CHAPTER V
CYCLOAROMATIZATION OF 2-LITHIOMETHYLTHIAZOLES
WITH \( \Delta \)-OXOKETENE DITHIOACETALS: SYNTHESIS OF
SUBSTITUTED AND FUSED THIAZOLE[3,2-\( a \)]PYRIDINIUM
COMPOUNDS

V.1 INTRODUCTION

Formation of carbon–carbon bond is one of the most fundamental
reactions in organic synthesis. The synthesis of complex molecules
from simple fragments would not be possible without this reaction.
One of the most intensively studied synthetic methodologies for the
construction of new carbon–carbon bond is by the addition of an
organometallic reagent to a suitable electrophilic carbon centre.

Oxoketene dithioacetals have been a subject of intense investigation
in this laboratory and elsewhere for the chemo-, stereo- and regio-
selective construction of new C–C bonds using organometallic reagents\(^1\).
The new C-C bond can be formed either by a 1,2-nucleophilic addition to the keto carbonyl or 1,4-conjugate addition to the β-carbon of the enone system. The 1,2- and 1,4-nucleophilic addition reactions can be effected separately or sequentially by suitable selection of the nucleophilic reagents and appropriate reaction conditions. A number of organolithium and magnesium reagents have been shown to add to α-oxoketene dithioacetals in a 1,2-manner to give the alcohol acetals which are suitable for other transformations. A brief account of some of these reactions which are relevant to the present study is given in the following section.

The foregoing discussion is restricted to the reports on C-C bond forming reactions via α-oxoketene dithioacetals which ultimately results in ring forming reactions to afford aromatic and heteroaromatic systems. The general strategy involves 1,2-addition of a suitable carbon nucleophile to α-oxoketene dithioacetals to give the allyl alcohol which on subsequent Lewis acid assisted cationic cyclization to form six membered ring followed by aromatization. The overall reaction can generally be termed as aromatic annelation or cycloaromatization and many variations of this approach have been reported in the literature. The other common methods for the construction of six membered rings consists of the union of two fragments, one with two atom fragment and other with four atom fragment (Diels-Alder reaction and Robinson annelation). The present method involving the union of two three atom fragments usually proceeds with high regiocontrol.
It is reported from this laboratory that the allylmagnesium bromide undergoes a 1,2-addition with \( \alpha \)-oxoketene dithioacetals of general formula 1 to afford the corresponding alcohol acetals 2 in nearly quantitative yields. These carbinols in the presence of boron trifluoride etherate were cyclized to give the benzoannelated products 3 \(^{14}\). The reaction appears to proceed through intramolecular \( \pi \)-participation of the allylic double bond to form a cationic species which on loss of proton and methylmercaptan yield the aromatized products 3 (Scheme 1). The reaction of allyl and crotyl magnesium bromide with cinnamoylketene dithioacetals 4 is also reported\(^ {15}\) to give the substituted stilbenes of the general formula 5 (Scheme 1). Subsequently, the reaction of benzylmagnesium bromide 6 with \( \alpha \)-oxoketene dithioacetals has been reported\(^ {16}\). The bulky benzylmagnesium bromide 6 underwent a 1,4-conjugate addition followed by a 1,2-addition to give carbinol 7 which in the presence of boron trifluoride etherate gave the naphthalene derivatives 8 (Scheme 2).

A benzoannelation approach for the synthesis of fused thioresorcinol dimethylethers is also reported\(^ {17}\) by the reaction of propargylmagnesium bromide with \( \alpha \)-oxoketene dithioacetals 1 prepared from cyclic ketones. The cyclization proceeds by the intramolecular participation of the propargyl triple bond in the carbinol acetal 9 with concommitant attack of methanol on the incepient vinyl cation, followed by loss of methylmercaptan to yield the thioresorcinol dimethylethers 10 in good yields (Scheme 3).
Scheme-1
Scheme 2

\[ \text{MgBr} \quad \text{H}_2 \text{C} \quad \text{SMe} \quad \text{R}^1 \quad \text{R}^2 \]

\[ \text{BF}_3 \cdot \text{Et}_2 \text{O} \quad \text{C}_6 \text{H}_6 / \Delta \]

\[ \text{CH}_2 \text{C}_6 \text{H}_5 \]

\[ \text{R}^1 = \text{C}_6 \text{H}_5, 4\text{-MeOC}_6 \text{H}_4, 4\text{-MeC}_6 \text{H}_4, 2\text{-naphthyl}; \text{R}^2 = \text{H}; 58\text{-}65\% \]

