CHAPTER III
CYCLOAROMATIZATION OF α-OXOKETENE DITHIOACETALS WITH 3-METHYL-5-LITHIOMETHYL ISOXAZOLE: A NEW GENERAL METHOD FOR THE SYNTHESIS OF SUBSTITUTED AND ANNELATED 1,2-BENZISOXAZOLES*

III.1 INTRODUCTION

The α-oxoketene dithioacetals have been a subject of intense investigation in this laboratory. They possess 1,3-electrophilic centres with differential electrophilicity and undergo either 1,2- or 1,4-regioselective additions depending on the nature of the nucleophiles. The differential reactivity pattern has been fully exploited by a number of workers leading to many novel transformations.

involving new C-C bond formation. Thus the organomanganese reagents have been shown to undergo both 1,2- or 1,4-addition, whereas various organolithium compounds exhibit high regioselectivity yielding compounds arising through 1,2-additions. Also the organocuprates have been shown to add in a regioselective 1,4-manner.

The foregoing discussion displays the reports on C-C bond forming reactions via α-oxoketene dithioacetals, which results in ring forming reactions leading to aromatic and heteroaromatic systems. The general strategy involves 1,2-addition of a suitable carbon nucleophile to α-oxoketene dithioacetals to give the allylic alcohols which on subsequent Lewis acid assisted cationic cyclization form six membered ring followed by aromatization. The overall reaction can be generally termed as aromatic annelation or cycloaromatization. The present method involves the union of two three atom fragments one with 1,3-electrophilic and other with 1,3-nucleophilic centres.

The α-oxoketene dithioacetals were shown to undergo facile 1,2-reduction with sodiaborohydride to give the intermediate alcohols which undergo facile solvolysis in the presence of boron trifluoride etherate to give the corresponding ene esters. The ene ester synthesis was further extended to the addition of alkyl and arylmagnesium halides to study the scope of the method. Interestingly when allylmagnesium bromide was added to α-oxoketene dithioacetals, exclusive 1,2-addition took place to afford the corresponding alcohol acetals in nearly quantitative yields, which were shown to undergo intramolecular cationic cycloaromatization to the aromatic compounds. The
reaction appears to proceed through intramolecular \( \pi \)-participation of the allylic double bond to form a cationic species which on elimination of methyl mercaptan yield the aromatized product 3 (Scheme 1). The formation of these benzenoids from the \( \omega \)-oxoketene dithioacetals derived from wide structural variants of active methylenes ketones, provides unique one pot reaction to yield regiospecifically substituted aromatic ring systems. The method has been shown to be general for both aliphatic and aromatic substituents in the open-chain precursors. The oxketene dithioacetals derived from fused ring systems yield the corresponding condensed aromatic systems in identical yields. Similarly the reaction of \( \omega \)-cinnamoylketene dithioacetals 4 with allyl and crotyl magnesium bromide is also reported to give regiospecifically substituted trans stilbenes 5 in good yields (Scheme 1)\(^7\). This approach of stilbene synthesis is of considerable synthetic importance for it allows one of the benzene rings with appropriate, substituents suitably placed in the open-chain precursors.

A benzoannelation approach for the synthesis of fused thioreosorcinol dimethylethers is also reported\(^8\) by the reaction of propargyl magnesium bromide with \( \omega \)-oxoketene dithioacetals 1 prepared from cyclic ketones. It was considered of interest that the cyclization proceeds by the intramolecular participation of the propargyl triple bond in the carbinol acetal 6 with concommitant attack of methanol on the incipient vinyl cation, followed by loss of methyl mercaptan to yield the thioreesorcinol dimethylethers 7 in good yields (Scheme 2). However when the oxketene dithioacetal derived from cyclopentanone 8 was reacted with
Scheme 1
1. \[ \equiv-\text{CH}_2\text{MgBr} \] in Ether

\[ \text{MeOH} \]

\[ \text{R}^1\text{H} \]

\[ \text{R}^2\text{Me} \]

\[ \text{MeOH} \]

\[ \text{BF}_3\text{Et}_2\text{O} / \text{MeOH} \]

\[ \text{BF}_3\text{Et}_2\text{O} / \text{MeOH} \]

\[ \text{H}_2\text{O} / \text{MeSH} \]

1-6, 7, \( \text{R}^1=\text{R}^2=(\text{CH}_2)_n, n=4,5; \text{R}^3=\text{R}^2=\text{R}_3=\text{H, Me, MeO} \)

\[ \text{R}^1=\text{R}^2=\text{C}_6\text{H}_{12-x}(\text{CH}_2)_n, n=1,2, x=0, S \]

\[ 1. \equiv-\text{CH}_2\text{MgBr} \]

\[ 2. \text{BF}_3\text{Et}_2\text{O} / \text{MeOH} \]

\[ \text{CO}_2\text{Me} \]

\[ \text{CO}_2\text{Me} \]

Scheme-2
propargylmagnesium bromide, the corresponding allyl alcohol though formed in quantitative yield failed to undergo the described cationic aromatic annelation to give the corresponding indanes, instead the corresponding propargyl ene esters arising from solvolysis of mercaptal functionality was obtained. Similarly the oxoketene dithioacetal derived from indanone underwent addition with propargylmagnesium bromide to yield the ene ester. The failure of the cycloaromatization in these systems appears to be due to unfavourable geometry of the five membered rings.

Interestingly the idea of acetonitrile nucleophile participation through the terminal double bond was extended usefully for the synthesis of pyridine derivatives. Thus lithioacetonitrile underwent smooth 1,2-addition to to give the corresponding allyl alcohol in nearly quantitative yields. The alcohol thus obtained underwent smooth intramolecular cyclization through the formation of new C-N bond with concurrent migration of thiomethyl group to yield the corresponding 2,6-bis(methylthio)-3,4-substituted or annelated pyridine derivatives (Scheme 3), in high yields which on Raney Nickel desulfurization yielded the parent compound in quantitative yield. The method has been extended to a number of substituents to prove the efficacy of its synthetic potential.

The reaction of benzylmagnesium chloride with oxoketene dithioacetals was considered of special interest since the corresponding allyl alcohol should undergo cycloaromatization through the participation of aromatic ring double bond yielding corresponding naphthalene and other fused ring systems. However when benzylmagnesium halide was reacted with
it underwent initial 1,4-conjugate addition to yield the corresponding more reactive ketone 16, followed by 1,2-addition, finally leading to the formation of naphthoannelated product 18 through 17 with benzyl group as substituent in place of thiomethyl group. This method is shown to be of general application, not only to naphthalene derivatives but also to many polycyclic hydrocarbons depending on the structure of 1 (Scheme 4)\(^{10}\).

