPh₂SH; Z = S) which undergoes cyclocondensation with dimethoxymethane to give 3,4,5,5-tetraphenyl-5H-[1,3]dithiino[4,5-c]pyridazine (**123**, 66%),⁵⁸ which is a representative of a new ring system (1,3-dithiano-[4,5-c]pyridazine).¹¹⁷



121

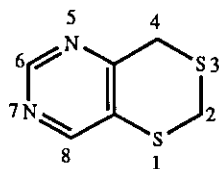


122



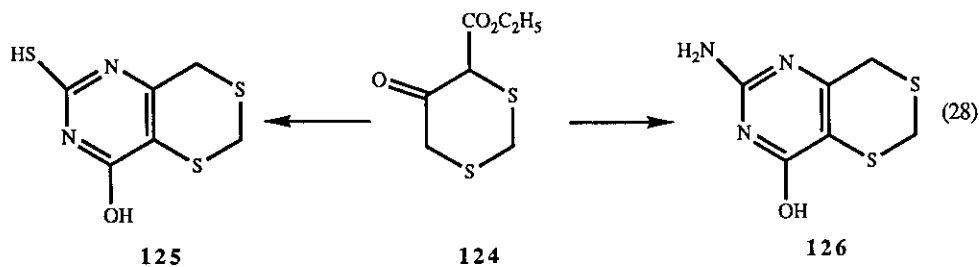
123

8. 4H-1,3-DITHIINO[5,4-d]PYRIMIDINES

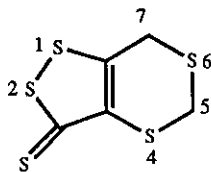


21

6-Mercapto-4H-1,3-dithiino[5,4-d]pyrimidin-8-ol (125) was prepared (26%) from ethyl 5-oxo-1,3-dithiane-4-carboxylate (124) and thiourea.⁵⁹ The 6-amino derivative (126) was prepared similarly from compound 124 and with guanidinium thiocyanate. Condensation of the methyl ester of 124 gave the 6,8-dihydroxy compound.⁵⁷

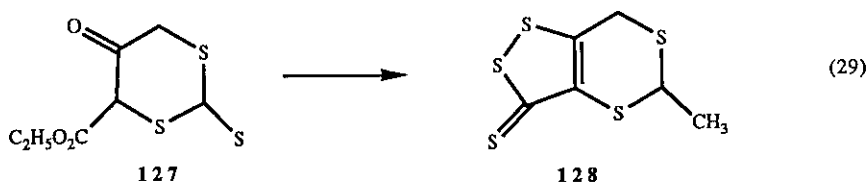


9. 1,2-DITHIOLO[4,3-d]-1,3-DITHIIN



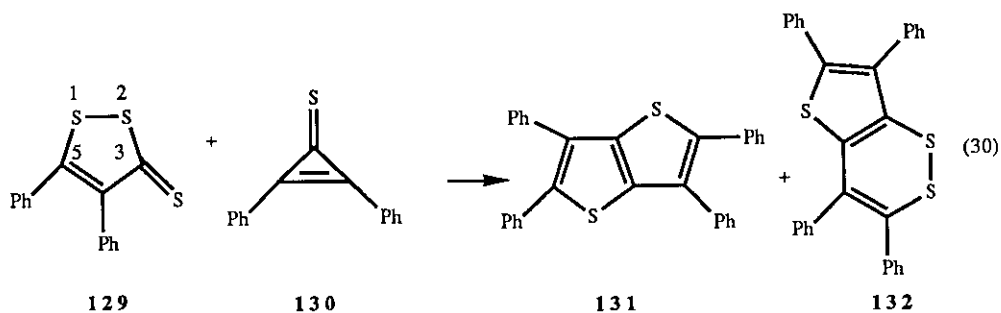
22

Treatment of 2-methyl-1,3-dithia-4-carbethoxycyclohexan-5-one (**127**) with P_4S_{10} , S, and CS_2 gave 5-methyl-1,2-dithiolo[4,3-d]-1,3-dithiin-(7H)-thione (**128**) which appears to be the only reported member of this family.⁶⁰