\[ \text{R}^1 = \text{R}^2 = (\text{CH}_2)_n; 81\% \]

\[ n = 1; 62\% \]

\[ n = 2; 71\% \]

\[ \text{R}^3 \text{= } \text{H; } n = 1; 58\% \]

\[ \text{R}^3 \text{= } \text{Me; } n = 2; 68\% \]

\[ \text{R}^3 \text{= } \text{H; } n = 2; 67\% \]
Scheme 3

1. R1=R2=-(CH2)4-; 76 %
   R1=R2=-(CH2)5-; 71 %
2. R1=R2= R3=H; 76 %
   R3=MeO; 66 %
   R3=Me; 77 %
3. R1=R2=R3=H; X=S, O;
   n=1, 2; 68-81 %
The above strategy of aromatic annelation is also extended for the synthesis of fused five and six membered heteroaromatic compounds. Thus, 5-lithiomethyl-3-methylisoxazole \( \text{12} \) underwent an exclusive 1,2-addition to \( \alpha \)-oxoketene dithioacetal to give the carbinol acetal \( \text{13} \). These carbinol acetals were cyclized to the corresponding 1,2-benzisoxazoles \( \text{14}\text{18} \) in the presence of boron trifluoride etherate (Scheme 4). Another related example reported \( \text{19} \) is the reaction of 2-picolyllithium \( \text{15} \) with \( \alpha \)-oxoketene dithioacetals resulting in the formation of substituted and fused quinolizinium ring systems. The 2-picolyllithium which bears an azaallyl moiety adds to dithioacetals \( \text{1} \) to give the alcohol acetals \( \text{16} \), which underwent cycloaromatization to the quinolizinium salts \( \text{17} \) through the participation of pyridine ring (Scheme 5).

As an extension of the above described strategy for the construction of aromatic and heteroaromatic ring systems (heteroaromatic annelation), it was considered of interest to explore the possibility of synthesizing other bridgehead aromatic nitrogen heterocycles using this approach. A nitrogen heterocycle with a methyl group on the carbon atom adjacent to the imino nitrogen can generate an azaallyl anion moiety by deprotonation with suitable base, provided competing sites are not present in the molecule. This structural requirement

\[
\begin{align*}
\text{Y-X} \text{CH}_3 & \xrightarrow{\text{Base}} \text{Y-X} \text{CH}_2 \text{M}^+ \\
\text{Z-N} &
\end{align*}
\]

is met in 2-methyl-4-substituted thiazoles which are selected for the
Scheme 4

R = C₆H₅, 4-ClC₆H₄, 4-MeOC₆H₄, 2-naphthyl, Me, 2-furyl, 2-thienyl; R₂ = H; 54-73 °/o

R₁ = R₂ = (CH₂)ₙ; n = 4: 65%; n = 5: 67%

R₁ = R₂ = (CH₂)₂; 57%

R₁ = R₂ = (CH₂)₂; 76%

R₁ = R₂ = (CH₂)₂; 81%

R₁ = R₂ = (CH₂)₂; 91%
R₁ = R₂ = -(CH₂)₄⁻; 82%  
R₁ = R₂ = -(CH₂)₅⁻; 79%

R₁ = R₂ =  
X = CH₂; n = 1; R¹ = H, MeO, Me; 78-85% 
X = S; n = 2; R¹ = Me; 80% 
X = O; n = 2; R¹ = H; 81%

R¹ = C₆H₅; 4-MeC₆H₄, 4-MeOC₆H₄, 2-naphthyl,  
2-furyl, 2-thienyl, 2-(styryl), R² = H; 73-86%

Scheme-5
present study. The reaction of $\alpha$-oxoketene dithioacetals withazaallyl anion generated from 2-methylthiazole should in principle lead to the formation of thiazolopyridines following the sequence described in the above examples. The reaction was found to be successful for the synthesis of thiazolo[3,2-\(a\)]pyridinium salts which are described in this chapter. The following section reviews some of the literature methods for the synthesis of these class of compounds.

