Chapter 2

The synthetic utility of β-oxodithioesters- a review

1. Introduction

β-oxodithioesters (ODEs) are the sulphur analogues of β-ketoesters[1]. These are the valuable three carbon precursors for a number of heterocyclic compounds having sulphur as a ring member or as a substituent and are widely used as a synthon in diversity-oriented synthesis (DOS). Such sulphur containing compounds exhibit various biological activities such as antibacterial, antifungal, antitumor and antimicrobial properties.

2. β-Oxodithioesters :– Reaction profiles

There are five active centres in β-oxodithioesters; out of which two are electrophilic and three are nucleophilic (**Fig.1**)[2]. The carbon atom of the carbonyl group and the carbon atom of the thiocarbonyl group act as electrophilic centres. At the same time, the oxygen atom of the carbonyl group, sulphur atom of the thiocarbonyl group and carbon atom present in between the carbonyl and thiocarbonyl group act as nucleophilic centres. The multiple reactive sites can be selectively tuned for a particular target molecule. Therefore, the presence of these active centres accompanied with the versatile reactivity of this framework qualifies it as a potential synthon for various heterocyclic compounds.

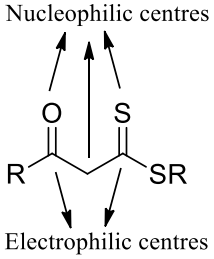
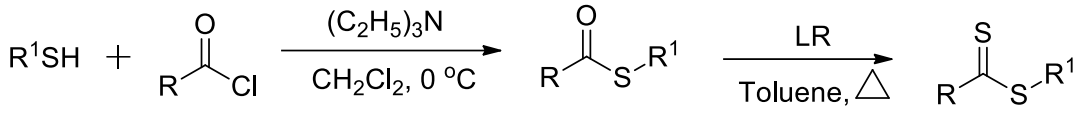


Fig. 1 Reactive sites of β-oxodithioesters

3. Methodologies for the synthesis β-oxodithioesters

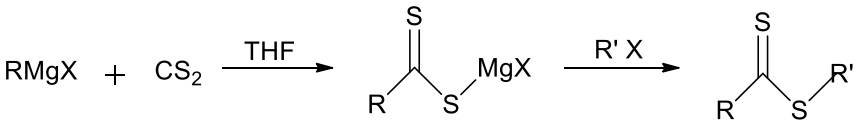
A number of methods have been reported in the literature for the synthesis of β-oxodithioesters. These include synthesis from carboxylic acids, aldehydes, ketones, thiols, dithioesters, Grignard reagents, ketene dithioacetals etc.[3].

Cerda and co-workers synthesised dithioesters **4** by the reaction between thiol **1** and acid chloride **2** in the presence of triethylamine and subsequent thionation using Lawesson's reagent[4] (**Scheme 1**). Dithioesters **8** can also be synthesised by the reaction between alkyl/aryl Grignard reagent **5** and carbon disulphide **6** followed by alkylation using alkyl halide[5] (**Scheme 2**).



1 **2** **3** **4**

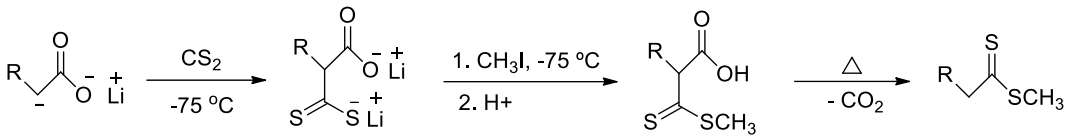
Scheme 1



5 **6** **7** **8**

Scheme 2

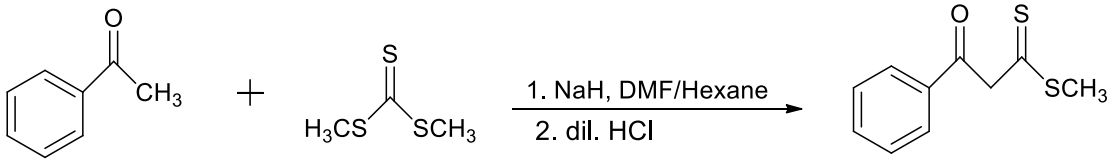
Konen *et al.* devised a synthetic protocol for dithioesters from carboxylic acids[6]. In this work, lithium enolates of carboxylic acids **9** were treated with carbon disulphide to get the corresponding dithiocarboxylate salt **10** which upon alkylation using methyl iodide followed by acidification yielded the dithioacid **11**. Decarboxylation of the dithioacid afforded corresponding dithioesters **12** (**Scheme 3**).



9 **10** **11** **12**

Scheme 3

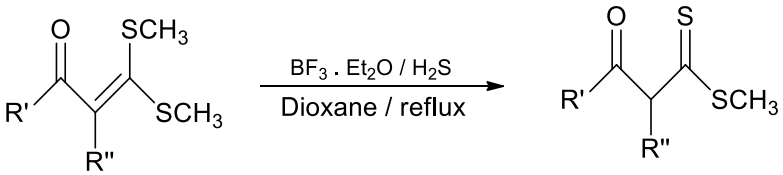
Samuel *et al.* reported a convenient approach for the synthesis of β-oxodithioesters **15** by the reaction between acetophenone **13** and dimethyl trithiocarbonate (DMTC) **14** in the solvent N,N-dimethylformamide (DMF)/hexane[7] (**Scheme 4**). The reaction was carried out at room temperature in the presence of sodium hydride (NaH).



13 **14** **15**

Scheme 4

Nair and Asokan introduced a new protocol for the synthesis of β-oxodithioesters **17** by sulphohydrolysis of acyl ketene dithioacetals **16** using hydrogen sulphide in the presence of boron trifluoride etherate in dioxane[8] (**Scheme 5**).

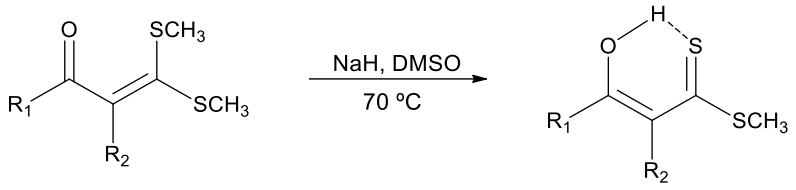


16 **17**

Scheme 5

In another synthetic method, α-oxo ketene dithioacetals **18** when treated with dimsyl sodium (sodium methylsulphinylmethylide) prepared in situ from DMSO and NaH undergo S-demethylation to afford the corresponding β-oxodithiocarboxylates **19**

(**Scheme 6**)[9]. S-Demethylation was achieved by nucleophilic attack of dimsyl anion at one of the methylthio groups.



18 **19**

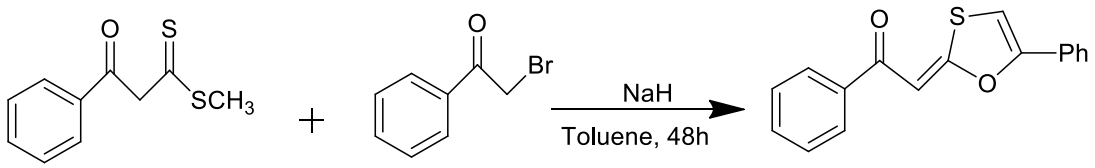
Scheme 6

4. Significance of β-oxodithioesters in organic synthesis

β-Oxodithioesters are promising synthons having valuable impact in modern synthetic organic chemistry. The diverse chemical properties promise wide synthetic utility of this framework in various synthetic transformations. It provides the scope for the development of new synthetic strategies that have to be explored. It finds application in the synthesis of monocyclic and polycyclic hetero aromatic compounds with one or more hetero atoms.

4.1. Synthesis of monocyclic heteronuclear aromatic compounds

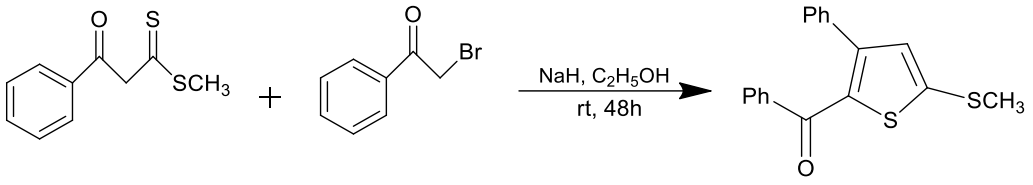
Samuel *et al.* reported the synthesis of 2-ylidene-1,3-oxathioles from β-oxodithiocarboxylate[7]. In this method β-oxodithiocarboxylate **20** was treated with α-haloketones **21** in the presence of NaH in toluene (**Scheme 7**). The reaction was completed in 48h affording substituted 2-ylidene-1,3-oxathioles **22** in good yields.