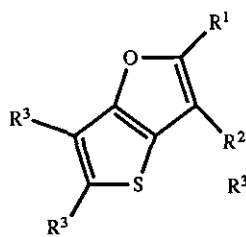
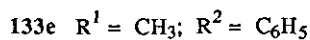
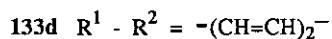
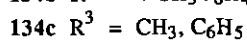
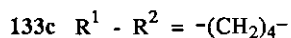
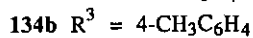
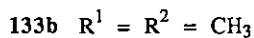
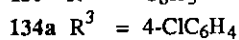
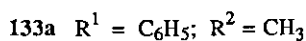
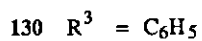
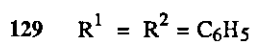
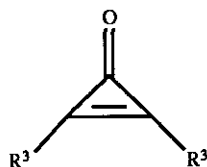
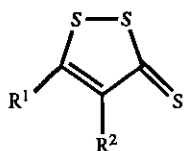


10. OTHER DERIVATIVES OF 4H-1,3-DITHIINS

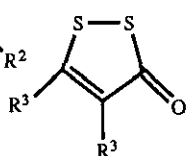
4,5-Diphenyl-1,2-dithiole-3-thione (1,2-trithione, **129**) reacts with 2,3-diphenylcyclopropenethione (**130**) to give thieno[3,2-b]thiophene (**131**) and tetraphenylthieno[3,2-c]-1,2-dithiin (**132**).¹¹⁸



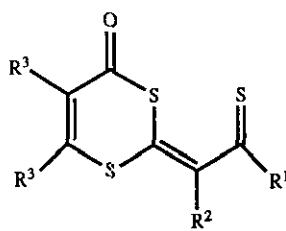
1,2-Trithiones (129, 133) react with 2,3-diarylcyclopropenones (130, 134) to give the corresponding thieno[3,2-b]furans (135), 1,2-dithiole-3-ones (136), and 4H-1,3-dithiin 137a and/or 137b. A mechanism for formation of 137a and 137b is shown in Scheme V.¹¹⁸