The thiazolo[3,2-\(a\)]pyridine ring systems can in principle be synthesized from a preconstructed 2-thiopyridine or from a thiazole derivative. Most of the literature methods make use of a suitably substituted pyridine derivatives and the approaches starting from thiazole precursors are scanty. The first synthesis of thiazolopyridinium salts is accomplished by Bradsher and Lohr \(^{20,21}\) starting from the corresponding pyridylsulfide \(18\) having a carbonyl function $\beta$- to the sulfide linkage. These sulfides can be prepared by the reaction of $\alpha$-haloketones or $\alpha$-haloacetals with 2-mercaptopyridine. The keto-sulfide \(18\) was treated with concentrated sulphuric acid to bring about the cyclization, which on perchloric acid treatment gave the thiazolo[3,2-\(a\)]pyridinium perchlorate \(19\) (Scheme 6). Alternatively, the cyclization can be effected in the opposite direction starting from a quaternized nitrogen intermediate as reported \(^{22}\) by Blank and coworkers. Thus, 2-bromopyridines were quaternized with phenacyl bromide to produce the 2-bromopyridinium salt \(20\). These salts were converted to pyridine 2-thiones \(21\) by treatment with aqueous sodium hydrosulfide. The ring closure of pyridine-2-thiones \(21\) to the
1. Concentrated H$_2$SO$_4$

2. HClO$_4$

**Scheme 6**

18-19 $R^1$=H, Me, COMe, C$_6$H$_5$;  
$R^2$=H, Me, C$_6$H$_5$;  
$R^3$=$R^4$=Cl, NO$_2$

20-22 $R$=H, Me, $R^1$=C$_6$H$_5$, 4-BrC$_6$H$_4$, 3-NO$_2$C$_6$H$_4$, 4-MeSO$_2$C$_6$H$_4$, 3-AcNH$_2$C$_6$H$_4$
thiazolopyridinium salts 22 is effected by concentrated sulphuric acid (Scheme 6).

Undheim and coworkers have extensively studied 23 dihydrothiazolo [3,2-α]pyridinium-9-olate systems and the literature on the chemistry of these compounds have been reviewed by the same authors 23. The initial studies on thiazolo/dihydrothiazolo[3,2-α]pyridinium 8-olates and related systems were initiated by the isolation of strongly blue fluorescent substance from bovine liver hydrolysates. The substance was identified as 5-methyl-8-hydroxydihydrothiazolo[3,2-α]pyridinium-3-carboxylate 26 24. This compound was synthesized 23 in 65% optical purity through the sequence of reactions shown in Scheme 7. The bromopyridine 23 was reacted with the (R)-cysteine to give the amino acid 24. The bromo compound 25 was prepared from the diazonium salt of the amino acid 24 with inversion of configuration. In basic conditions, the bromo compound 25 was cyclized stereospecifically to the optically active (S)-dihydrothiazolo[3,2-α]pyridinium-3-carboxylate 26.

The general method for the synthesis of thiazolo[3,2-α]pyridinium salts consists of an acid catalyzed cyclization of 2-(2-oxoethylthio) pyridines 27. The substituent effects 25 in the cyclization step is also studied by the same group of workers. The reaction is sensitive to the steric interference from the pyridine 6-substituent. Thus, the methylketone 27a and the corresponding aldehyde 27b cyclized to the pyridinium salt 29a and 29b in the presence of cold sulphuric acid, while the 6-methyl compound 27c required heating for cyclization to give 29c (Scheme 7).
In the following two examples given in the Scheme 8, the construction of thiazolopyridinium ring systems starts from a thiazole ring rather than pyridine ring. The base catalyzed condensation of N-substituted 2-methyl thiazolinium salt 30 with 1,2-diketones 31 affords the thiazolopyridinium salts 32. Similarly, the thiazolopyridone 35 was prepared by the condensation of 2-cyanomethylthiazole 33 and ethylacetoacetate through the intermediate 34.

From the reviewed examples given above, it is evident that the synthesis of thiazolo[3,2-a]pyridinium salts makes use of preformed pyridine or a thiazole nucleus. Both the approaches are known and only a few reports are available making use of the latter approach. Also, both the approaches do not offer much scope for substituent variation in the pyridine ring. The following section describes the successful application of the aromatic annelation approach for the synthesis of these class of compounds.