20 **21** **22**

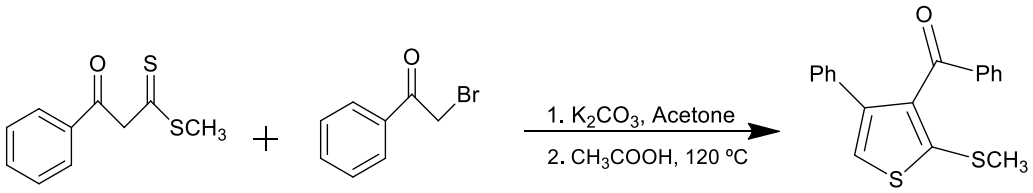
Scheme 7

In another method, β-oxodithioesters were alkylated with α-haloketones to afford substituted thiophenes[10]. Different derivatives of thiophenes were synthesised by changing the reaction conditions, base and solvent used. The reaction between β-oxodithioesters **23** and phenacyl bromide **24** in the presence of sodium hydride in ethanol as solvent led to alkylation and subsequent intramolecular aldol reaction that resulted in the synthesis of aryl[5-(methylsulphanyl)-3-phenyl-2-thienyl]methanone **25** (**Scheme 8**). However, when the alkylation of β-oxodithioesters **26** was carried out in the presence of potassium carbonate as the base using acetone as solvent followed by heating at 120 ºC in acetic acid resulted in aryl[2-(methylsulphanyl)-4-phenyl-3-thienyl]methanone **28** (**Scheme 9**).



23 **24** **25**

Scheme 8

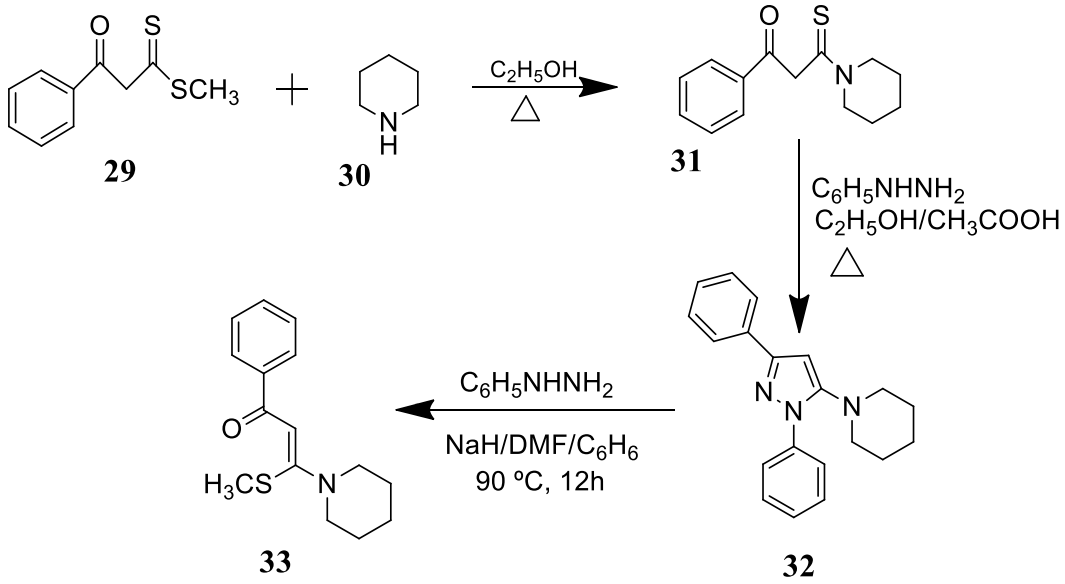


26 **27** **28**

Scheme 9

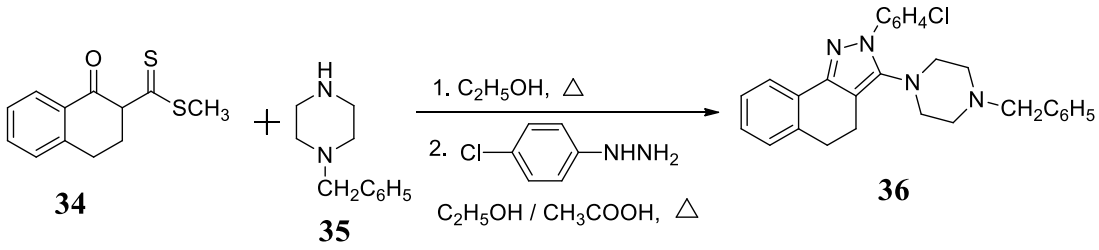
β-Oxodithioesters can be efficiently transformed to S,S- or N,S- acetals which are also useful as synthons in organic synthesis. Singh *et al*. reported a highly regioselective synthetic strategy for 5-amino substituted pyrazoles such as 1-aryl-3,4-substituted-5-(cycloamino)-pyrazoles and 1-aryl-3,4-substituted-5-(alkylamino)-pyrazoles from β-oxodithioesters[11]. In this method, β-oxodithioester **29** was converted to corresponding β-oxothioamides by refluxing it with piperidine **30** in ethanol. The β-oxothioamide **31**

prepared in situ was then refluxed with phenylhydrazine in ethanol in the presence of the catalytic amount of acetic acid which resulted in the cyclisation of β-oxothioamide to provide the target molecules **33** (**Scheme 10**). Synthesis of the 5-amino substituted pyrazole by the reaction of N,S-acetals with phenylhydrazine in the presence of the catalytic amount of NaH in DMF was also reported by the same group.

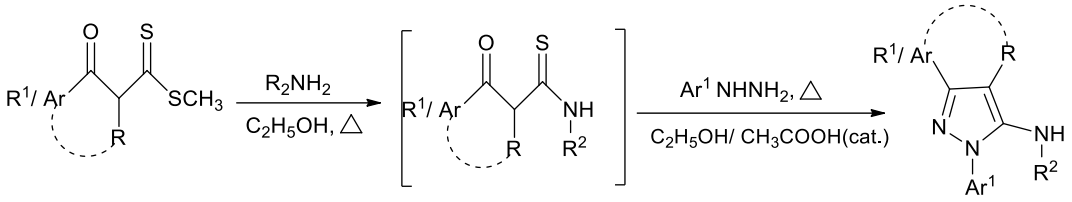


Scheme 10

β-Oxodithioesters **34** derived from cyclic ketones like cyclohexanone and 1-tetralone when treated with N-substituted piperazine **35** and substituted arylhydrazines afforded 3,4-fused 1-aryl-5-(cycloamino)pyrazoles **36** (**Scheme 11**). The reaction between β-oxodithioesters **37**, arylhydrazines and aliphatic amines in refluxing ethanol in the presence of the catalytic amount of acetic acid afforded 1,3-substituted-5-(alkylamino)pyrazoles **39 (Scheme 12)**[11].