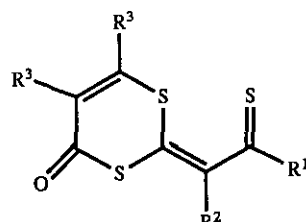
135



136

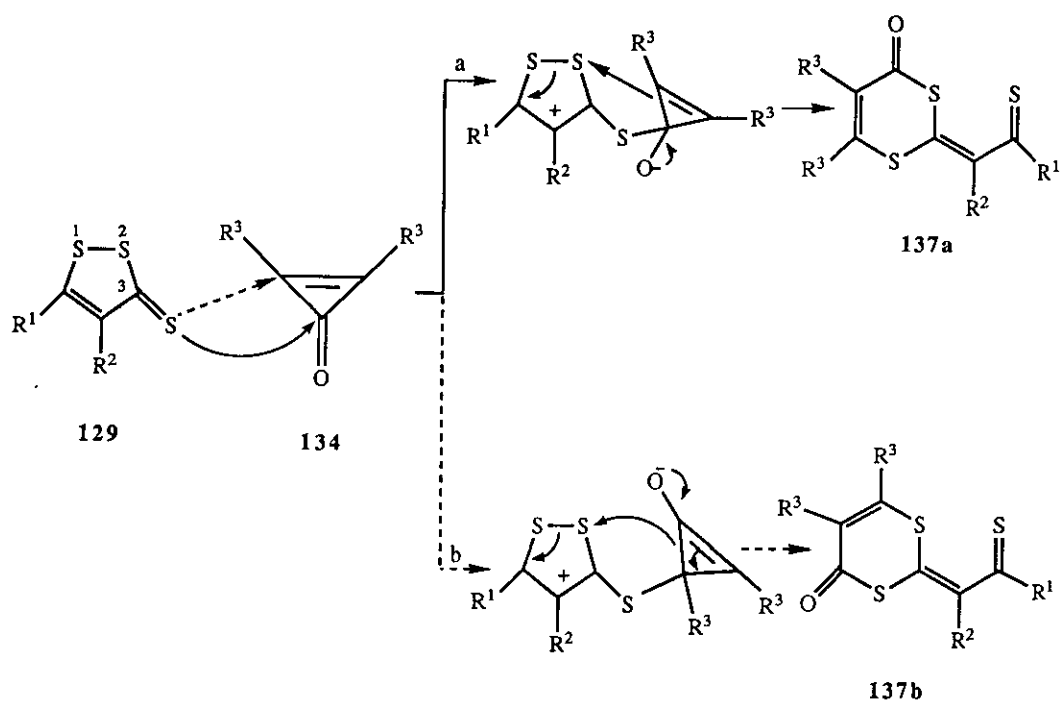


137a

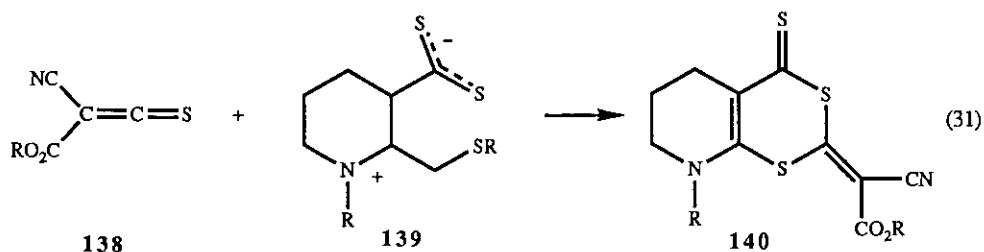


137b

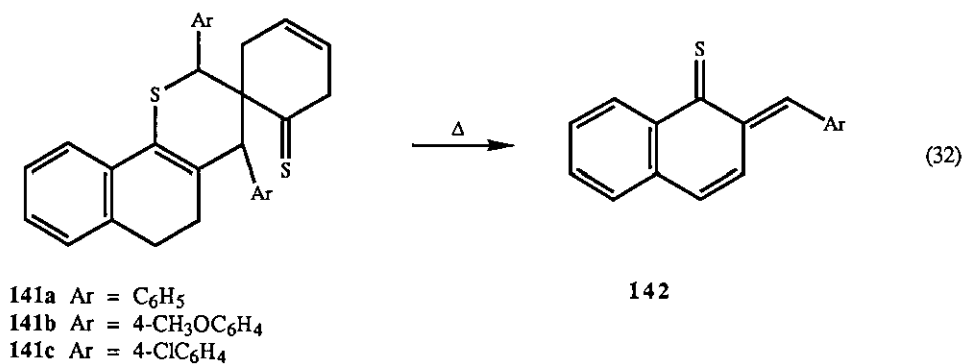
Scheme V

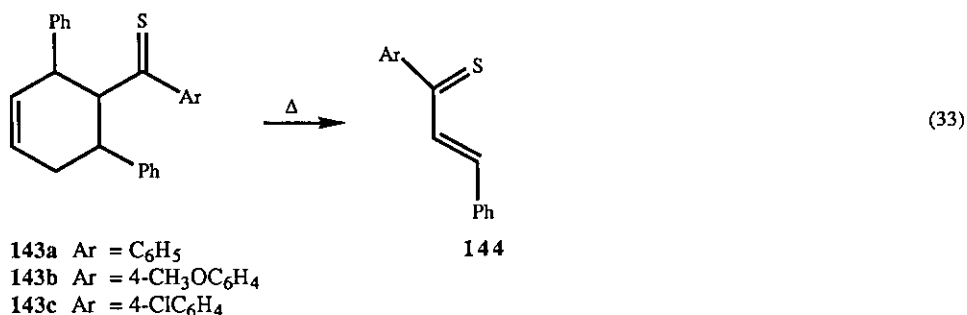


The 1,4-dipole (139) reacts with thioketene (138) to give the cycloadduct (140).^{119,120}

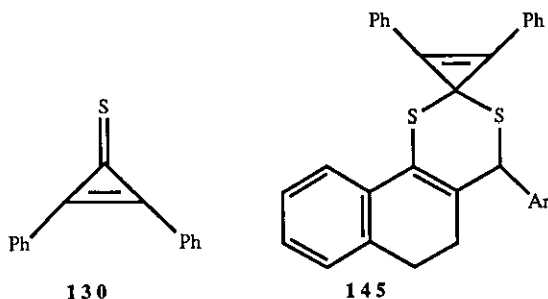


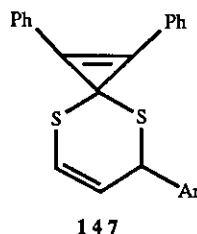
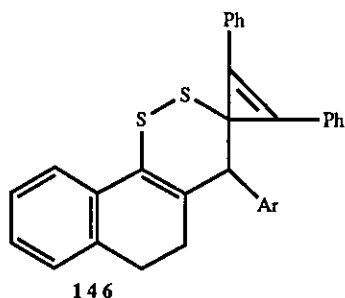
2-(Arylmethylene)tetralin-1-thiones (142) and thiochalcones (144), which were generated by thermolysis of their respective dimers (141 and 143), undergo cycloaddition reactions with various dienophiles to give a wide variety of products.^{64,121}