V.2 RESULTS AND DISCUSSION

The required 2,4-dimethylthiazole and 2-methyl-4-phenylthiazole were prepared by a modified reported procedure by the reaction of thioacetamide with chloroacetone or phenacyl bromide. The detailed procedure is given in the experimental section. The selected ketene dithioacetals 1a-g, 41a-e and 43a-c were prepared by the general procedure described in Chapter II. The procedure for the preparation of known cinnamoyl-ketene dithioacetal is given in the experimental section of Chapter III. The authenticity of all these ketene dithioacetals is confirmed by comparison of their i.r. and n.m.r. spectral data with those of reported values.
Scheme-8

Bu₂NH → R₁

0°C

R=COC₆H₅, CN, CO₂C₂H₅
R₁=CH₃, C₆H₅, 2-furyl

Scheme-8
In an optimized reaction condition, the 2-lithiomethyl-4-methylthiazole 36a was generated by deprotonation at 2-methyl group by butyllithium in dry THF maintained at -78°C under an efficient atmosphere of nitrogen. The α-oxoketene dithioacetal 1a was added as a THF solution maintaining the same temperature. The usual work up of the reaction (experimental) afforded the alcohol acetal 37a in nearly quantitative yield. However, the alcohol 37a was found to be not stable enough for purification and characterization and was subjected as such to borontrifluoride-ether catalyzed cyclization in refluxing benzene. Work up of the reaction mixture afforded a pale yellow solid, which was characterised as 3-methyl 5-methylthio-7-phenylthiazolo[3,2-a]pyridinium tetrafluoroborate 39a formed in 55% yield. The structure of this compound is assigned on the basis of spectral and analytical data. The product 39a was analyzed for C$_{15}$H$_{14}$NS$_{2}$BF$_{4}$ and its mass spectrum displayed characteristic peaks at m/z 272 (34%, M$^+$-BF$_{4}$), 271(100%) and 256(62%), Infrared spectrum of this compound showed a broad band between 1020-1120 cm$^{-1}$ which is characteristic of tetrafluoroborate salt. The $^1$H n.m.r.(TFA) spectrum of 39a showed singlets at $\delta$ 2.92(3H) and 3.30(3H) due to methyl and methylthio protons respectively. The multiplet between $\delta$ 7.56-7.93 was assigned for seven aromatic protons and the singlet at $\delta$ 8.31 was assigned for 8-H proton. The other thiazolopyridines 39b-R were obtained by the same sequence by the reaction of 1b-R with 2-lithiomethylthiazole 36a in 61-68% overall yield (Scheme 9). Spectral and analytical data in support of the assigned structure is given in the experimental. The cinnamoylketene dithioacetal 4 was reacted with lithiomethylthiazole
Scheme 9

1, 37-39

a $R^1 = C_6H_5$

b $R^1 = 4$-MeC$_6$H$_4$

c $R^1 = 4$-MeOC$_6$H$_4$

d $R^1 = 2$-naphthyl

e $R^1 = 2$-furyl

f $R^1 = 2$-thienyl

g $R^1 = $Me

H$_2$Li

$\text{MeS(C)}$ \( \rightarrow \)

R$_1$ CO $\text{MeS(C)}$

BF$_3$·Et$_2$O

$\text{MeS(C)}$

$\text{MeS(C)}$

38

39

1, 37-39
with a view to generalize the method for the synthesis of thiazolo-
pyridines with 7-styryl substitution. Although alcohol acetal was
formed in quantitative yield the cyclization was found to be sluggish
leading to lower yield (42%) of 40. Spectral and analytical data is
given in the experimental.

The reaction of 2-lithiomethylthiazole 36a with α-oxoketene dithioacetals
derived from cyclic ketones were next investigated. Thus, treatment of
dithioacetal 41a with lithiomethylthiazole 36a gave the alcohol acetal
in good yield. However, subsequent cyclization of alcohol in the
presence of BF$_3$.Et$_2$O gave the tetrahydroisoquinolinium salt 42a
in low yield (33%)(Scheme 10). The characteristic signals due to
2-H and 10-H protons appeared at 5.656 and 6.81 in its $^1$H n.m.r. spectrum.
The other spectral and analytical data are given in the experimental.

In an analogous reaction condition, the ketene dithioacetals 41b-d
prepared from benzocyclic ketones gave the tetracyclic thiazolopyri-
dinium salts 42b-d in 60-64% overall yield (Scheme 11). Interestingly
the yields 42b-d were found to be reasonably good compared to that of
the product 42a. The structures of 42b-d were fully established by
spectral and analytical data (experimental). The ketene dithioacetal
41e derived from benzothiepinone also afforded the thiazolopyridinium
salt 42e in 62% yield on reaction with 36a followed by BF$_3$.Et$_2$O treatment.
Spectral and analytical data of 42e are given in the experimental.