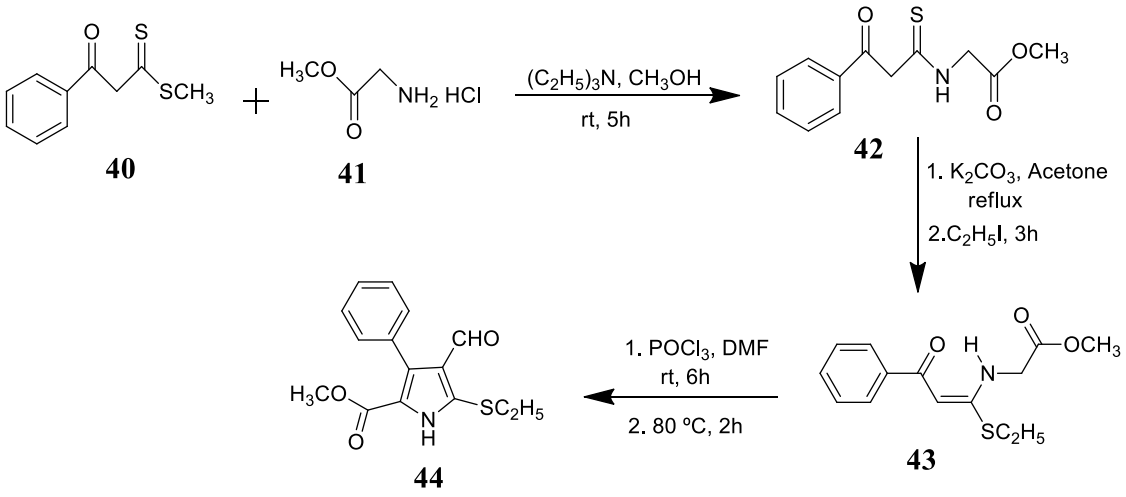
Scheme 11



37 **38** **39**

Scheme 12

Mathew and Asokan reported the synthesis of substituted pyrroles by the cyclisation of α-oxoketene-N,S-acetals synthesised from β-oxodithioesters[12]. In this method, the condensation reaction between β-oxodithioester **40** and methyl glycinate hydrochloride **41** using triethylamine as the base and methanol as solvent afforded the corresponding β-oxodithioamide **42**. It was then alkylated using ethyl iodide in the presence of potassium carbonate as the base and acetone as the solvent to afford the corresponding α-oxoketene-N,S-acetals **43**. Vismeier-Haack reaction of α-oxoketene-N,S-acetals with $POCl_3$ and DMF followed by hydrolysis using saturated aqueous solution of potassium carbonate afforded substituted pyrroles **44** (**Scheme 13**).

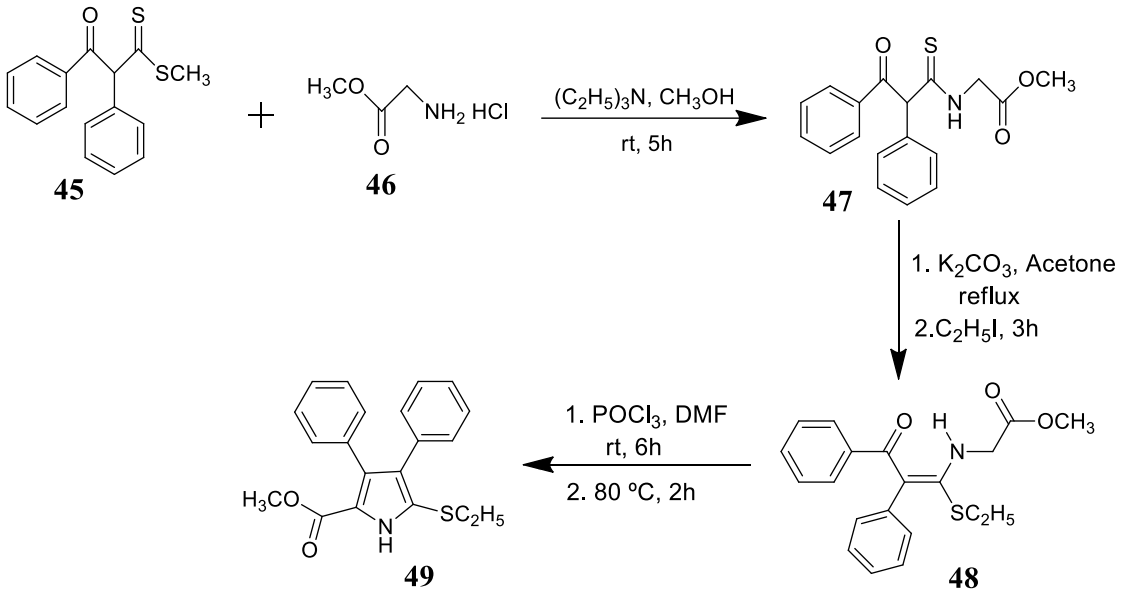


40 **41** **42** **43** **44**

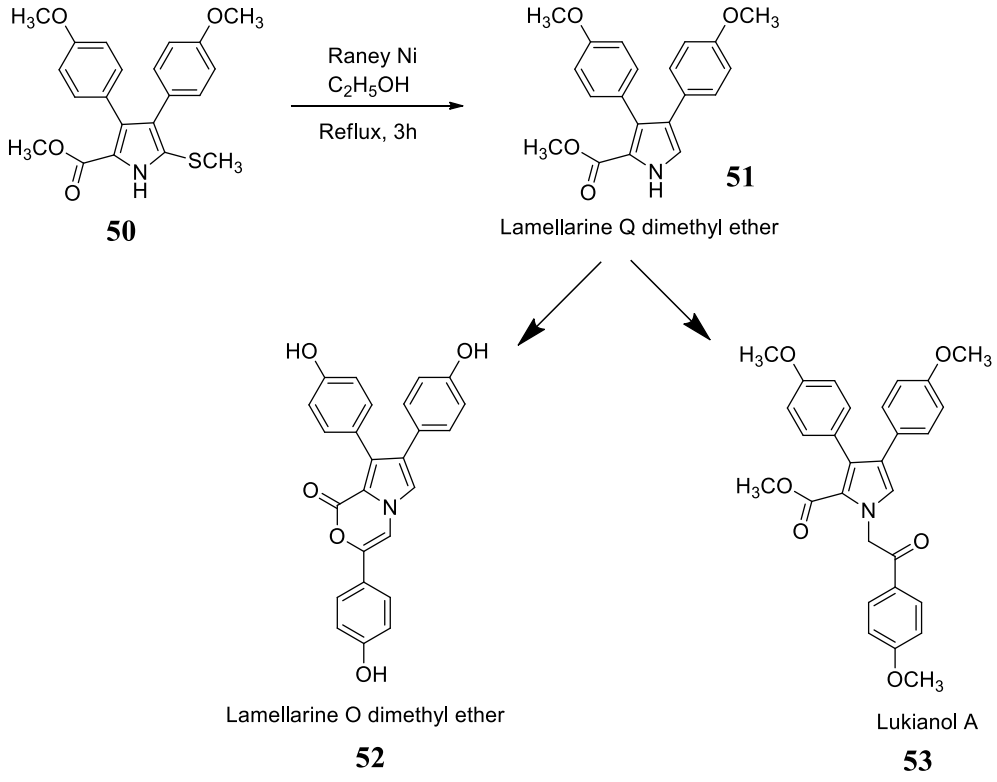
Scheme 13

A similar reaction on α-substituted β-oxodithioester **45** as synthon resulted in a structurally different pyrrole **49** (**Scheme 14**)[12]. Treatment of suitably substituted pyrrole derivative **50** with Raney Ni in ethanol afforded lamellarin Q dimethyl ether

(Furstner intermediate) **51** (**Scheme 15**)[12] which was reported as a precursor of lamellarin O dimethyl ether **52** and lukinol A **53**.

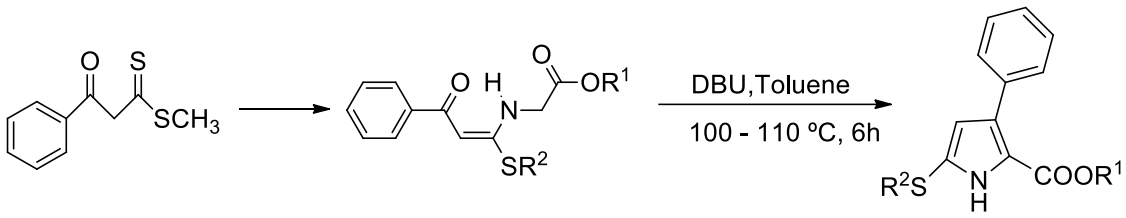


Scheme 14



Scheme 15

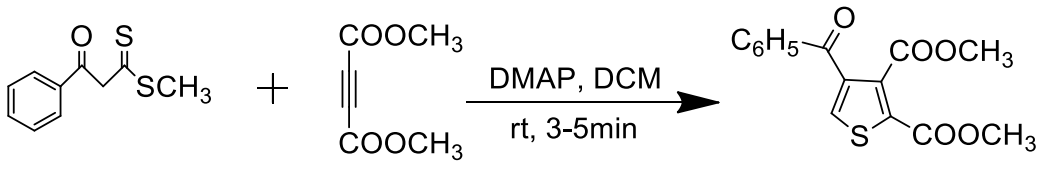
Mathew and Asokan devised a protocol for the synthesis of pyrrole derivatives from β-oxodithioesters[13]. In this method, α-oxo ketene-N,S-acetals **55** synthesised from β-oxodithioesters **54** when treated with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in toluene at a temperature of 100-110 ºC afforded trisubstituted pyrrole **56** within 6h (**Scheme 16**)[12].