Treatment of the thione (142) with 2,3-diphenyl-2-propene-1-thione (130) in refluxing benzene (1 h) gave 1:1 adducts (56-63%) for which the regioisomeric structures (145) (5',6'-dihydro-2,3,4'-triarylspiro[2-cyclopropene-1,2']-[4H]-naphthol[1,2-d][1,3]dithiin)) and 146 are reason-able.¹²³ Structure 145 was preferred owing to the extrusion of a phenylmethanethial molecule in the mass fragmentation pattern. Similarly the reaction of 130 and 143 gave the 6'-aryl-2,3,4'-triphenylspiro[2-cyclopropene-1,2']-[4H][1,3]dithiins (147, 62-88%).¹²¹

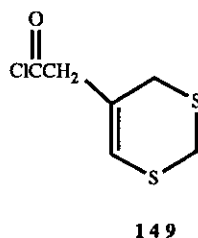
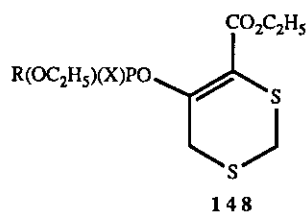




11. BIOACTIVITY

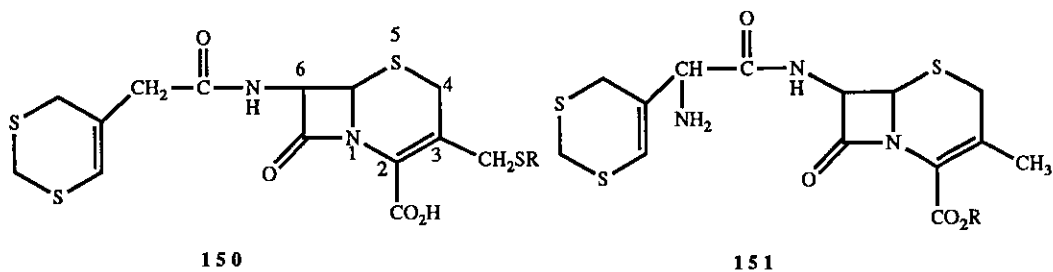
3-Ethenyl-3,4-dihydro-1,2-dithiin (11) and 2-ethenyl-4H-1,3-dithiin (12) show antithrombotic activity.⁵³

Although the garlic constituents (E/Z) ajoene and diallyl disulfide strongly inhibited prostaglandin synthase and 5-lipoxygenase, which are involved in prostaglandin and leukotriene biosynthesis, respectively, 3-ethenyl-3,4-dihydro-1,2-dithiin (11) and 2-ethenyl-4H-1,3-dithiin (12) did not inhibit the enzymes to any appreciable extent.¹²² 1,3-Dithiacyclohexenyl (thiono)(thiolo)phosphoric(phosphonic) acid esters (148, X = S, R = OC₂H₅, SC₃H₇, C₂H₅, Ph; X = O, R = OC₂H₅) have found applications as insecticides.¹²³ Compound 148 (X = S, R = OC₂H₅) at 5 ppm gave 100% kill of *Porbia antiqua* larvae in soil.



The cephalosporin derivatives (150, R = 5-methyl-1,3,4-thiadiazol-2-yl, 1-methyl-5-tetrazolyl) were prepared by the reaction of 7-aminocephalosporanic acid with 149, followed by reaction with 5-methyl-2-thioxo-

1,3,4-thiadiazoline or 1-methyl-5-thioxotetrazoline. Compounds **150** are useful as bactericides, e.g. at 0.1-0.5 $\mu\text{g}/\text{cm}^3$ in vitro against *Staphylococcus aureus* Smith.¹²⁴



Other cephalosporin derivatives (**151**, $R = H$, $\text{CHR}^1\text{O}_2\text{CR}^2$; $R^1 = H$, C_{1-4} alkyl; $R^2 = \text{C}_{1-4}$ alkyl, cyclohexyl) and their salts were prepared for use as bacteriocides.^{125,126}