The aromatic annelation was further extended to construct bridge head nitrogen compounds of the general formula 21 (Scheme 5). Thus 2-picolyllithium was selected as representative of lithio-3-azaallyl system with oxoketene dithioacetals, to enhance the scope of the method for aromatic annelation and further extend it to important heteroaromatic annelation. Thus 2-picolyllithium underwent facile 1,2-addition with 1 to give the expected allyl alcohols 19 in nearly quantitative yields (Scheme 5)\(^{11}\). These carbinol acetics when directly subjected to cycloaromatization in the presence of boron trifluoride etherate formed the quinolizinium ring systems 20 involving new C-N bond formation in high yields. Similarly when 2-lithiomethyl quinoline was reacted with 1 the corresponding quinolizinium fluoroborate salt 21 was obtained in high yields\(^{12}\). The generality of the method has been shown to be applicable to many structural variants of oxoketene dithioacetals.

Interestingly unlike benzylmagnesium chloride, when oxo-naphthylmethylmagnesium halide was reacted with 1, only 1,2-adduct 22 was formed in high yields which underwent facile boron trifluoride assisted ring
1. $C_6H_5CH_2MgCl$ addition

1,4-addition

1. $C_6H_5CH_2MgCl$ addition

1,2-addition

1. $C_6H_5CH_2MgCl$ addition

1,2-addition

$-\text{H}_2\text{O}$

$-\text{MeSH}$

$R^1 = \text{aryl, 2-naphthyl, 2-furyl, 2-thienyl}$, $R^2 = \text{H}$

$R^1 = R^2 = -(CH_2)_n$, $n = 3,4,5$

$R^1 = R^2 = R^3 - \text{(CH}_2\text{)}_n$, $n = 1,2$, $R^3 = \text{H, MeO}$

$R^1 = R^2 = \text{aryl} - \text{(CH}_2\text{)}_n$, $X = \text{O, S}$, $n = 1,2$

Scheme-4
closure to yield the corresponding thiomethylphenanthrene $^{23}$ in high yields (Scheme 6)$^{13}$. Thus the oxoketene dithioacetals $^1$ are of considerable synthetic importance as useful precursors, for the synthesis of regiospecifically substituted phenanthrene derivatives in one pot synthetic operations. When the reagent was reacted with oxoketene dithioacetal derived from tetralone $^{24}$ the corresponding dihydro-1,2-naphthophenanthrene $^{25}$ was obtained in high yields. These reactions amply demonstrate that the aromatic annelation is possible to construct benzenoids, naphthalenes, anthracenes, phenanthrenes, benzanthracenes, naphthophenanthrenes and many other condensed aromatic systems starting from appropriately substituted oxoketene dithioacetals.

In the proceeding examples it has been shown that the aromatic or heteroaromatic annelation is possible for the construction of the aromatics and heteroaromatics and its possible extension to construct aromatic ring over the five membered heterocycles would provide an alternative efficient approach for the synthesis of important class of benzo heterocycles. The reported approaches for the synthesis of this class of compounds generally involve the construction of five membered heterocycles over the preconstructed benzene ring. Though this approach has been extensively investigated it requires often highly functionalized benzene derivatives, which are not always easy to make in overall high yields. Thus it was contemplated to extend the aromatic annelation approach to yet another broad based plan to explore the possibilities of annelating the aromatic ring over the preconstructed five membered heterocycles. Such an approach would
Scheme 6

1. BrMgH₂C → 1,2-addition

2. BF₃·Et₂O → C₆H₆

Ar = C₆H₅, 4-MeC₆H₄, 4-ClC₆H₄

1,2,23, Ar = C₆H₅, 4-MeC₆H₄, 4-ClC₆H₄

BF₃·Et₂O
C₆H₆
provide possibly easy general methods for the synthesis of benzoheterocycles. As a part of this programme the reaction of 3-methyl-5-lithiomethylisoxazole with \( \Delta \)-oxoketene dithioacetals 1 has been investigated to yield the corresponding substituted and annelated 1,2-benzisoxazoles in high yields. The broad approach envisaged in the present investigation is described in Scheme 7.

![Scheme 7]

However the success of the general approach envisaged in the present investigation will depend upon the availability of lithiomethyl heterocycles of the general formula.

\[
\begin{array}{c}
\text{X} \\
\text{CH}_2\text{Li}
\end{array}
\]

; \( X = O, N, S \)

A few classical approaches indeed are reported in the literature for the construction of benzene ring over the five membered heterocycles. For example the reaction of 2-lithio-N-methyl pyrrole 28 with functionalized ketals to yield the corresponding alcohols 29 (Scheme 8) have been shown to afford after acid assisted ring closure to the 4-(3-methyl-2-butenyl) indole 30. Similarly the grignard reagent 32 was shown to react with 2-aryltiophenes and the resulting ketal alcohols 33 were found to undergo acid catalyzed ring closure to
yield the corresponding benzo[b] thiophenes 34 in good yields (Scheme 8)\textsuperscript{15}.

III.2 RESULTS AND DISCUSSION

In the present investigation 3-methyl-5-lithiomethyl isoxazole was selected as an allylanion system and as a representative of the 5-membered heterocycles in general. Thus anion 35 underwent facile 1,2-addition to yield the corresponding allyl alcohol 36 in near quantitative yields and the alcohol was insitu cycloaromatized in the presence of boron trifluoride etherate by the elimination of methylmercaptan from 37 to yield the corresponding benzisoxazole 38 (Scheme 9). Results of the detailed investigation are described herein.

When 1a was reacted with 3-methyl-5-lithiomethyl isoxazole 35 at \(-78^\circ\text{C}\), the corresponding carbinol acetal 36 was formed in quantitative yield which was directly subjected to cyclization in the presence of boron trifluoride etherate in refluxing benzene to give the colourless crystalline product characterized as 3-methyl-4-methylthio-6-phenyl-1,2-benzisoxazole 38a in 73\% yield (Scheme 10). The structure of this compound was assigned on the basis of analytical and spectral data. Thus it was analyzed for C\textsubscript{15}H\textsubscript{13}NOS and its mass spectrum displayed molecular ion peak at m/z 255 (M\textsuperscript{+},100\%). Its infrared spectrum (KBr) exhibited bands at 1600, 1566, 1425, 1388, 1345 cm\textsuperscript{-1}, where the 1600 band was due to \textit{C=\textit{N}} group. The \textit{\textsuperscript{1}H n.m.r. (CCl\textsubscript{4})} spectrum of 38a showed a singlet (3H) at \(\delta\) 2.50 which was assigned to the methyl protons. The signal at \(\delta\) 2.68 appeared as a singlet (3H) and was attributed to the methylthio protons. The
broad singlet at $\delta$7.02 was assigned to the $H$-7 proton whereas the aromatic protons appeared as broad multiplet between $\delta$7.20-7.67 (6H). The structure of 38a was also confirmed by its $^{13}$C n.m.r. spectrum which showed signals at $\delta$11.47 (CH$_3$), 17.23 (CH$_3$S), 103.80 (C-7), 114.59 (C-5), 125.45, 127.24, 128.35 (CH, arom), 128.36, 140.20, 142.66, 142.41 (quaternary C), 159.71 (C-3), 168.07 (C-8). Thus the structural assignment of 38a was fully confirmed. The method was found to be quite general and a number of benzisoxazoles 38b-h were obtained in 54-68% overall yields by reacting 35 with the corresponding $\omega$-oxoketene dithioacetals 1b-h. The structures of all these benzisoxazoles were fully confirmed by their analytical and spectral data and are given in the experimental section.