54 **55** **56**

Scheme 16

An efficient one-pot synthetic strategy for functionalized thiophenes from β-oxodithioesters was reported by Nandi *et al.* According to this protocol, β-keto dithioesters **57** when stirred with dialkyl acetylenedicarboxylate **58** in dichloromethane, in the presence of lewis base 4-dimethylaminopyridine (DMAP), afforded 2,3,4-trisubstituted thiophenes **59** within 3-5min. at room temperature (**Scheme 17**)[14]. This method was conveniently used for the synthesis of 2,3-dicarboalkoxy-4-aroyl/alkanoyl/heteroaroyl thiophenes where [3+2] heteroannulation between β- keto dithioesters and dialkyl acetylenedicarboxylate via 1-2 (C-S) and 3-4 (C-C) bond formation furnished the thiophenes.

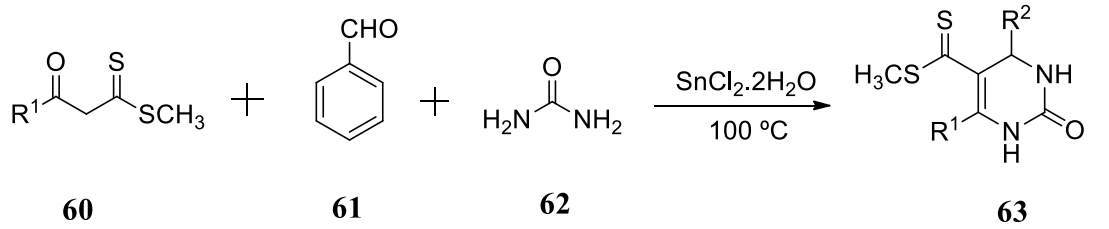


57 **58** **59**

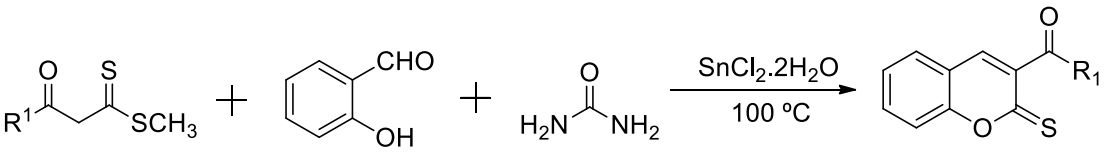
Scheme 17

Singh and Devi reported the synthesis of substituted 2H-chromene-2-thiones and 5-methylmercaptothiocarbonyl-4-aryl-3,4-dihydropyrimidin-2(1H)-ones using β-oxodithioesters as synthons. Dihydropyrimidinones **63** have been synthesised through three component Biginelli reaction of β-oxodithioesters **60** with aldehydes **61** and urea **62** in the presence of the catalytic amount of $SnCl_2.2H_2O$ at 100 ºC under solvent-free

conditions[15]. Whereas, the reaction between β-oxodithioesters **64**, salicylaldehyde **65** and urea **66** under the same conditions resulted in the synthesis of 2H-chromene-2-thiones **67** (**Scheme 18**). In this reaction urea act as the promotor. The reaction when carried out in the absence of urea provided only moderate yields, but in the presence of urea, an increase in the yield of the product was observed.



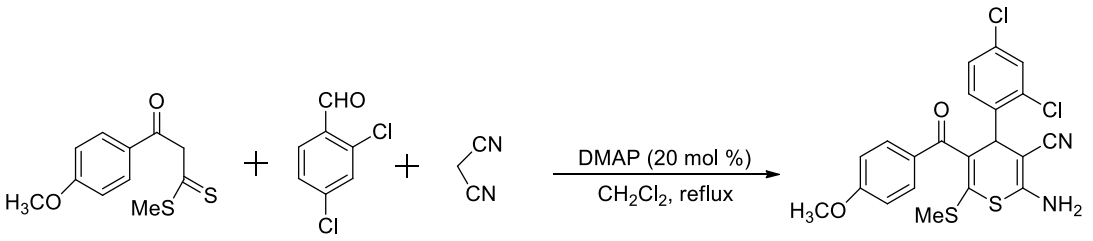
60 **61** **62** **63**



64 **65** **66** **67**

Scheme 18

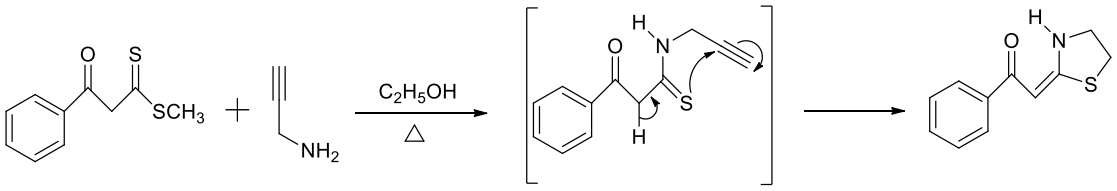
A highly efficient and regioselective one-pot three-component heteroannulation protocol has been developed for the synthesis of highly functionalized 4H-thiopyrans[16]. The three-component coupling (3CC) of β-oxodithioesters **68**, aldehyde **69** and an active methylene compound containing cyano group **70** catalysed by 4-dimethylamino pyridine (DMAP) under solvent-free conditions or using dichloromethane (DCM) as solvent afforded 4H-thiopyrans **71** (**Scheme 19**). The synthesis involves a sequence of knoevenagel condensation, Michael addition and intramolecular cyclisation resulting in two C-C bonds, one C-S bond and one stereocentre.



68 **69** **70** **71**

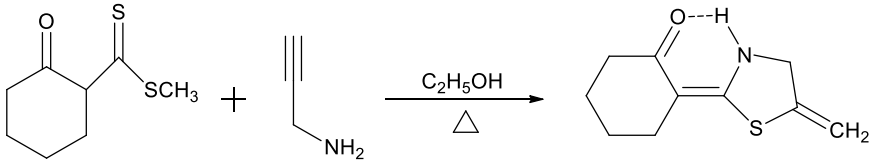
Scheme 19

Chandrasekharam *et al.* reported a synthetic strategy for thiazolidines from β-oxodithioesters[17]. This method includes the treatment of β-oxodithioesters **72** with propargylamine **73** in ethanol as solvent to afford β-oxo-N-propargyl thioamide **74** as intermediate. This is followed by intramolecular rearrangement caused by nucleophilic attack of thiocarbonyl sulphur on triple bond present in the β-oxo-N-propargyl thioamide to yield 2-(acylalkylidene)-5-(methylene)-thiazolidines **75** (**Scheme 20**). In the same way, cyclic β-oxodithioesters **76** reacted with propargylamine **77** in ethanol to afford thioamide which upon intramolecular nucleophilic attack transformed to 2-(2-oxocycloalkylidene)-5-(methylene) thiazolidines **78** (**Scheme 21**).