Despite its success as a general method for the synthesis of thiazolo-
pyridinium salts, the method failed to give the products in the case
of ketene dithioacetals 43a-c (Scheme 12). The enolacetals 44a-c were
indeed formed in quantitative yield, which however failed to undergo
Scheme 11

1. LiH₂C⁺⁻gni⁻N⁺SMe
defined chemicals reaction conditions
2. BF₃·Et₂O/C₆H₆/Δ

41, 42 b R¹=H
42 c R¹=OMe

36 a
36 b
36 c

LiH₂C⁺⁻gni⁻N⁺SMe

41, 42 a
42 d

36 a
36 b
36 c
cyclization to yield the thiazolopyridinium salts \( 45a-c \). It appears that in the case of \( 44a \) the mercaptal double bond assumes an unfavourable geometry through rotation of carbon–carbon bond pushing the \( R^2 \) substituent towards the thiazole ring.

To check the efficacy and generality of the method, 2-methyl-4-phenylthiazole \( 36b \) was metallated and reacted with \( \beta \)-oxoketene dithioacetals under the described conditions. Thus, lithiation of thiazole \( 36b \) with butyllithium at \(-78^\circ C\) followed by reaction with dithioacetal \( 1 \) and BF\(_3\).Et\(_2\)O treatment afforded an yellow crystalline solid after usual work up and column chromatography. The compound was characterized as the thioester \( 49 \) on the basis of spectral and analytical data. Thus, the thioester \( 49 \) was analyzed for \( C_{20}H_{17}NOS_2 \) and exhibited molecular ion peak at \( m/z \) 305 (100\%) in its mass spectrum. Its i.r. spectrum displayed characteristic band at 1656 cm\(^{-1}\) due to the thioester carbonyl group. In its \( ^1H \) n.m.r. spectrum (CDCl\(_3\)) the thiomethyl protons appeared as a singlet at \( \delta 2.21(3H) \) and the signal due to 2-methyl protons of the thiazole ring was present at \( \delta 2.69(s,3H) \). The signal due to the olefinic proton appeared at \( \delta 6.70(s,1H) \) and the aromatic protons appeared as two multiplets between \( \delta 7.12-7.46(8H) \) and \( 7.60-7.74(2H) \) confirming the structural assignment. Evidently the compound \( 49 \) is formed by the hydrolysis of the alcohol acetal \( 48 \) formed by the reaction of lithiated thiazole \( 47 \) with dithioacetal \( 1 \) (Scheme 13). The thiazolopyridinium salt \( 51 \) which can be formed by the reaction 2-lithiomethyl species \( 46 \) could not be isolated and considerable amount of thiazole \( 36b \) was isolated from the reaction mixture.
The literature search at this stage revealed that the observed change in the behaviour of 2-methylthiazole by replacing the 4-methyl group with a phenyl group as in thiazole 36b is not unusual and Meyers and Knaus have made similar observations 29-31 in the lithiation of 2-methyl-4-phenylthiazole 36b. They observed that the lithiation of thiazole 36b takes place both at the 2-methyl and 5-position at low temperature. The lithio derivative 46 and 47 do not exchange hydrogen or metal and the products arising from 46 and 47 are the result of independent metallation of 2-methyl and 5-position in a kinetically controlled process. Although it is reported that both the specious 46 and 47 react independently only the product arising from the 5-lithiated thiazole 47 could be isolated on reaction with dithioacetal 1.

Surprisingly, in an analogous reaction condition the dithioacetal 41b derived from tetralone gave the 3-phenyl thiazolopyridinium salt 53 in 43% yield (calculated on the basis of recovered thiazole 36b). The thioester 55 which can be formed by the reaction of 5-lithiated thiazole 47 could not be isolated from the reaction mixture (Scheme 14). The dithioacetal 41c also gave the thiazolopyridinium salt 53c through the alcohol 52c. The spectral and analytical data in favour of the thiazolopyridinium salts 53b and 53c are given in the experimental section. The reason for the difference in the reactivity of the acyclic and cyclic dithioacetals towards lithiated thiazeles 46 and 47 is difficult to explain and further work is in progress to understand this anomalous observation.