The oxoketene dithioacetals derived from ethyl methyl ketone 1i and propiophenone 1j failed to yield the desired alcohols 36i and 36j and therefore corresponding benzisoxazoles 39i and 39j could not be isolated. It appears that the $\omega$-methyl protons of 1i and 1j undergo rapid competitive deprotonation to give the allyl anions that do not participate in the reaction sequence (Scheme 10). However, the cyclic oxoketene dithioacetals also underwent the sequence of reaction to yield the corresponding benzisoxazoles. Thus oxoketene dithioacetal 40 derived from cyclohexanone reacted with 3-methyl-5-lithiomethylisoxazole 35 and underwent cycloaromatization to yield the corresponding 3-methyl-4-methylthio-5,6,7,8-tetrahydronaphtho[b]isoxazole 41 in 65% yield (Scheme 11). The analytical and spectral data of 41 are in conformity with the assigned structure. Similarly the oxoketene dithioacetals 42 derived from cycloheptanone also reacted with 35 to yield 43 in 67%
yield. The spectral and analytical data in favour of 43 were given in the experimental section. The \( \alpha \)-oxoketene dithioacetal 8 derived from cyclopentanone though yielded the alcohol 44, failed to undergo cycloaromatization under the described conditions to yield the corresponding isoxazole 45. No well defined compound could be isolated from the reaction mixture (Scheme 11). However in an analogous reaction condition oxoketene dithioacetal derived from indanone 10 did react with 35 and underwent cyclization to yield the corresponding fused ring isoxazole 46 in 57% yield. The analytical and spectral data of 46 are in agreement with the assigned structure (experimental). Similarly the oxoketene dithioacetals 24a-b also reacted with isoxazole to yield the corresponding 5,6-annelated benzisoxazoles 47a-b in 76% and 78% yields respectively (Scheme 12). The analytical and spectral data of these compounds are described in the experimental section.

The oxoketene dithioacetals 48 and 50 similarly yielded fused benzisoxazoles 49 and 51 in 69% and 81% yields respectively (Scheme 13) whose analytical and spectral data are described in experimental section.

In a few cases the validity of benzoannelation over the isoxazole ring was examined on \( \beta \)-methylthio-\( \alpha \)-\( \beta \)-unsaturated enones 52 so that the product isoxazoles are formed without thiomethyl group on the ring. Thus the oxoketene dithioacetals 1a-c were subjected to Nickel boride reduction as reported in one of our earlier papers 16 to yield the corresponding \( \beta \)-methylthio-\( \alpha \)-\( \beta \)-unsaturated ketones 52a-c in 60-70% overall yields (Scheme 14). These compounds were confirmed for their
Scheme-12

1. 35
2. BF$_3$Et$_2$O/C$_6$H$_6$

\[ \text{R} \rightarrow \text{R} \]

24, 47: \( g, R = H \)
\( b, R = \text{MeO} \)
Scheme 14

Naphthalene derivatives

1. $\text{NMe}_2$\textsubscript{2} $\rightarrow$ 2. BF$_3$Et$_2$O / C$_6$H$_6$

1. $\text{NaBH}_4$/ NiCl$_2$ $\rightarrow$ 2. BF$_3$Et$_2$O / C$_6$H$_6$

1. 1.5, 2.5 $\rightarrow$ 2. $\text{NaBH}_4$/ NiCl$_2$

Naphthalene derivatives with different substitutions on the aromatic rings.
structural authenticity and reacted with 3-methyl-5-lithiomethyl isoxazole and the corresponding sulfur free benzisoxazole 53a-c were obtained in 70-90% overall yields. The absence of thiomethyl singlet at $\delta 2.68$ fully confirmed the formation of sulphur free benzisoxazoles. The analytical and spectral data of these compounds are described in the experimental section. Similarly 54a-b were formed from 24a-b in 75-85% yields as per reported method and when reacted with isoxazole 35 the corresponding 5,6-annellated benzisoxazoles 55a-b were obtained in 85% and 88% overall yields. The absence of thiomethyl signal and the other spectral data (experimental) confirmed the formation of benzisoxazoles.

The approach of stilbene synthesis was extended to benzisoxazole synthesis as depicted in Scheme 15. Thus the cinnamoylketene dithiaoacetals 4a was reacted with isoxazole 35 to yield the corresponding allyl alcohol 56a in quantitative yield and cyclized in the presence of boron trifluoride etherate to yield the corresponding 6-styryl benzisoxazole 57a in 68% yield. The structure of 57a was confirmed from its analytical and spectral data. Thus it was analyzed for C$_{17}$H$_{15}$NOS and its mass spectrum showed the molecular ion peak at m/z 281 (M$^+$, 100%). The spectral data of 57a were described in experimental section. The 6-styryl benzisoxazoles 57b-g were also obtained similarly from the corresponding cinnamoylketene dithiaoacetals 4b-g in 60-70% overall yields (Scheme 15). The structures of these compounds were confirmed from their analytical and spectral data (experimental).

Interestingly, although dienoylketene dithiaoacetals 58 failed to undergo cyclocondensation with allylmagnesium halide the 3-methyl-5-lithiomethyl
Scheme 15

4, 56, 57 a, Ar = C6H5
b, Ar = 4-MeC6H4
c, Ar = 4-(MeO)C6H4
d, Ar = 3, 4, 5-(MeO)2C6H4
e, Ar = 3, 4, 5-(MeO)3C6H2
f, Ar = 4-(Cl)C6H4
g, Ar = [Diagram of molecular structures]
isoxazole 35 reacted smoothly with 58a-b in near quantitative yields followed by cyclocondensation to yield the corresponding 6-(4-aryl-1,3-butadienyl)benzisoxazoles 59a-b in 55% and 65% yields respectively. The structural assignment of both 59a and b are in agreement with the spectral data and are described in experimental section. The 6-(6-phenyl-1,3,5-hexatrienyl)benzisoxazole 61 was similarly obtained by reacting 35 with 60 (Scheme 16). The structure of 61 was confirmed by its analytical and spectral data.