72 **73** **74** **75**

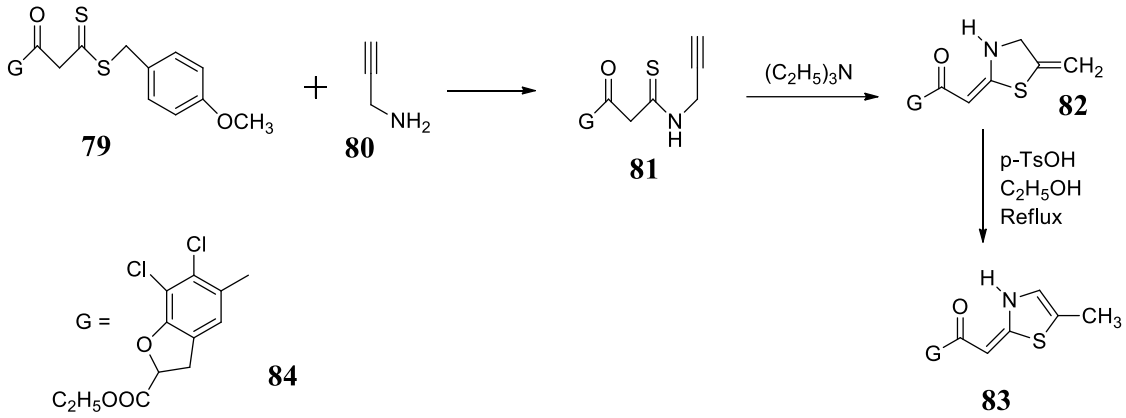
Scheme 20



76 **77** **78**

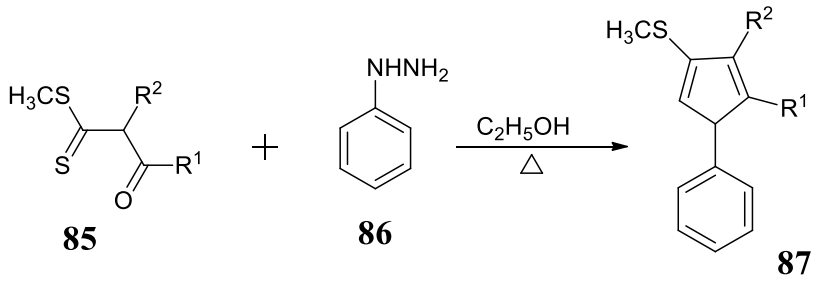
Scheme 21

Eiichi *et al.* synthesised thiazoles from thioamide derived from corresponding β-oxodithioesters[18]. Treatment of β-oxodithioesters **79** with propargyl amine **80** afforded the corresponding thioamide **81**. The reaction of the synthesised thioamide with triethylamine resulted in the intramolecular cyclisation of the thioamide providing the thiazole ring with an exocyclic double bond **82** which underwent isomerisation in the presence of p-TsOH in ethanol to afford thiazoles **83** (**Scheme 22**).



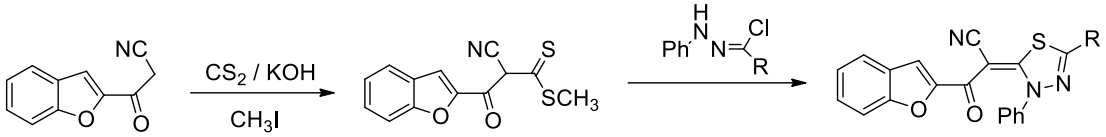
Scheme 22

Synthesis of 1-aryl-3-(methylthio)-4,5-substituted pyrazoles *via* cyclocondensation of β-oxodithioesters and arylhydrazines have been reported by Junjappa and co-workers[19]. Treatment of β-oxodithioesters **85** with arylhydrazines **86** in refluxing ethanol resulted in cyclocondensation along with the elimination of H_2S yielding pyrazoles **87** (**Scheme 23**).



Scheme 23

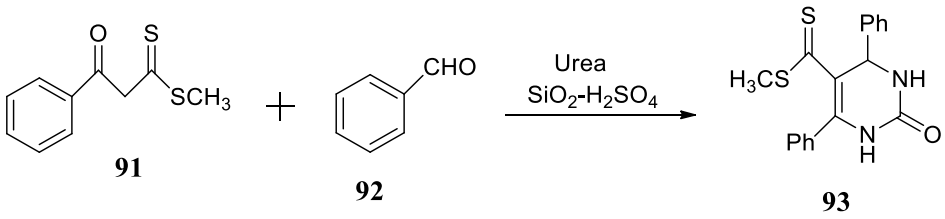
Abdelhamid *et al.* reported a new synthetic strategy for thiadiazoles from β-oxodithioesters[20]. The dithioesters required for the synthesis were prepared by the reaction between 3-(benzofuran-2-yl)-3-oxopropanenitrile **88** and carbon disulphide using potassium hydroxide as base and DMF as solvent. The synthesised dithioester **89** was then treated with hydrazonyl halide to afford 2,3-dihydro-1,3,4- thiadiazole derivative **90** (**Scheme 24**).



88 **89** **90**

Scheme 24

Nandi *et al.* developed a synthetic protocol for dihydropyrimidinones using β-oxodithioesters as synthons[21]. Three component cyclocondensation reaction of β-oxodithioesters **91**, aromatic aldehyde **92** and urea in the presence of SiO_2-H_2SO_4 afforded dihydropyrimidinones **93** (**Scheme 25**).

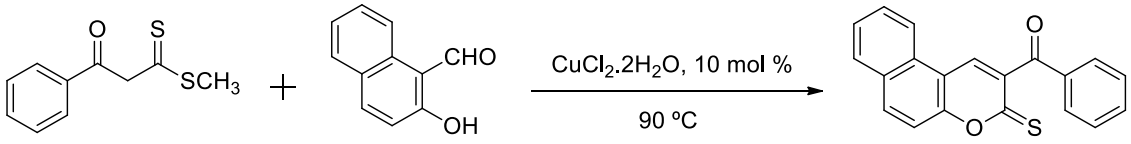


91 **92** **93**

Scheme 25

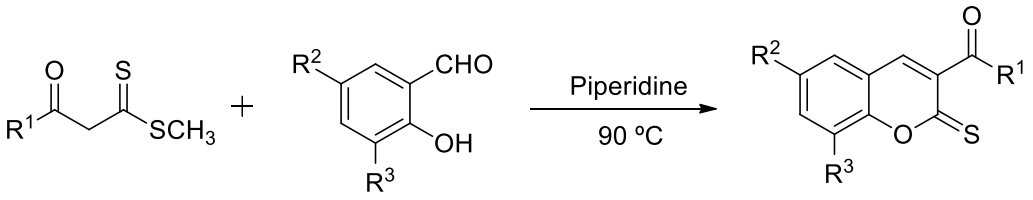
4.2. Synthesis of polycyclic heteronuclear aromatic compounds

Singh *et al.* introduced a facile and efficient synthetic strategy for coumarins from β-oxodithioesters[22]. Thiocoumarins **96** have been synthesised by cupric chloride catalysed condensation of β-oxodithioesters **94** with 2-hydroxy-1-naphthaldehyde **95** under solvent-free conditions (**Scheme 26**). A facile and high yielding synthesis of 3-alkanoyl/aroyl/heteroaroyl-2H-chromene-2-thiones using β-oxodithioesters as synthons have been reported by the same group[23]. The piperidine mediated condensation of β-oxodithioesters **97** with salicylaldehyde **98** or substituted 2-hydroxybenzaldehyde afforded the corresponding 2H-chromene-2-thiones **99** under solvent-free conditions (**Scheme 27**).