References

1. F. Freeman, D.S.H.L. Kim, and E. Rodriquez, *Sulfur Reports*, 1989, **9**, 207.
2. U. Eisner and T. Krishnamurthy, *Int. J. Sulfur Chem.*, 1972, **7B**, 101.
3. C.M. Buess, *Mech. React. Sulfur Cpds.*, 1968, **3**, 15.
4. K. Kobayashi, C.L. Gajurel, *Sulfur Reports*, 1986, **7**, 123.
5. W.E. Parham, 'Org. Sulfur Cpds.', Vol. 1, ed. by N. Kharasch, Pergamon Press, New York, 1961, p. 248.
6. F. Freeman, D.H.S.L. Kim, C. Lee, and W.J. Hehre, unpublished data from work in progress.
7. F. Freeman, C. Lee, and W.J. Hehre, unpublished data from work in progress.
8. D.S. Sappenfield, and M. Kreevoy, *Tetrahedron*, 1963, **19**, 157.
9. W. Schroth, M. Hassfeld, and A. Zschunke, *Z. Chem.*, 1970, **10**, 296.
10. W. Schroth, R. Borsdorf, R. Herzsuh, and J. Seidler, *Z. Chem.*, 1970, **10**, 147.
11. S. Saebo, L. Radom, and G.L.D. Ritchie, *J. Mol. Struct.*, 1984, **108**, 59.
12. J. Kao, C. Eyermann, E. Southwick, and D. Leister, *J. Am. Chem. Soc.*, 1985, **107**, 5323.
13. B.A. Hess, Jr. and L.J. Schaad, *J. Am. Chem. Soc.*, 1973, **95**, 3907.
14. V. Galasso, *J. Mol. Struct.*, 1981, **85**, 159.

15. M. Kreevoy, *J. Am. Chem. Soc.*, 1958, **80**, 5543.
16. N.K. Ray and P.T. Narashimhan, *J. Mol. Struct.*, 1968, **1**, 489.
17. K. Hayakawa, N. Mibu, E. Osawa, and K. Kanematsu, *J. Am. Chem. Soc.*, 1982, **104**, 7136.
18. W.C. Herndon and C. Parkanyi, *Tetrahedron*, 1978, **34**, 3419.
19. N.K. DasGupta and F.W. Birss, *Tetrahedron*, 1980, **36**, 2711.
20. S. Inagaki and Y. Hirabayashi, *J. Am. Chem. Soc.*, 1977, **99**, 7418.
21. R. Borsdorf, H.J. Hofmann, H.-J. Koehler, M. Scholz, and J. Fabian, *Tetrahedron*, 1970, **26**, 3227.
22. J. Fabian and H. Hartmann, *Z. Chem.*, 1978, **18**, 145.
23. G. Geiseler and J. Sawistowsky, *Z. Phys. Chem. (Liepzig)*, 1973, **253**, 333.
24. F. Freeman, D.S.H.L. Kim, and E. Rodriguez, unpublished data from work in progress.
- 25a. K. Steliou, private communication.
- 25b. K. Steliou, Y. Gareau, G. Milot, and P. Salama, XIII International Symposium on the Organic Chemistry of Sulfur, 7-12 August 1988, Odense, Denmark, p. 13.
26. E. Rodriguez, M. Aregullin, T., Nishida, S. Uehara, R. Wrangham, Z. Abramowski, A. Finlayson, and G.H.N. Towers, *Experientia*, 1985, **41**, 419.
27. R.A. Norton, A.J. Finlayson, and G.H.N. Towers, *Phytochem.* 1985, **24**, 356.
28. E.G. Cosio, R.A. Norton, E. Towers, A.J. Finlayson, E. Rodriguez, and G.H.N. Towers, *J. Plant. Physiol.*, 1986, **124**, 155.