III.3 CONCLUSION

Thus, it has been demonstrated that the oxoketene dithioacetals with diverse structural features react with 3-methyl-5-lithiomethyl isoxazole resulting in the synthesis of hitherto unreported benzisoxazoles in high yields. Starting from benzene derivatives, apparently the synthesis of these benzisoxazoles is uneconomic, tedious and involve many steps with possible overall poor yields of the product benzisoxazoles. The present method therefore makes a definite contribution for the synthesis of benzisoxazoles in high yields in one step from oxoketene dithioacetals. Conceptually this approach can be extended to any five membered heterocycles to build aromatic ring over five membered heterocycles. However, the success and the extension of this methodology to other five membered heterocycles largely depends upon the possibility of regiospecific generation of lithiomethyl anions which are not always easy to generate since these heterocycles undergo ring deprotonation in preference to methyl side-chain deprotonation. The further work in this direction is in progress in our laboratory.
III.3 EXPERIMENTAL

Melting points were determined on a Thomas Hoover melting point (capillary method) apparatus and are uncorrected. $^1$H n.m.r. spectra were recorded on a Varian EM-390, 90 MHz spectrometer and the chemical shift values are expressed as $\delta$(ppm) downfield from Me$_4$Si as internal standard. $^{13}$C n.m.r. spectra were recorded on a 67.89 MHz Brucker WH-270 spectrometer. I.r. and mass spectra were recorded on a Perkin-Elmer 297 spectrometer and a Jeol D-300 mass spectrometer respectively. Carbon, hydrogen and nitrogen elemental analysis were done at RSIC, Central Drug Research Institute, Lucknow, India.

Starting Materials

The commercial samples of acetone, acetophenone, 4-methylacetophenone, 4-methoxyacetophenone, 4-chloroacetophenone, 2-acetyl-naphthalene, 2-acetylfuran, 2-acetylthiophene, cyclopentanone, cyclohexanone, cycloheptanone, 1-tetralone, 6-methoxytetralone, benzaldehyde, 4-methylbenzaldehyde, 4-methoxybenzaldehyde, piperonaldehyde were purified before use wherever necessary. The cyclic ketones i.e. 1-indanone$^{17}$, 1-benzsuberanone$^{18}$, benzthiopenone$^{19}$, 4-methoxycinnamaldehyde, 5-phenyl-2,4-pentadienal$^{20}$, and 3,5-dimethylisoxazole$^{21}$ were prepared according to the reported procedure.

The known $\alpha$-oxoketene dithioacetics 1a–j, 8, 10, 24, 40, 42, 48, 50, $\beta$-methylthio-$\alpha$–$\beta$-unsaturated enones 52a–c, 54a–b, 1,1-bis (methylthio)-1,4-pentadiene-3-ones 4a–g, 1,1-bis(methylthio)-7-aryl-1,4,6-heptatriene 3-ones 58a–b and 1,1-bis(methylthio)-
9-aryl,1,4,6,8-nonatetraene-3-one \(\text{9a,16,22-27}\) were prepared according to the reported procedures given below.

**General method for the preparation of \(\omega\)-oxoketene dithioacetals \((1a-j, 8, 10, 24, 40, 42, 48, 50)\):**

A mixture of ketone (0.2 mol) and carbondisulphide (0.2 mol) was added dropwise to an ice cold and well stirred suspension of sodium \(t\)-butoxide (0.4 mol) in dry benzene (200 ml) and the reaction mixture was allowed to stir at room temperature for 5-6 hrs. Acid free dimethyl sulphate (0.2 mol) was then gradually added with stirring and cooling and the reaction mixture was allowed to stir at room temperature for 6-10 hr. The reaction mixture was poured over ammonium chloride solution (250 ml) and the layers were separated. The aqueous layer was extracted with benzene (100 ml) and the combined benzene extracts were washed with water (4x250 ml), dried (\(\text{Na}_2\text{SO}_4\)) and evaporated. Trituration of the oily residue with hexane gave the dithioacetals as yellow crystalline solid in good yields. The physical and spectral data were compared with that of reported values.

**General method for the preparation of 2-methylthio-1-alkenyl ketones \((52a-c, 54a-b)\):**

To a stirring suspension of nickel chloride hexahydrate (0.16 mol) in ethanol (150 ml), sodium borohydride (0.2 mol) was slowly added (15 min.). Fresh addition was made only when effervescence due to evolution of hydrogen has stopped. The mixture was further stirred for 10 min. and a solution of ketene S,S-acetal \(\text{1} \) (0.06 mol) in ethanol (50 ml) was added to the black suspension and the mixture
was further stirred at room temperature for 10 min. It was then heated under reflux in an oil bath with stirring (9-36 hr), until the starting material has disappeared completely (TLC). The mixture was filtered hot through a sintered funnel and the black residue was washed with boiling chloroform (3x200 ml). The combined filtrate was washed with water (2x300 ml), the organic layer dried with sodium sulphate and evaporated to give a dark brown viscous liquid which was then purified by column chromatography. Elution with hexane/benzene (9:1). The physical and spectral data were compared with that of reported values.

Condensation of α-acylketene dithioacetals with aldehydes; General procedure for the preparation of compounds (4a-g, 58a-b, 60):

To a cooled and stirred solution of sodium ethoxide in ethanol, prepared by dissolving sodium (0.06 mol) in ethanol (30 ml), a solution of the α-acylketene dithioacetal (0.03 mol) and the aldehyde (0.03 mol) in minimum amount of ethanol was added dropwise over a period of 5 minutes. The reaction mixture was brought to room temperature stirred for 4-5 hrs. The mixture was diluted with cold water (100 ml) and the solid separated out was filtered, washed with water (4x100 ml) and dried. The physical and spectral data were found to be in confirmity with that of reported values.

3,5-Dimethyl isoxazole:

To a solution of hydroxylamine hydrochloride (7g) in water (15 ml) in a 100 ml round bottomed flask a solution of acetylacetone (10g) in ethanol (10 ml) was added. The mixture was heated under reflux until a negative ferric chloride test is given (ca 1 hr) and the
reaction mixture was poured into cold water (60 ml). Extracted with ether, dried (Na$_2$SO$_4$), and distilled. B.P. 140-142°C.

Generation and reaction of 3-methyl-5-lithiomethyl isoxazole with oxoketene dithioacetals; General procedure:
To a stirred solution of freshly distilled 3,5-dimethyl isoxazole (0.015 mol) in dry THF (25 ml), butyllithium (0.015 mol) was added under nitrogen atmosphere at -78°C. The solution was stirred for 30 min. and a solution of L (0.01 mol) in THF (25 ml) was added to 35 at -78°C, stirred for 1 hr, slowly warming the mixture to room temperature. The reaction mixture was poured over saturated ammonium chloride solution. The aqueous layer was extracted with ether (2x50 ml) and the combined organic layer was washed with water (100 ml), dried (Na$_2$SO$_4$) and evaporated to give the crude alcohol 36 in nearly quantitative yield.