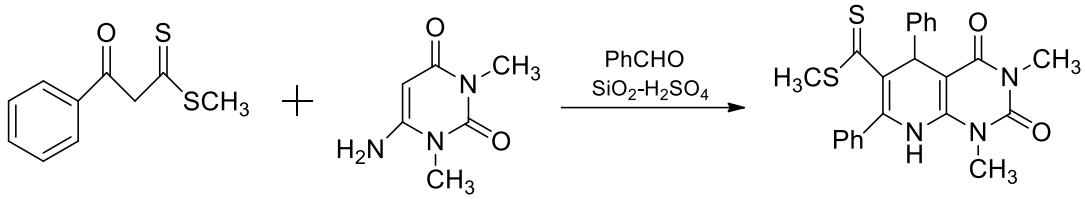
94 **95** **96**

Scheme 26

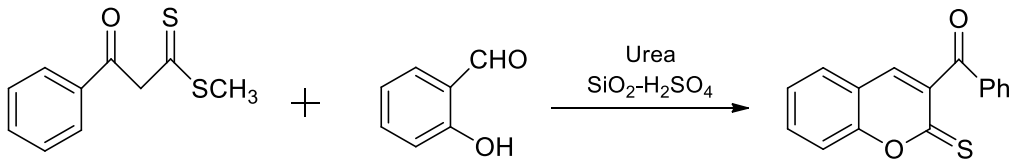


97 **98** **99**

Scheme 27



100 **101** **102**

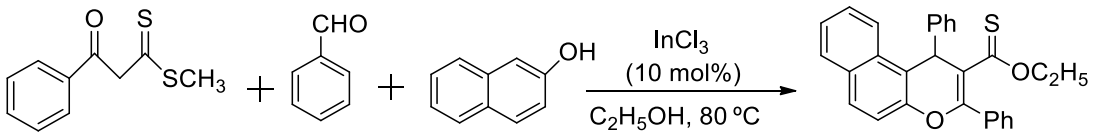


103 **104** **105**

Scheme 28

Nandi *et al*. developed diversity oriented synthesis (DOS) of bioactive heterocyclic frameworks such as dihydropyrimidinones, dihydropyridopyrimidinones and 3-aroyl/heteroaroyl-2H-chromen-2-thiones using β-oxodithioesters as synthons[21]. Three component cyclocondensation reaction of β-oxodithioesters **100**, aromatic aldehyde and 6-amino-1, 3-dimethyluracil **101** in the presence of SiO_2-H_2SO_4 afforded dihydropyridopyrimidinones **102**. On the other hand, when β- oxodithioesters **103**, salicylaldehyde **104** and urea were allowed to react under similar reaction conditions yielded 3-aroyl/heteroaroyl-2H-chromen-2-thiones **105** (**Scheme 28**).

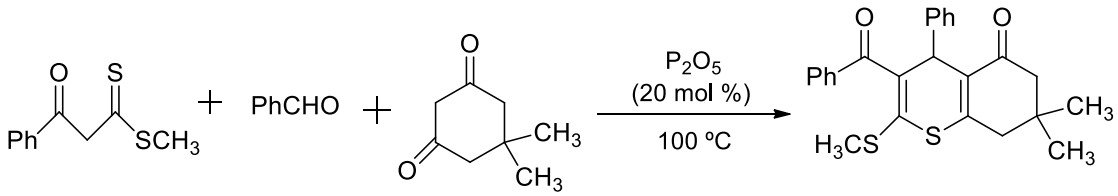
Samai *et al.* reported an efficient and facile regioselective synthetic method for 4H-benzo[f] chromenes from β- oxodithioesters[24]. In this protocol, β- oxodithioesters **106** upon reaction with aromatic aldehyde **107**, β-naphthol **108** and primary alcohols in the presence of $InCl_3$ undergo one-pot four component coupling reaction along with trans esterification yielding 4H-benzo[f] chromenes **109** (**Scheme 29**).



106 **107** **108** **109**

Scheme 29

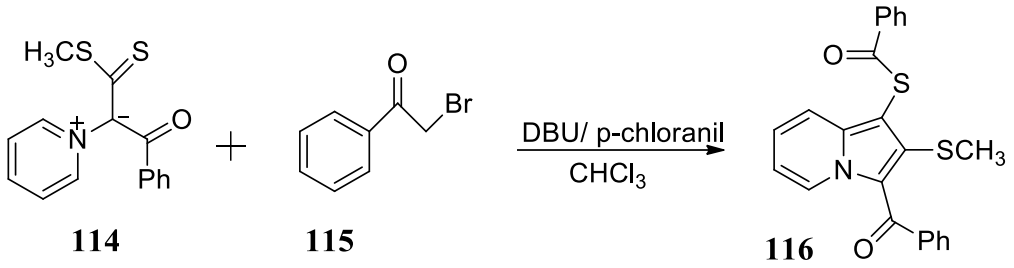
Chowdhury *et al.* reported an efficient regioselective one-pot synthetic method for 4-aryl-3-aroyl-2-methylsulphanyl-4,6,7,8-tetrahydrothiochromene-5-one from β-oxodithioesters. Here, β-oxodithioester **110** was treated with aldehyde **111** and cyclic 1,3-diketones **112** in the presence of P_2O_5 under solvent-free conditions when Knoevenagel coupling reaction and subsequent Michael addition occurs leading to the formation of two C-C bonds, one C-S bond and one stereo centre resulting in the target molecule **113**[25] (**Scheme 30**).



110 **111** **112** **113**

Scheme 30

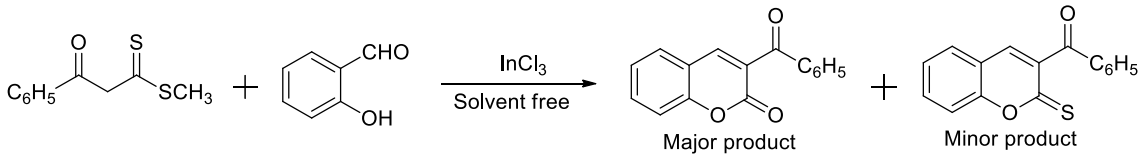
Kakehi *et al.* succeeded in synthesising substituted indolizine **116** by the DBU/ρ-chloranil catalysed reaction between pyridine substituted β-oxodithioesters **114** and 2-bromoacetophenone **115** in chloroform[26] (**Scheme 31**).



114 **115** **116**

Scheme 31

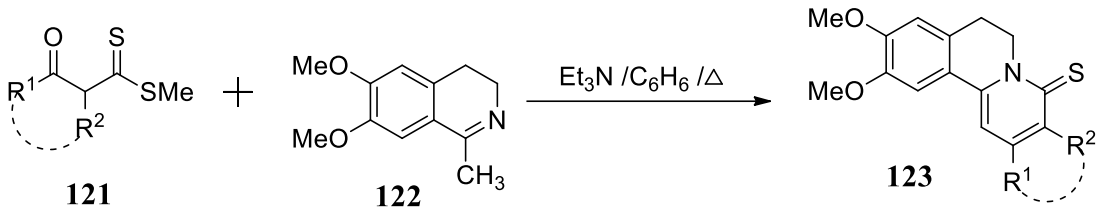
One-pot solvent-free synthesis of coumarin derivatives **119** as well as substituted 2H-chromene-2-thione **120** by the indium trichloride mediated condensation of β-oxodithioesters **117** and salicylaldehyde **118** has been reported by Singh and coworkers[27]. Urea acting as a promotor play a major role in the selectivity of the reaction. In the presence of urea, the product obtained was exclusively chromene-2-thione **120**. Whereas, in the absence of urea the major product obtained was coumarin derivatives **119** along with chromene-2-thione **120** as a minor product (**Scheme 32**). The chromene-2-thiones were less toxic to human beings and were found to exhibit cytotoxicity and antileishmanial activity[28].



117 **118** **119** **120**

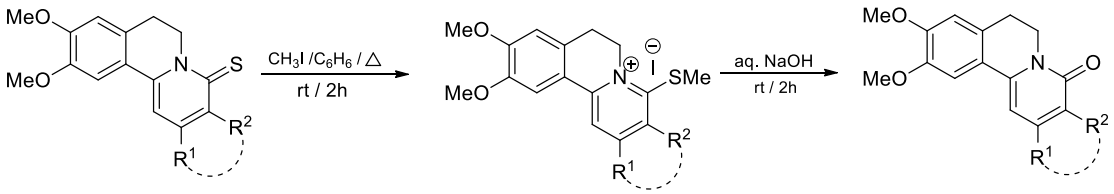
Scheme 32

Junjappa *et al.* developed an efficient synthetic protocol for 2,3-substituted benzo[a]quinolizine-4-thiones **123** via ring annulation of cyclic and acyclic β-oxo dithioesters **121** with 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline **122**. The ring annulation reaction was carried out in the presence of triethylamine in refluxing benzene (**Scheme 33**). Junjappa and coworkers successfully converted the benzo[a]quinolizine-4-thiones **123** to benzo[a]quinolizine-4-ones **125**. The methodology of this transformation involves alkylation of benzo[a]quinolizine-4-thiones **123** using methyl iodide to get benzo[a]quinolizinium salts **124** which was then subjected to dethiomethylative hydrolysis to afford benzo[a]quinolizine-4-ones **125**[29] (**Scheme 34**).