29. E.G. Cosio, G.H.N. Towers, and J. McPherson, *J. Plant. Physiol.*, 1987, **129**, 1.
30. F. Bohlmann, T. Burkhardt, and C. Zdero, *Naturally Occurring Acetylenes*, Academic Press, London, 1973.
31. N.H. Fischer and L. Quijano, *ACS Symp. Ser.*, 1985, **268**, 133; *Chem. Abstr.*, 1985, **102**, 128809.
32. F. Bohlmann, J. Jakupovic, and A. Schuster, *Phytochem.*, 1983, **22**, 1637.
33. F. Bohlmann, C. Zdero, R.M. King, and H. Robinson, *Phytochem.*, 1982, **21**, 2329.
34. F. Bohlmann, J. Jakupovic, H. Robinson, and R.M. King, *Phytochem.*, 1980, **19**, 881.
35. F. Bohlmann, A.A. Natsu, and P.K. Mahanta, *Phytochem.*, 1978, **17**, 483.
36. F. Bohlmann and M. Lonitz, *Chem. Ber.*, 1978, **111**, 254.
37. F. Bohlmann and C. Zdero, *The Chemistry of Heterocyclic Compounds: Thiophene and Its Derivatives*, ed. by S. Gronowitz, Wiley, New York, 1985, **44**, 261.
38. F. Bohlmann, C. Zdero, and M. Grenz, *Phytochem.*, 1976, **15**, 1309.
39. F. Bohlmann and C. Zdero, *Phytochem.*, 1978, **17**, 2302.
40. F. Bohlmann and C. Zdero, *Phytochem.*, 1979, **18**, 492.
41. F. Bohlmann, M. Grenz, R.K. Gupta, A.K. Dhar, M. Ahmed, R.M. King, and H. Robinson, *Phytochem.*, 1980, **19**, 2391.
42. F. Bohlmann and Le Van Ngo, *Phytochem.*, 1977, **16**, 1765; *Chem. Abstr.*, 1977, **88**, 101545.

43. J.T. Mortensen, J.S. Sørensen, and N.A. Sørensen, *Acta Chem. Scand.*, 1964, **18**, 2392.
44. F. Bohlmann and K.M. Kleine, *Chem. Ber.*, 1965, **98**, 3081.
45. F. Bohlmann and C. Zdero, *Phytochem.*, 1977, **16**, 780.
46. R. Tressl, D. Bahri, M. Holzer, and T. Kossa, *J. Agric. Food Chem.*, 1977, **25**, 459.
47. E. Block, S. Ahmad, J.L. Catalfamo, M.K. Jain, and R. Apitz-Castro, *J. Am. Chem. Soc.*, 1986, **108**, 7045.
48. M.H. Brodnitz, J.V. Pascale, and L. Van Derslice, *J. Agric. Food Chem.*, 1971, **19**, 273.
49. M.S. Legendre, H.P. Dupuy, E.T. Rayner, and W.H. Schuller, *J. Am. Oil Chem. Soc.*, 1980, **57**, 361.
50. B. Tokarska and K. Karwowski, *Nahrung*, 1983, **27**, 443; *Chem. Abstr.*, 1983, **99**, 69118.
51. M. G.B. Zoghbi, L.S. Ramos, J.G.S. Maia, M.L. Da Silva, and A.I.R. Luz, *J. Agric. Food Chem.*, 1984, **32**, 1009; *Chem. Abstr.*, 1984, **101**, 126818.
52. M. Voight and E. Wolf, *Dtsch. Apoth. Ztg.*, 1986, **126**, 591; *Chem. Abstr.*, 1986, **104**, 193276.
53. H. Nishimura, C.H. Wijaya, and J. Mizutani, *J. Agric. Food Chem.*, 1988, **36**, 563; *Chem Abstr.*, 1988, **108**, 203507.
54. A Lüttringhaus and K. Hagele, *Angew. Chem.*, 1955, **67**, 304.
55. K. Yui, Y. Aso, T. Otsubo, and F. Ogura, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 953.
56. A. Martani, *Ann. Chim. (Rome)*, 1959, **49**, 1844; *Chem. Abstr.*, 1947, **41**, 952.