General procedure for the cycloaromatization of hydroxy dithioacetals; Synthesis of substituted and annelated 1,2-benzisoxazoles (38a-h, 41, 43, 46-47, 49, 51, 53a-c, 55a-b, 57a-g, 59, 61):
To a solution of crude alcohol 36 in dry benzene (50 ml), boron trifluoride etherate (2 ml) was added and the reaction mixture was refluxed with stirring for 1 hr. The reaction mixture was cooled and poured over cold saturated NaHCO$_3$ solution, extracted with chloroform (2x50 ml), washed with water, dried (Na$_2$SO$_4$) and evaporated to give a viscous residue which was purified by passing through silica gel column (hexane as eluent) to give 38 as colourless crystals (chloroform).
The spectral and analytical data of the 1,2-benzisoxazoles are given below.

3-Methyl-4-methylthio-6-phenyl-1,2-benzisoxazole (38a); colourless crystals; yield 73%; m.p. 70°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1566, 1425, 1388, 1345 \text{ cm}^{-1}$; $^1H$ n.m.r. (CCl$_4$): $\delta 2.50$ (s, 3H, CH$_3$); 2.68 (s, 3H, SCH$_3$); 7.02 (brs, 1H, H-7); 7.20-7.67 (m, 6H$_\text{arom}$); $^{13}C$ n.m.r. (CDCl$_3$): 511.47 (CH$_3$); 17.23 (SCH$_3$); 103.80, 114.59 (C-7 and C-5); 125.45, 127.24, 128.35 (CH, phenyl); 128.36, 140.20, 142.66, 142.41 (quaternary C); 159.71 (C-3); 168.07 (C-8). (Found: C, 70.42; H, 5.11; N, 5.44. Calc. for C$_{15}$H$_{13}$NOS (255.31): C, 70.56; H, 5.13; N, 5.48%). m/z 255 (M$^+$, 100%).

3-Methyl-4-methylthio-6-(4-chlorophenyl)-1,2-benzisoxazole (38b); colourless crystals; yield 66%; m.p. 155°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1575, 1430, 1390, 1335 \text{ cm}^{-1}$; $^1H$ n.m.r. (CDCl$_3$): $\delta 2.56$ (s, 3H, CH$_3$); 2.68 (s, 3H, SCH$_3$); 7.02 (brs, 1H, H-7); 7.21-7.67 (m, 6H$_\text{arom}$). (Found: C, 62.03; H, 4.13; N, 4.80. Calc. for C$_{15}$H$_{12}$ClNOS (289.76): C, 62.17; H, 4.17; N, 4.83%). m/z 289 (M$^+$, 60%).

3-Methyl-4-methylthio-6-(4-methoxyphenyl)-1,2-benzisoxazole (38c); colourless crystals; yield 68%; m.p. 130°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1580, 1430, 1345, 1385 \text{ cm}^{-1}$; $^1H$ n.m.r. (CDCl$_3$): $\delta 2.60$ (s, 3H, CH$_3$); 2.70 (s, 3H, SCH$_3$); 3.80 (s, 3H, OCH$_3$); 7.02 (brs, 1H, H-7); 6.80-6.93 (d, J=7Hz, A$_2$B$_2$, 2H$_\text{arom}$); 7.33-7.63 (d, J=7Hz, A$_2$B$_2$, 2H$_\text{arom}$); 7.36 (s, 1H$_\text{arom}$). (Found: C, 67.15; H, 5.22; N, 4.88. Calc. for C$_{16}$H$_{15}$NO$_2$S (285.34): C, 67.34; H, 5.29; N, 4.90%). m/z 285 (M$^+$, 100%).

3-Methyl-4-methylthio-6-(4-methylphenyl)-1,2-benzisoxazole (38d); colourless crystals; yield 65%; m.p. 120°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1580, 1425, 1385, 1345 \text{ cm}^{-1}$; $^1H$ n.m.r. (CDCl$_3$): $\delta 2.40$ (s, 3H, CH$_3$);
2.56(s,3H,CH₃); 2.66(s,3H,SCH₃); 7.03(brs,1H,H-7); 7.16-7.53
(м,5Hₐr om). (Found: C,71.24; H, 5.60; N,5.18. Calc. for
C₁₆H₁₅NOS (269.35): C,71.34; H,5.61; N,5.19%). m/z 269(M⁺,100%).

3-Methyl-4-methylthio-6-(2-naphthyl)-1,2-benzisoxazole (38e);
colourless crystals; yield 64%; m.p. 145°C; i.r.(KBr): υmax = 1600,
1590, 1425, 1380, 1345 cm⁻¹; ¹H n.m.r.(CDCl₃): δ 2.60(s,3H,CH₃);
2.73(s,3H,SCH₃); 7.10(brs,1H,H-7); 7.26(s,1Hₐr om); 7.36-7.66(m,3Hₐr om);
7.72-8.01(m,4H). (Found: C,74.58; H,4.92;N,4.50. Calc. for
C₁₉H₁₅NOS (305.37): C,74.72; H,4.95; N,4.58%). m/z 305(M⁺,100%).

3-Methyl-4-methylthio-6-(2-furyl)-1,2-benzisoxazole (38f); colour­
less crystals; yield 59%; m.p. 85°C; i.r.(KBr): υmax = 1601, 1517,
1429, 1387, 1347 cm⁻¹; ¹H n.m.r.(CDCl₃): δ 2.56(s,3H,CH₃); 2.66(s,
3H,SCH₃); 6.43(m,1H,H-4'); 6.73(d,J=3Hz,1H,H-3'); 7.20(s,1H,H-7);
7.56(d,J=3Hz,2H,H-5 and 2H-5'). (Found: C,63.55; H,4.48; N,5.69.
Calc. for C₁₃H₁₁NO₂S (245.28): C,63.65; H,4.52; N,5.70%). m/z 245
(M⁺,100%).

3-Methyl-4-methylthio-6-(2-thienyl)-1,2-benzisoxazole (38g); colour­
less crystals; yield 61%; m.p. 125°C; i.r.(KBr): υmax = 1602, 1573,
1427, 1388, 1341 cm⁻¹; ¹H n.m.r.(CDCl₃): δ 2.63(s,3H,CH₃); 2.76(s,
3H,SCH₃); 7.10-7.30(m,2Hₐr om); 7.41-7.62(m,3Hₐr om). (Found: C,59.63;
H,4.19; N,5.32. Calc. for C₁₃H₁₁NOS₂ (261.34): C,59.74; H,4.24;
N,5.35%). m/z 261(M⁺,100%).