121 **122** **123**

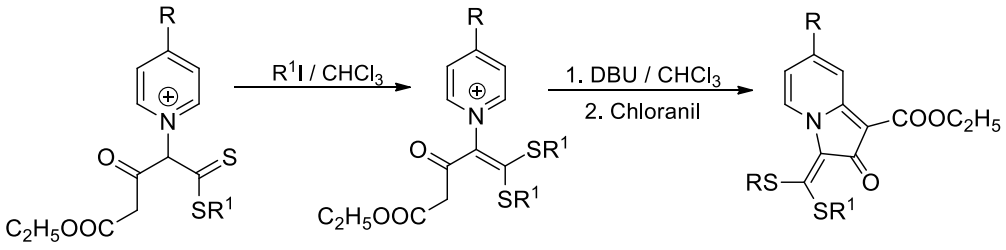
Scheme 33



123 **124** **125**

Scheme 34

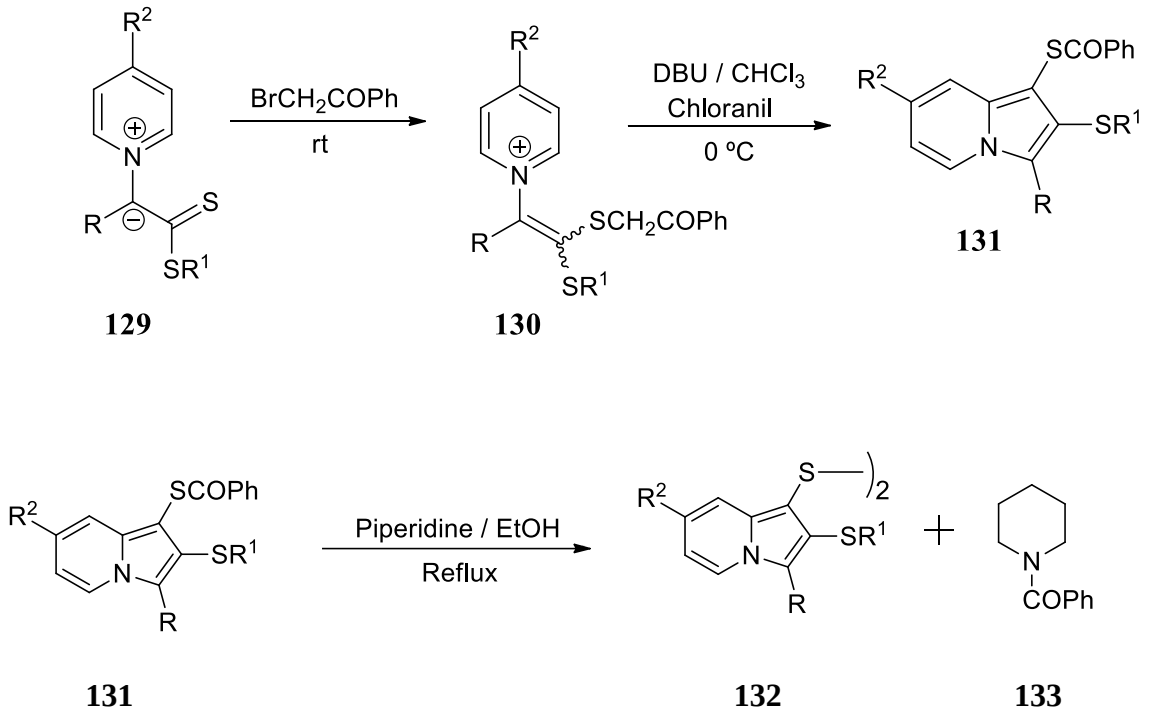
Kakehi *et al.* reported the synthesis of indolizinones from pyridinium salts of dithioesters[30]. In this synthetic protocol, they converted the pyridinium salts of dithioesters **126** to corresponding dithioacetals **127** by treatment with methyl/ethyl iodide. This was followed by the treatment with DBU/$CHCl_3$ and the subsequent addition of chloranil to afford indolozinones **128** (**Scheme 35**). The influence of water, base, solvents and additives in this reaction was investigated. It was found that the presence of water resulted in the formation of side products. Trifluoroacetic acid was proved to be the best additive for the synthesis of indolizinones.



126 **127** **128**

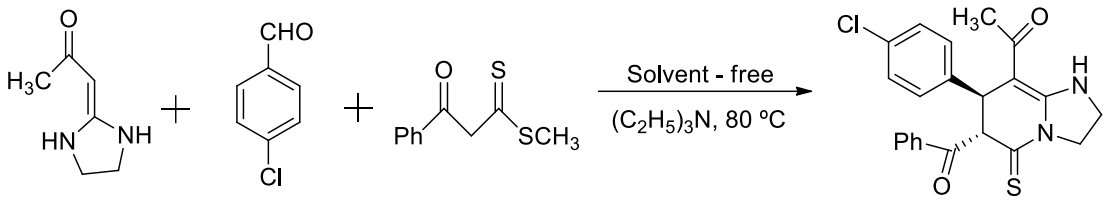
Scheme 35

Through another synthetic approach, Kakehi and co-workers succeeded in synthesising bis(indolizin-1-yl)disulphide from pyridinium salts of β-oxodithioesters[26]. In this method, pyridinium salts of β-oxodithioesters **129** were converted to 1-(benzoylthio)indolizines **131** by treatment with DBU and chloranil using chloroform as solvent. The synthesised1-(benzoylthio)indolizines **131** were transformed to bis(indolizin-1-yl)disulphide **132** upon treatment with piperidine in refluxing ethanol (**Scheme 36**).



Scheme 36

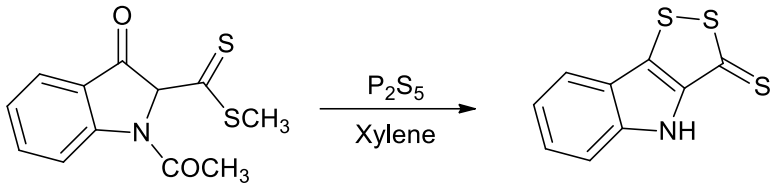
A highly efficient and regioselective green synthetic protocol has been developed for substituted imidazo[1,2-a]pyridine by Li and co-workers[31]. The synthesis involves triethylamine catalysed solvent-free annulation of heterocyclic ketene aminals **134**, aldehydes **135** and β-oxodithioesters **136** (**Scheme 37**). This one-pot three component reaction is an easy access to the imidazo[1,2-a]pyridine **137**.



134 **135** **136** **137**

Scheme 37

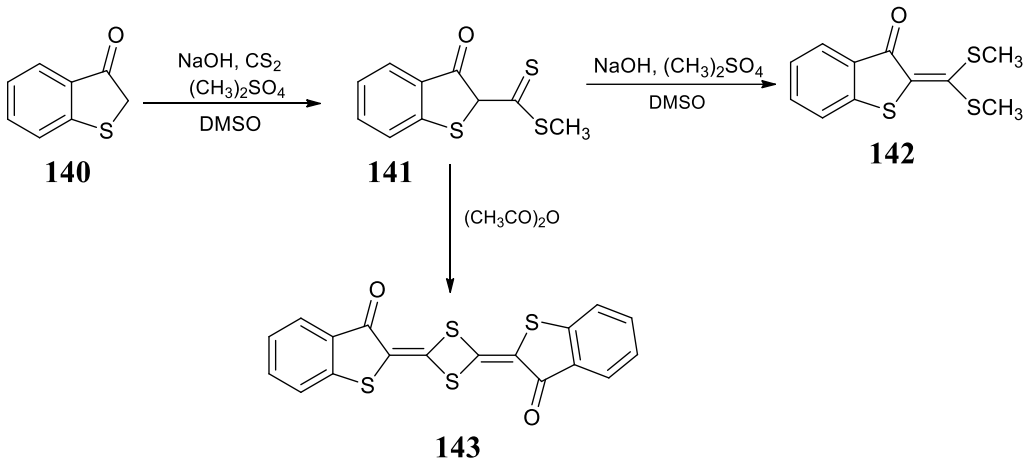
Tominaga and co-workers succeeded in synthesising a system of fused tricyclic indole from β-oxodithioesters derived from N-acetyl indoline-3-one **138**[32]. In this method, the β-oxodithioester upon reaction with phosphorous pentasulphide in xylene at refluxing temperature was transformed to fused tricyclic [1, 2]dithiolo[4,3-b]indole-3-(4H)-thione **139** (**Scheme 38**).