57. A. Martani, *Ann. Chim. (Rome)*, 1959, **49**, 1844; *Chem. Abstr.*, 1960, **54**, 19689.
58. N.A. Shams, E.I. Enayat, A.A. Ebtisam, and S.A. El-Abbady, *J. Prakt. Chem.*, 1987, **329**, 271; *Chem. Abstr.*, 1988, **108**, 56021.
59. E.G. Howard, Jr. and R.V. Lindsey, Jr., *J. Am. Chem. Soc.*, 1960, **82**, 158.
60. A. Lüttringhaus and H. Prinzbach, *Liebigs Ann. Chem.*, 1959, **624**, 79.
- 61a. G. Vermeersch, J. Marko, N. Febray-Garot, S. Caplain, A. Couture, and A. Lablache-Combier, *Tetrahedron*, 1978, **34**, 2453.
- 61b. D.L. Boger and S.N. Weinreb, '*Hetero Diels-Alder Methodology in Organic Synthesis*', Academic Press, New York, 1987, p. 214.
- 61c. H. Bock, S. Mohamand, T. Hirabayashi, and A. Semkov, *J. Am. Chem. Soc.*, 1982, **104**, 312.
- 61d. H. Bock, S. Mohamand, T. Hirabayashi, and A. Semkov, *Chem. Ber.*, 1982, **115**, 1339.
62. E. Vedejs, T.H. Eberlein, and D.L. Varie, *J. Am. Chem. Soc.*, 1982, **104**, 1445.
63. P. Breslin, *J. Heterocycl. Chem.*, 1983, **20**, 1753.
- 64a. T. Karakasa, S. Sadayoshi, and S. Motoki, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 335.
- 64b. T. Karaskasa, *Nippon Shika Daigaku Kiyo, Ippan Kyoiku-kei*, 1985, **14**, 103; *Chem. Abstr.*, 1987, **107**, 153669.
65. H.G. Giles, R.A. Marty, and P. de Mayo, *J. Chem. Soc., Chem. Commun.*, 1974, 409.

66. H.G. Giles, R.A. Marty, and P. de Mayo, *Can. J. Chem.*, 1976, **54**, 537.
67. P. Breslin, D. Lagain, and J. Vialle, *Tetrahedron Lett.*, 1979, 2677.
68. P. Breslin, D. Lagain, J. Vialle, and C. Minot, *Tetrahedron*, 1981, **37**, 3839.
69. E. Baumann and F. Fromm, *Chem. Ber.*, 1895, **28**, 895.
70. E. Campaigne, *J. Am. Chem. Soc.*, 1944, **66**, 684.
71. E. Campaigne, W.B. Reid, Jr., and J.D. Pera, *J. Org. Chem.*, 1959, **24**, 1229.
72. D.J. Pasto and M.P. Serve, *J. Org. Chem.*, 1962, **27**, 4665.
73. W.H. Linnell and V.R. Sharma, *Quart. J. Pharm. Pharmacol.*, 1939, **12**, 263; *Chem. Abstr.*, 1939, **33**, 8596.
74. E. Campaigne and B.E. Edwards, *J. Org. Chem.*, 1962, **27**, 3760.
75. E. Campaigne and B.E. Edwards, *J. Org. Chem.*, 1962, **27**, 4488.
76. C. Demuyne, M. Prudhomme, and A. Thuillier, *Bull. Soc. Chim. Fr.*, 1966, **6**, 1970.
77. M. Pulst, M. Weissenfels, E. Kleinpeter, and L. Beyer, *Tetrahedron*, 1975, **31**, 3107.
78. U. Eisner and T. Krishnamurthy, *Tetrahedron*, 1971, **27**, 5753.
79. A. Lüttringhaus, M. Mohr, and N. Englehard, *Liebigs Ann. Chem.*, 1963, **661**, 84.
80. F. Duus and S.O. Lawesson, *Arkiv Kemi*, 1968, **29** 127.
81. E. Schaumann, *Tetrahedron*, 1988, **44**, 1827.
82. G. Schmerse, Ph.D. Thesis, University of Hamburg, West Germany, 1983.

83. C. Heibl, Ph.D. Thesis, University of Hamburg, West Germany, 1985.
84. A. J. Fatiadi, *Synthesis*, 1978, 165, 241.
85. F. Freeman, *Chem. Rev.*, 1969, **69**, 591.
86. F. Freeman, *Chem. Rev.*, 1980, **80**, 329.
87. F. Freeman, *Synthesis*, 1981, 925.
88. F. Freeman, Ed., The Chemistry of Malononitrile, in preparation.
89. J. Jentzsch and R. Mayer, *J. Prakt. Chem.*, 1962, **18**, 211; *Chem. Abstr.*, 1964, **60**, 1583.
90. R. Gompper and U. Heinemann, *Synthesis*, 1982, 227.
91. K. Gewald, *Chem. Ber.*, 1968, **101**, 383.
92. K. Hiratani, T. Nakai, and M. Okawara, *Chem. Lett.*, 1974, 1041.
93. T. Nakai, K. Hiratani, and M. Okawara, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 827.
94. Y. Ueno, A. Nakayama, and M. Okawara, *Synthesis*, 1975, 277.
95. F. Wudl, D. Wobschall, and E.J. Hufnagel, *J. Am. Chem. Soc.*, 1972, **94**, 670.
96. K. Hiratani, H. Shiono, and M. Okawara, *Chem. Lett.*, 1973, 867.
97. E. Campaigne and N.W. Jacobsen, *J. Org. Chem.*, 1964, **29**, 1703.
98. K. Hiratani, T. Nakai, and M. Okawara, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 2339.
99. J.L. Massingill, M.G. Reinecke, and J.E. Hodgkins, *J. Org. Chem.*, 1970, **35**, 823.
100. G. Karmas, *J. Org. Chem.*, 1967, **32**, 3147.
101. M. Tomoeda, M. Ishizaki, H. Kobayashi, S. Kanamoto, T. Koga, M. Inuzaka, and T. Furuta, *Chem. Pharm. Bull.*, 1964, **12**, 383.