3-Methyl-4-methylthio-6-methyl-1,2-benzisoxazole (38h); colourless
 crystals; yield 54%; m.p. 85°C; i.r.(KBr): υmax = 1601,1517,1429,1387,
1347 cm⁻¹; ¹H n.m.r.(CDCl₃): δ 2.43(s,3H,CH₃); 2.51(s,3H,CH₃); 2.68
(s,3H,SCH$_3$); 7.01(brs,1H,H-7); 6.86(s,1H$_{arom}$). (Found: C,62.02; H,5.68; N,7.20. Calc. for C$_{10}$H$_{11}$NOS (193,26): C,62.14; H,5.73; N,7.24%). m/z 193(M$^+$,100%).

3-Methyl-4-methylthio-5,6,7,8-tetrahydronaphtho[b]isoxazole (41);
colourless crystals; yield 65%; m.p. 42°C; i.r.(KBr): $\gamma_{max}$ = 1605, 1580, 1430, 1330, 1300 cm$^{-1}$; $^1$H n.m.r.(CDCl$_3$): $\delta$ 1.61-1.98(m,4H,ring CH$_2$); 2.34(s,3H,CH$_3$); 2.66(s,3H,SCH$_3$); 2.60-3.13(m,4H, ring CH$_2$); 7.01(brs,1H$_{arom}$). (Found: C,66.80; H,6.47; N,6.02. Calc. for C$_{13}$H$_{15}$NOS (233.32): C,66.91; H,6.48; N,6.00%). m/z 233 (M$^+$,92%).

3-Methyl-4-methylthio-6,7,8,9-tetrahydro-5H-cyclohepta[b]benzisoxazole (43); colourless crystals; yield 67%; m.p. 62°C; i.r.(KBr): $\gamma_{max}$ = 1600, 1580, 1430, 1380, 1300 cm$^{-1}$; $^1$H n.m.r.(CDCl$_3$): $\delta$ 1.30-1.80(m,6H,ring CH$_2$); 2.13(s,3H,CH$_3$); 2.53(s,3H,SCH$_3$); 2.83(m,2H,ring CH$_2$); 7.01(brs,1H$_{arom}$). (Found: C,67.86; H,6.88; N,5.62. Calc. for C$_{14}$H$_{17}$NOS(247.35): C,67.97; H,6.92; N,5.65%). m/z 247 (M$^+$,100%).

3-Methyl-4-methylthio-5H-indano[2,1-b]benzisoxazole (46); colourless crystals; yield 57%; m.p. 160°C; i.r.(KBr): $\gamma_{max}$ = 1600, 1588, 1420, 1388, 1320 cm$^{-1}$; $^1$H n.m.r.(CDCl$_3$): $\delta$ 2.36(s,3H,CH$_3$); 2.73(s,3H,SCH$_3$); 3.99(brs,2H,ring CH$_2$); 7.26-7.50(m,3H$_{arom}$); 7.63-7.83(m,2H$_{arom}$).
(Found: C,71.80; H,4.88; N,5.21. Calc. for C$_{16}$H$_{15}$NOS (267.26): C,71.90; H,4.90; N,5.23%). m/z 267 (M$^+$,89%).

3-Methyl-4-methylthio-5,6-dihydrophenanthro[2,1-b]isoxazole (47a);
colourless crystals; yield 76%; m.p. 152°C; i.r.(KBr): $\gamma_{max}$ = 1600, 1585, 1513, 1430, 1380, 1330, 1300 cm$^{-1}$; $^1$H n.m.r.(CDCl$_3$): $\delta$ 2.30(s,3H,CH$_3$); 2.80(s,3H,SCH$_3$); 2.72-3.43(m,A$_2$B$_2$,4H,CH$_2$); 7.16-7.38(m,3H$_{arom}$);
7.60-7.83 (m, 2H<sub>arom</sub>); <sup>13</sup>C n.m.r. (CDCl<sub>3</sub>): δ 12.75 (CH<sub>3</sub>); 20.14 (SCH<sub>3</sub>); 26.04 (CH<sub>2</sub>); 29.16 (CH<sub>2</sub>); 105.61, 124.88, 127.24, 127.97, 128.60 (CH<sub>arom</sub>); 123.03, 128.91, 134.24, 134.26, 138.17, 138.26, 155.83, 162.50 (quaternary C). (Found: C, 72.45; H, 5.29; N, 4.92. Calc. for C<sub>17</sub>H<sub>15</sub>NOS (281.36): C, 72.56; H, 5.37; N, 4.97%). m/z 281 (M<sup>+</sup>, 100%).

3-Methyl-4-methylthio-8-methoxy-5,6-dihydrophenanthro[2,1-b]isoxazole (47b); colourless crystals; yield 78%; m.p. 135°C; i.r. (KBr): ν<sub>max</sub> = 1600, 1580, 1512, 1420, 1385, 1325, 1300 cm<sup>-1</sup>; 1H n.m.r. (CDCl<sub>3</sub>): δ 2.33 (s, 3H, CH<sub>3</sub>); 2.83 (s, 3H, SCH<sub>3</sub>); 2.73-3.36 (m, A<sub>2</sub>B<sub>2</sub>, 4H, CH<sub>2</sub>); 3.83 (s, 3H, OCH<sub>3</sub>); 6.63-6.93 (m, 2H<sub>arom</sub>); 7.56-7.86 (m, 2H<sub>arom</sub>). (Found: C, 69.31; H, 5.48; N, 4.08. Calc. for C<sub>18</sub>H<sub>17</sub>NOS (311.38): C, 69.42; H, 5.50; N, 4.49%). m/z 311 (M<sup>+</sup>, 100%).

3-Methyl-4-methylthio-6,7-dihydro-5H-benzocyclohepta[2,1-b]benzisoxazole (49); colourless crystals; yield 69%; m.p. 175°C; i.r. (KBr): ν<sub>max</sub> = 1600, 1560, 1430, 1390, 1345 cm<sup>-1</sup>; 1H n.m.r. (CDCl<sub>3</sub>): δ 2.23-2.36 (brs, 4H, ring CH<sub>2</sub>); 2.86 (s, 3H, SCH<sub>3</sub>); 3.43-3.96 (m, 2H, ring CH<sub>2</sub>); 7.36-7.83 (m, 5H<sub>arom</sub>). (Found: C, 73.07; H, 5.78; N, 4.71. Calc. for C<sub>18</sub>H<sub>17</sub>NOS (295.38): C, 73.18; H, 5.80; N, 4.73%). m/z 295 (M<sup>+</sup>, 100%).