V.3 SUMMARY

A new general heteroaromatic annelation strategy has been developed
for the synthesis of substituted and fused thiazolo[3,2-\(a\)]pyridinium salts. Annihilation of a pyridine ring onto a thiazole ring is achieved by the generation and reaction of an azaallyl anion equivalent with \(\Delta\)-oxoketene dithioacetals. The Lewis acid induced cyclization of the alcohol acetal can be considered as a special case of aromatic annelation in which the electrophilic attack occurs on an aromatic heterocyclic nitrogen atom rather than a carbon atom. Most of the reported methods make use of a preconstructed pyridine ring and have obvious limitation in introducing substitutions in the pyridine ring. A number of hitherto inaccessible thiazolo[3,2-\(a\)]pyridine fused polycyclic ring systems are synthesized by the present method. Despite its moderate yields in a few cases the method developed can be of choice for the construction of these ring systems.

V.4 EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded as KBr discs on a Perkin-Elmer 297 spectrophotometer. N.m.r. spectra refer to those run on a Varian EM-390 (90 MHz) spectrometer using TMS as internal standard. Chemical shifts are expressed as ppm downfield from TMS. Mass spectra were recorded on a Jeol JMS D-300 spectrometer. Elemental analysis were carried out on a Heraus CHN-O-RAPID instrument.

Starting Materials
Chloroacetone (90%, stabilized by 0.5% CaCO\(_3\)) was purchased (Aldrich) and was used without further purification. Phenacyl bromide was prepared according to the standard procedure. Thioacetamide was purchased (Loba Chemicals) and was used without purification.
α-oxoketene dithioacetals were prepared by the earlier reported procedure and the structural assignment was confirmed by comparing the spectral data with the reported values.

2,4-Dimethylthiazole:

To a stirred suspension of thioacetamide (37.5 g, 0.5 mol) in benzene (100 ml) was added chloroacetone (51 g, 0.5 mol) in benzene (50 ml) over a period of 45 minutes. The reaction mixture was initially warmed to initiate the exothermic reaction. The mixture was further refluxed for 30 minutes, cooled and the upper benzene layer was removed by decantation. To the thiazolonium hydrochloride remained as solid mass was added cold 20% NaOH solution until the solution is alkaline. The upper thiazole layer was separated and the aqueous layer is extracted with ether (3 x 75 ml). The combined extracts were washed once with water (100 ml), dried (Na₂SO₄) and distilled. B.P. 143-145°C, yield 39.5 g (70%).

2-Methyl-4-phenylthiazole (36b) was prepared by the above method using phenacyl bromide and thioacetamide, and was obtained as colourless crystals, yield 68%, m.p. 67°C.

Generation and reaction of 2-lithiomethylthiazoles with oxoketene dithioacetals; General Procedure:

To a stirred solution of freshly distilled 2,4-dimethylthiazole (1.70 g, 0.15 mol) in dry THF (25 ml), butyllithium (0.015 mol) was added under an efficient atmosphere of nitrogen, maintaining the temperature at -78°C. The lithiation was indicated by the appearance of reddish brown colour. The solution is stirred for 15 min. at -78°C. The oxoketene dithioacetal (0.01 mol) was added as a THF (15-25 ml depending
on solubility) solution in one portion and further stirred for 1 hr., slowly warming the mixture to room temperature. The reaction mixture was poured into saturated ammonium chloride solution and the layers were separated. 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 in nearly quantitative yield.

General procedure for the cycloaromatization of hydroxy dithioacetals;

**Synthesis of thiazolo[3,2-a]pyridinium tetrafluoroborates 39a-g, 40, 42a-e, 53b, c:**

To a solution of crude hydroxy dithioacetal (Ca.0.01 mol) in dry benzene (50 ml), boron trifluoride etherate (8 ml) was added and the reaction mixture was refluxed with stirring for 1.5 hr. The reaction mixture was cooled and the benzene layer was removed by decantation. The remaining residue was dissolved in minimum amount of ethyl acetate and neutralized with saturated sodium bicarbonate solution. The solid separated was collected by filtration, washed with water (3x50 ml) and diethylether (2x20 ml). Analytically pure products were obtained by recrystallization from ethylacetate.