102. M. Tomoeda, M. Ishizaki, H. Kobayashi, S. Kanamoto, T. Koga, M. Inuzaka, and T. Furuta, *Tetrahedron*, 1965, **21**, 733.
103. L.F. Fieser, C. Yuan, and T. Goto, *J. Am. Chem. Soc.*, 1960, **82**, 1996.
104. J.E. Ellis, J.H. Fried, I.T. Harrison, E. Rapp, and C.H. Ross, *J. Org. Chem.*, 1977, **42**, 2891.
105. Y. Kishi, T. Fukuyama, and S. Nakatsuka, *J. Am. Chem. Soc.*, 1973, **95**, 6490.
106. T. Takeshima, N. Fukada, T. Ishii, and M. Muraoka, *J. Chem. Soc., Perkin Trans. I*, 1976, 1706.
107. R.E. Kohrman and G.A. Berchtold, *J. Org. Chem.*, 1971, **36**, 3971.
108. A.A. El-Barbay, K. Clausen, and S.-O. Lawesson, *Tetrahedron*, 1980, **36**, 3309.
109. A.A. El-Barbay, H.A. Hammouda, and M. El-Borai, *Indian J. Chem., Sect. B*, 1984, **23B**, 770; *Chem. Abstr.*, 1985, **102**, 6342.
110. K. Yui, Y. Aso, T. Otsubo, and F. Ogura, *Chem. Lett.*, 1986, 551.
111. R. Gleiter and J. Uschumann, *J. Org. Chem.*, 1986, **51**, 370.
112. W.B. Price and S. Smiles, *J. Chem. Soc.*, 1928, 2372.
113. M. Takagi, R. Ishihara, and T. Matsuda, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 2193.
114. S. Tamagaki and S. Oae, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 960.
115. H. Bock, G. Brahler, D. Dauplaise, and J. Meinwald, *Chem. Ber.* 1981, **114**, 2622.
116. B.A. Clark, C. Holstead, and J.M. Simons, *Brit. UK Pat. Appl. GB 2,136,980* (1984); *Chem. Abstr.* 1985, **102**, P103656.

117. It appears that there are no reports of 2H-[1,3]dithiino[4,5-c]pyridazine and its derivatives.
118. H. Behringer and E. Meinetsberger, *Liebigs Ann. Chem.*, 1982, 315.
119. R. Gompper and W. Elser, *Angew Chem. Int. Ed. Engl.*, 1967, 6, 366.
120. R. Gompper, *Angew. Chem. Int. Ed. Engl.*, 1969, 8, 312.
121. T. Karakasa, S. Takeda, T. Saito, and S. Motoki, *Bull. Chem. Soc. Jpn.*, 1986, 59, 3279.
122. H. Wagner, M. Wierer, and B. Fesler, *Planta Med.*, 1987, 53, 305; *Chem. Abstr.* 1987, 107, 89878.
123. H.J. Riebel and B. Homeyer, *Ger. Offen.* 2,545,028 (1977); *Chem. Abstr.* 1977, 87, P53322.
124. C. Berger, D. Farge, and C. Moutonnier, *Ger. Offen.* 2,702,025 (1977); *Chem. Abstr.*, 1977, 87, P135372.
125. C. Berger, D. Dominique, D. Farge, C. Moutonnier, and G. Wolfe, *Ger. Offen.* 2,825,426 1978; *Chem. Abstr.*, 1979, 91, P57033.
126. C. Berger, D. Dominique, D. Farge, C. Moutonnier, and G. Wolf, *Ger. Offen.* 2,825,426 (1978); *Chem. Abstr.*, 1979, 90, P168616.

Received, 24th January, 1989