3-Methyl-4-methylthio-10-methyl-5,6-dihydrobenzothiepinob[2,1-b]benzisoxazole (51); colourless crystals; yield 81%; m.p. 185°C; i.r. (KBr): ν<sub>max</sub> = 1600, 1580, 1430, 1380, 1320 cm<sup>-1</sup>; 1H n.m.r. (CDCl<sub>3</sub>): δ 2.43 (s, 3H, CH<sub>3</sub>); 2.46 (s, 3H, SCH<sub>3</sub>); 2.36-2.73 (m, 1H, CH, benzylic); 2.83-3.16 (m, 1H, CH, benzylic); 3.43-3.63 (m, 1H, SCH); 3.83-4.13 (m, 1H, SCH); 7.16-7.53 (m, 4H<sub>arom</sub>). (Found: C, 85.99; H, 4.88; N, 4.05.
Calc. for $C_{18}H_{16}NO_2$ (327.44): C, 66.02; H, 4.92; N, 4.27%. m/z 327($M^+$, 100%).

3-Methyl-6-phenyl-1,2-benzisoxazole (53a); colourless crystals; yield 87%; m.p. 62°C; i.r. (KBr): $\nu_{\text{max}}$ = 1600, 1580, 1500, 1430, 1390, 1340 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.60 (s, 3H, CH$_3$); 7.26-7.93 (m, 8H arom). (Found: C, 78.35; H, 4.52; N, 5.78. Calc. for $C_{14}H_{11}NO$ (209.23): C, 78.46; H, 4.55; N, 5.80%). m/z 241($M^+$, 100%).

3-Methyl-6-(4-methylphenyl)-1,2-benzisoxazole (53b); colourless crystals; yield 82%; m.p. 134°C; i.r. (KBr): $\nu_{\text{max}}$ = 1600, 1560, 1420, 1380, 1320 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.36 (s, 3H, CH$_3$); 2.56 (s, 3H, CH$_3$); 7.16-7.33 (m, 2H arom); 7.43-7.76 (m, 5H arom). (Found: C, 80.58; H, 5.78; N, 6.24. Calc. for $C_{15}H_{13}NO$ (223.25): C, 80.69; H, 5.86; N, 6.27%). m/z 223($M^+$, 100%).

3-Methyl-6-(4-chlorophenyl)-1,2-benzisoxazole (53c); colourless crystals; yield 79%; m.p. 102°C; i.r. (KBr): $\nu_{\text{max}}$ = 1600, 1555, 1420, 1375, 1320 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.56 (s, 3H, CH$_3$); 7.23-7.96 (m, 7H arom). (Found: C, 68.88; H, 4.08; N, 5.72. Calc. for $C_{14}H_{10}ClNO$ (243.72): C, 68.98; H, 4.10; N, 5.74%). m/z 243($M^+$, 40%).

3-Methyl-5,6-dihydrophenanthro[2,1-b]isoxazole (55a); colourless crystals; yield 85%; m.p. 105°C; i.r. (KBr): $\nu_{\text{max}}$ = 1620, 1595, 1430, 1380, 1320 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.53 (s, 3H, CH$_3$); 2.73-3.03 (m, 4H, ring CH$_2$); 7.16-7.46 (m, 4H arom); 7.66-7.93 (m, 2H arom). (Found: C, 81.56; H, 5.48; N, 5.92. Calc. for $C_{16}H_{13}NO$ (235.26): C, 81.67; H, 5.56; N, 5.95%). m/z 235($M^+$, 90%).
3-Methyl-8-methoxy-5,6-dihydro-phenanthro[2,1-b]isoxazole (55b);
colourless crystals; yield 88%; m.p. 130°C; i.r. (KBr): $\gamma_{\text{max}} = 1600,
1556, 1488, 1440, 1345, 1250 \text{ cm}^{-1}; ^1H \text{n.m.r. (CDCl}_3): 6 2.46 (s, 3H,
CH$_3$); 2.66-3.03 (m, 4H, ring CH$_2$); 3.83 (s, 3H, OCH$_3$); 6.50-6.93 (m, 3H
$_\text{arom}$); 7.53 (brs, 1H$_\text{arom}$); 7.93 (d, 1H$_\text{arom}$). (Found: C, 76.85; H, 5.68; N, 5.23.
Calc. for C$_{17}$H$_{15}$NO$_2$ (265.29): C, 76.96; H, 5.69; N, 5.27%). m/z 265
(M$^+$, 100%).

3-Methyl-4-methylthio-6-styryl-1,2-benzisoxazole (57a); pale yellow
crystals; yield 68%. m.p. 145-149°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1570,
1510, 1430, 1390, 1350 \text{ cm}^{-1}; ^1H \text{n.m.r. (CDCl}_3): 6 2.60 (s, 3H, CH$_3$);
2.70 (s, 3H, SCH$_3$); 2.03-7.26 (m, 3H, 2H$_\text{olefinic}$ + 1H$_\text{arom}$); 7.36-7.83 (m,
6H, 5H$_\text{arom}$ + 1H$_\text{olefinic}$). (Found: C, 72.45; H, 5.04; N, 4.92. Calc. for
C$_{17}$H$_{15}$NOS (281.35): C, 72.56; H, 5.37; N, 4.97%). m/z 281 (M$^+$, 100%).

3-Methyl-4-methylthio-6(4-methylstyryl)-1,2-benzisoxazole (57b);
pale yellow crystals; yield 71%; m.p. 135°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1599,
1570, 1500, 1450 \text{ cm}^{-1}; ^1H \text{n.m.r. (CDCl}_3): 6 2.63 (s, 3H, CH$_3$);
2.66 (s, 3H, SCH$_3$); 7.03-7.30 (m, 2H$_\text{olefinic}$ + 1H$_\text{arom}$); 7.30-7.56 (m, 5H
$_\text{arom}$). (Found: C, 73.07; H, 5.78; N, 4.71. Calc. for C$_{18}$H$_{17}$NOS
(295.38): C, 73.18; H, 5.80; N, 4.73%). m/z 295 (M$^+$, 100%).