3-Methyl-5-methylthio-7-phenylthiazolo[3,2-a]pyridinium tetrafluoroborate (39a) was isolated as yellow solid (ethylacetate), yield 55%; m.p. 247-248°C; $\nu_{\text{max}}$ 1601, 1500, 1420, 1020-1119 (br) cm$^{-1}$; $\delta_{H}$ 2.91(3H,s, CH$_3$), 3.30(3H,s,SCH$_3$), 7.56-7.93(7H,m,arom), 8.31(1H,s,H-8). (Found: C,49.99; H,3.81; N,4.02. C$_{15}$H$_{14}$NS$_2$BF$_4$ requires: C,50.15; H,3.93; N,3.90%); m/z 272(34%,M$^+$-BF$_4$), 271(100), 256(62).
3-Methyl-5-methylthio-7-(4-methylphenyl)thiazolo[3,2-a]pyridinium tetrafluoroborate (39b) was isolated as yellow solid (ethylacetate), yield 58%; m.p. 281-182°C; υmax 1599, 1497, 1423, 1027-1115 (br) cm⁻¹; S_H 2.48(3H,s,CH₃), 2.90(3H,s,CH₃), 3.30(3H,s,SCH₃), 7.33-7.82(6H,m, arom), 8.24(1H,s,H-8). (Found: C, 51.61; H, 4.40; N, 3.88. C₁₆H₁₆NS₂BF₄ requires: C, 51.49; H, 4.32; N, 3.75%; m/z 286(75%,M⁺-BF₄), 285(74), 270(100).

3-Methyl-5-methylthio-7-(4-methoxyphenyl)thiazolo[3,2-a]pyridinium tetrafluoroborate (39c) was isolated as yellow solid (ethylacetate), yield 68%; m.p. 284-185°C; υmax 1604, 1505, 1433, 1021-1122(br) cm⁻¹; S_H 2.90(3H,s,CH₃), 3.29(3H,s,SCH₃), 4.00(3H,s,OCH₃), 7.27(2H,d,J=8.5Hz, arom), 7.61(1H,s,arom), 7.74(1H,s,arom), 7.89(2H,d,J=8.5Hz,arom), 8.30(1H,s,H-8). (Found: C, 49.21; H, 4.03; N, 3.71. C₁₆H₁₆NOS₂BF₄ requires: C, 49.37; H, 4.14; N, 3.60%; m/z 302(33%,M⁺-BF₄), 301(55), 287(100).

3-Methyl-5-methylthio-7-(2-naphthyl)thiazolo[3,2-a]pyridinium tetrafluoroborate (39d) was isolated as yellow solid (ethylacetate), yield 60%; m.p. 312-13°C; υmax 1601, 1491, 1434, 1030-1119(br) cm⁻¹; S_H 2.88(3H,s,CH₃), 3.20(3H,s,SCH₃), 7.44-7.68(5H,m,arom), 7.77-8.04(4H,m,arom), 8.22(1H,s,H-8). (Found: C, 55.58; H, 4.02; N, 3.60. C₁₉H₁₆NS₂BF₄ requires: C, 55.76; H, 3.94; N, 3.42%; m/z 322(24%,M⁺-BF₄), 321(48), 306(84).

3-Methyl-5-methylthio-7-(2-furyl)thiazolo[3,2-a]pyridinium tetrafluoroborate (39e) was isolated as yellow solid (ethylacetate), yield 53%; m.p. 249-250°C; υmax 1609, 1501, 1477, 1421, 1009-1122(br) cm⁻¹; S_H 2.91(3H,s,CH₃), 3.26(3H,s,SCH₃), 6.75(1H,brs,H-3' furyl), 7.41(1H,distorted t, H-4' furyl), 7.54(1H,s,arom), 7.70(1H,s,arom), 7.77(1H,d,H-5' furyl),
8.26(1H,s,H-8). (Found: C, 44.80; H, 3.53; N, 4.22. \( \text{C}_{13}\text{H}_{12}\text{NOS}_2\text{BF}_4 \) requires: C, 44.71; H, 3.47; N, 4.01%; m/z 262(42%,\( \text{M}^+\text{-BF}_4 \)), 261(96), 246(100).

3-Methyl-5-methylthio-7-(2-thienyl)thiazolo[3,2-a]pyridinium tetrafluoroborate (39f) was isolated as yellow solid (ethylacetate), yield 57%; m.p. 273-74°C; \( \nu \) max 1600, 1493, 1433, 1416, 1026-1120(br) cm\(^{-1} \); \( \delta \) \(_\text{H} \) 2.90(3H,s,CH\(_3\)), 3.23(3H,s,SCH\(_3\)), 7.29(1H,t,J=4.5Hz,H-4' thienyl), 7.53(1H,s,arom), 7.67(1H,brs,arom), 7.76(1H,d,J=4.5Hz,H-3' thienyl), 7.88(1H,d,J=4.0Hz,H-5' thienyl), 8.22(1H,s,H-8). (Found: C, 42.66; H, 3.32; N, 4.01. \( \text{C}_{13}\text{H}_{12}\text{NS}_3\text{BF}_4 \) requires: C, 42.75; H, 3.31; N, 3.84%); m/z 278(37%,\( \text{M}^+\text{-BF}_4 \)), 277(100), 262(97).