138 **139**

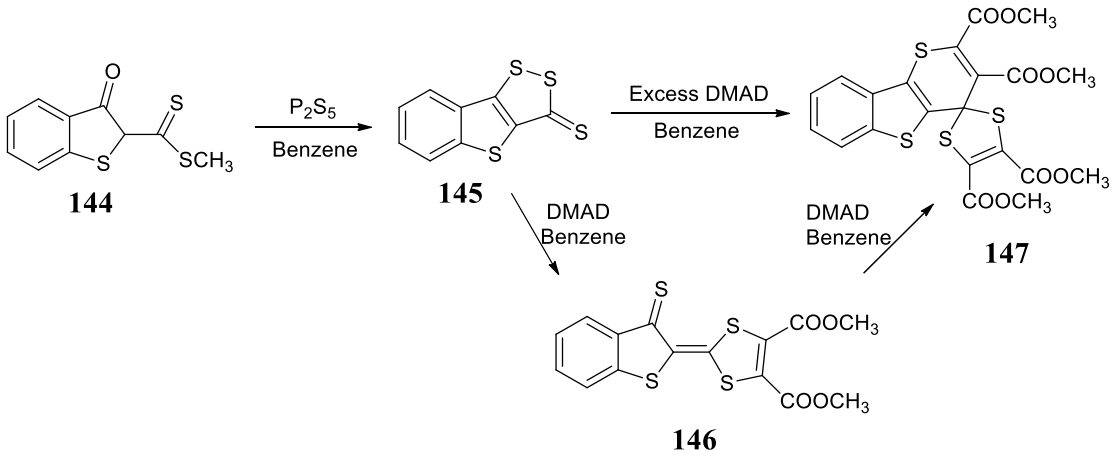
Scheme 38

The heterocyclic active methylene compound benzothiophene-3(2H)-one when treated with carbon disulphide and dimethyl sulphate in the presence of sodium hydroxide in DMSO gets converted to the corresponding β-oxodithioester. Tominago *et al.* reported the synthesis of a series of fused spiro heterocyclic systems containing sulphur using the β-oxodithioester derived from benzothiophene-3(2H)-one **140**[33]. The alkylation of the β-oxodithioester **141** using dimethyl sulphate and sodium hydroxide leads to the formation of ketenethioacetal derivative, 2-bis(methylthio)methylenebenzothiophen-3(2H)-one **142**. Whereas the β-oxodithioester **141** upon reaction with acetic anhydride afforded disarium type compound 2,4-bis(3-oxo-2,3-dihydrobenzothiophen-2-ylidene)-1,3-dithiacetane **143** (**Scheme 39**).



Scheme 39

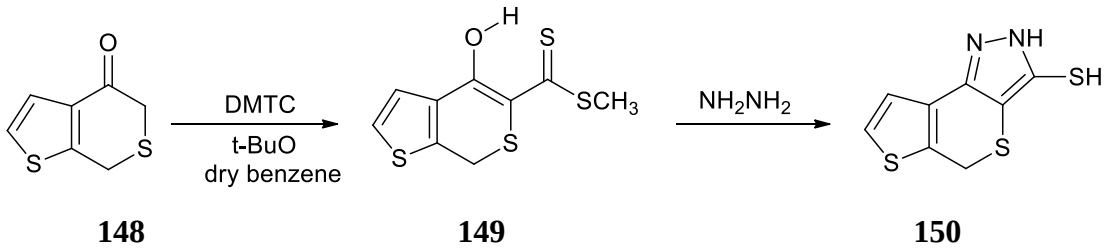
Tominago and co-workers further treated the β-oxodithioester obtained from benzothiophene-3-one **144** with phosphorus pentasulphide to afford 1,2-dithiolo[4,3-b]benzothiophen-3-thione **145**[33]. This compound formed, being a trithione derivative, when treated with dipolarophilic reagents such as dimethyl acetylenedicarboxylate (DMAD) furnished 1,3-dipole adduct **146**. Since the 1,3-dipole adduct thus formed a diene system containing a thioketone group, upon reaction with DMAD undergo Diels-Alder reaction affording 1,4-cycloaddition adduct **147**. The same 1,4-cycloaddition adduct **147** can also be obtained by the addition of an excess of DMAD to 1,2-dithiolo[4,3-b] benzothiophen-3-thione **145** (**Scheme 40**).



Scheme 40

Synthesis of a number of tricyclic compounds via annulation of nitrogen heterocycles onto thienothiopyran has been reported by De *et al.* Thienothiopyran **148** was converted to the corresponding β-oxodithioester **149** by treatment with dimethyl

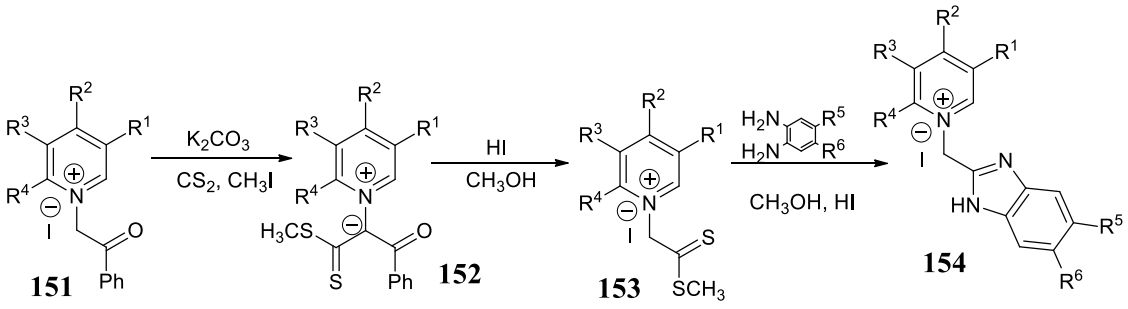
trithiocarbonate and potassium tert-butoxide in dry benzene. Further treatment of these β-oxodithioesters **149** with hydrazine hydrate in refluxing ethanol yielded the tricyclic compounds containing a thiophene ring, thiopyran ring and pyrazole ring **150**[34] (**Scheme 41**).



148 **149** **150**

Scheme 41

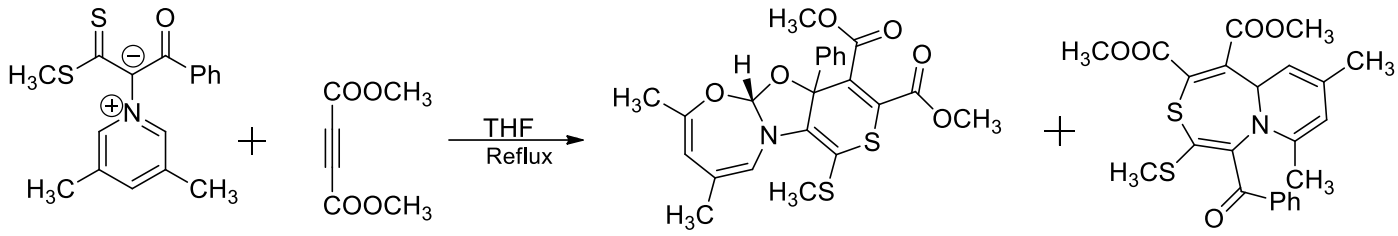
Cuardo *et al.* synthesised benzimidazole derivatives from N-[(methyithio) thiocarbonylmethyl] azinium salts[35]. Pyridinium salts **151** were converted to corresponding β-oxodithioesters **152** by treatment with carbon disulphide and methyl iodide in the basic medium. The conversion of pyridinium slats of β-oxodithioesters **152** into benzimidazole **154** derivatives was carried out by removal of benzoyl moiety using hydroiodic acid in methanol, followed by treatment with o-phenylenediamine, methanol and hydroiodic acid (**Scheme 42**).



151 **152** **153** **154**

Scheme 42

Kakehi and coworkers reported the unexpected formation of thiino-[3',4': 4,5]oxazolo[1,3-b]-[1,3]oxazepine derivatives[36]. Pyridinium-2-alkylthio-1-benzoyl-2-thioxoethylides **155** when refluxed with dimethyl acetylenedicarboxylate **156** in THF yielded dimethyl-2-alkylthio-4a-phenyl-4aH **157** and 5aH-thiino-[3',4':4,5]oxazolo[1,3-b][1,3] oxazepine-3,4-dicarboxylates **158** (**Scheme 43**).



155 **156** **157** **158**

Scheme 43

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