3-Methyl-4-methythio-6(4-methoxystyryl)-1,2-benzisoxazole (57c);
yellow crystals; yield 78%; m.p. 139°C; i.r. (KBr): $\gamma_{\text{max}} = 1600, 1590,
1500, 1440, 1380 \text{ cm}^{-1}; ^1H \text{n.m.r. (CDCl}_3): 6 2.70 (s, 3H, SCH$_3$);
3.76 (s, 3H, OCH$_3$); 6.76-7.03 (m, 4H$_\text{arom}$ + 1H$_\text{olefinic}$); 7.16-7.56 (m,
A$_2$B$_2$, 4H$_\text{arom}$ + 1H$_\text{olefinic}$). (Found: C, 69.31; H, 5.48; N, 4.45.
Calc. for C$_{18}$H$_{17}$NO$_2$S (311.38): C, 69.42; H, 5.50; N, 4.49%). m/z
311 (M$^+$, 100%).
3-Methyl-4-methylthio-6-[4-(3,4-dimethoxystyryl)]-1,2-benzisoxazole (57d); yellow crystals; yield 62%; m.p. 134°C; i.r. (KBr): \( \gamma_{\text{max}} = 1600, 1580, 1500, 1440, 1380 \text{ cm}^{-1} \); \(^1\text{H N.M.R.} (\text{CDCl}_3): \delta 2.46(\text{s}, 3\text{H}, \text{CH}_3); 2.66(\text{s}, 3\text{H}, \text{SCH}_3); 3.93(\text{d}, 6\text{H}, \text{OCH}_3); 6.23(\text{brs}, 2\text{H}, \text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}); 6.36-6.66(\text{m}, 2\text{H}_{\text{arom}}); 6.83-7.36(\text{m}, 3\text{H}, 2\text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}) \). (Found: C, 66.71; H, 5.58; N, 4.00. Calc. for C\(_{34}\)H\(_{23}\)NO\(_3\)S (341.4): C, 66.83; H, 5.60; N, 4.10%). m/z 341 (M\(^+\), 92%).

3-Methyl-4-methylthio-6-[4-(3,4,5-trimethoxystyryl)]-1,2-benzisoxazole (57e); yellow crystals; yield 63%; m.p. 179°C; i.r. (KBr): \( \gamma_{\text{max}} = 1600, 1590, 1505, 1420, 1380 \text{ cm}^{-1} \); \(^1\text{H N.M.R.} (\text{CDCl}_3): \delta 2.63(\text{s}, 3\text{H}, \text{CH}_3); 2.73(\text{s}, 3\text{H}, \text{SCH}_3); 3.86-4.16(\text{m}, 9\text{H}, \text{OCH}_3); 6.93(\text{brs}, 2\text{H}, \text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}); 7.23(\text{brs}, 2\text{H}_{\text{arom}}); 7.43-7.66(\text{m}, 2\text{H}, 1\text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}) \). (Found: C, 64.54; H, 5.68; N, 3.74. Calc. for C\(_{30}\)H\(_{21}\)NO\(_3\)S (371.43): C, 64.66; H, 5.69; N, 3.76%). m/z 371 (M\(^+\), 100%).

3-Methyl-4-methylthio-6-(4-chlorostyryl)-1,2-benzisoxazole (57f); pale yellow crystals; yield 60%; m.p. 120°C; i.r. (KBr): \( \gamma_{\text{max}} = 1600, 1580, 1430, 1410 \text{ cm}^{-1} \); \(^1\text{H N.M.R.} (\text{CDCl}_3): \delta 2.56(\text{s}, 3\text{H}, \text{CH}_3); 2.66(\text{s}, 3\text{H}, \text{SCH}_3); 6.93-7.13(\text{m}, 3\text{H}, 2\text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}); 7.33-7.63(\text{m}, 5\text{H}, 4\text{H}_{\text{arom}} + 1\text{H}_{\text{olefinic}}) \). (Found: C, 64.53; H, 4.42; N, 4.41. Calc. for C\(_{17}\)H\(_{14}\)ClNOS (315.84): C, 64.64; H, 4.43; N, 4.43%). m/z 315 (M\(^+\), 40%).

3-Methyl-4-methylthio-6-(3,4-methylenedioxy styryl)-1,2-benzisoxazole (57g); yellow crystals; yield 59%; m.p. 188°C; i.r. (KBr): \( \gamma_{\text{max}} = 1600, 1580, 1500, 1480, 1400 \text{ cm}^{-1} \); \(^1\text{H N.M.R.} (\text{CDCl}_3): \delta 2.63(\text{s}, 3\text{H}, \text{CH}_3); 2.73(\text{s}, 3\text{H}, \text{SCH}_3); 5.93(\text{brs}, 2\text{H}, \text{O-CH}_2-\text{O}); 6.73-7.40(\text{m}, 5\text{H}_{\text{arom}} + 2\text{H}_{\text{olefinic}}) \). (Found: C, 66.31; H, 4.58; N, 4.28. Calc. for C\(_{18}\)H\(_{15}\)NO\(_3\)S (325.36): C, 66.44; H, 4.64; N, 4.30%). m/z 325 (M\(^+\), 100%).
3-Methyl-4-methylthio-6(4-phenyl-1,3-butadienyl)-1,2-benzisoxazole (59a); yellow crystals; yield 55%; m.p. 153°C; i.r. (KBr): $\nu_{\text{max}}$ = 1605, 1599, 1440, 1400, 1340 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.56 (s, 3H, CH$_3$); 2.66 (s, 3H, SCH$_3$); 6.60-7.30 (m, 4H, olefinic); 7.13-7.56 (m, 7H, arom). (Found: C, 74.07; H, 5.53; N, 4.54. Calc. for C$_{19}$H$_{17}$NOS (307.39): C, 74.23; H, 5.57; N, 4.55%). m/z 307 (M$^+$, 100%).

3-Methyl-4-methylthio-6-[4-(4-methoxyphenyl)-1,3-butadienyl]-1,2-benzisoxazole (59b); deep yellow crystals; yield 65%; m.p. 162°C; i.r. (KBr): $\nu_{\text{max}}$ = 1600, 1580, 1510, 1395, 1355 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.56 (s, 3H, CH$_3$); 2.66 (s, 3H, SCH$_3$); 3.83 (s, 3H, OCH$_3$); 6.66-7.33 (m, 7H, 3H, arom + 4H, olefinic); 7.20-7.50 (m, 3H, arom). (Found: C, 70.99; H, 5.59; N, 4.12. Calc. for C$_{20}$H$_{19}$NO$_2$S (337.41): C, 71.18; H, 5.68; N, 4.14%). m/z 337 (M$^+$, 100%).

3-Methyl-4-methylthio-6-(6-phenyl-1,3,5-hexatrienyl)-1,2-benzisoxazole (61); deep yellow crystals; yield 55%; m.p. 172°C; i.r. (KBr): $\nu_{\text{max}}$ = 1600, 1570, 1435, 1400, 1335 cm$^{-1}$; $^1$H n.m.r. (CDCl$_3$): $\delta$ 2.63 (s, 3H, CH$_3$); 2.73 (s, 3H, SCH$_3$); 6.43-6.93 (m, 6H, olefinic); 7.20-7.56 (m, 7H, arom). (Found: C, 75.51; H, 5.71; N, 4.17. Calc. for C$_{21}$H$_{19}$NOS (333.42): C, 75.64; H, 5.74; N, 4.19%). m/z 333 (M$^+$, 100%).
REFERENCES