3-Methyl-5-methylthio-7-methylthiazolo[3,2-a]pyridinium tetrafluoroborate (39g) was isolated as colourless solid (ethylacetate), yield 51%; m.p. 154-155°C; \( \nu \) max 1609, 1515, 1457, 1440, 1422, 1025-1120(br) cm\(^{-1} \); \( \delta \) \(_\text{H} \) 2.65(3H,s,CH\(_3\)), 2.83(3H,s,CH\(_3\)), 3.23(3H,s,SCH\(_3\)), 7.44(1H,s,H-2), 7.59(1H,s,H-6), 7.97(1H,s,H-8). (Found: C, 40.58; H, 4.01; N, 4.88. \( \text{C}_{10}\text{H}_{12}\text{NS}_2\text{BF}_4 \) requires: C, 40.42; H, 4.07; N, 4.71%); m/z 210(44%,\( \text{M}^+\text{-BF}_4 \)), 194(28).

3-Methyl-5-methylthio-7-(3-methoxystyryl)thiazolo[3,2-a]pyridinium tetrafluoroborate (40) was isolated as yellow solid (ethylacetate), yield 42%; m.p. 293-294°C; \( \nu \) max 1604, 1530, 1461, 1430, 1030-1125(br) cm\(^{-1} \); \( \delta \) \(_\text{H} \) 2.88(3H,s,CH\(_3\)), 3.20(3H,s,SCH\(_3\)), 3.98(3H,s,OCH\(_3\)), 6.97-7.71 (8H,m,arom and olefinic), 8.13(1H,brs,H-8). (Found: C, 51.96; H, 4.30; N, 3.48. \( \text{C}_{18}\text{H}_{18}\text{NOS}_2\text{BF}_4 \) requires: C, 52.06; H, 4.37; N, 3.37%); m/z 328 (2%,\( \text{M}^+\text{-BF}_4 \)), 313(79), 312(44).
3-Methyl-5-methylthio-6,7,8,9-tetrahydrothiazolo[3,2-a]isoquinolinium tetrafluoroborate (42a) was isolated by silica gel column chromatography (ethylacetate:hexane 1:20 as eluent) as yellow solid, yield 33%; m.p. 56-58°C; \( \nu_{\text{max}} \) 1596, 1573, 1516, 1415, 1011-1123(br) cm\(^{-1}\); \( S_H \) 1.60-1.90 (4H, m, \( CH_2 \)), 2.40(3H, s, \( CH_3 \)), 2.56-2.90(4H, m, \( CH_2 \)), 3.20(3H, s, \( SCH_3 \)), 6.56(1H, s, H-2), 6.81(1H, s, H-10). (Found: C, 62.78; H, 6.69; N, 5.72. 
\( C_{13}H_{16}NS_2 \) requires: C, 62.36; H, 6.44; N, 5.59%).

3-Methyl-5-methylthio-6,7-dihydrothiazolo[3,2-a]phenanthroquinolinium tetrafluoroborate (42b) was isolated as yellow solid (ethylacetate), yield 62%; m.p. 193-194°C; \( \nu_{\text{max}} \) 1600, 1581, 1505, 1431, 1412, 1028-1125 (br) cm\(^{-1}\); \( S_H \) 2.57(3H, s, \( CH_3 \)), 3.11(2H, t, J=7.0Hz, \( CH_2 \)), 3.30(3H, s, \( SCH_3 \)), 3.64(2H, t, J=7.0Hz, \( CH_2 \)), 7.41-7.64(3H, m, arom), 7.77(1H, s, arom), 7.98 (1H, d, J=8.5Hz, arom), 8.69(1H, s, H-12). (Found: C, 53.21; H, 4.13; N, 3.70. \( C_{17}H_{16}NS_2BF_4 \) requires: C, 53.00; H, 4.19; N, 3.64%); m/z 283 [98%, M\(^+\)-(BF\(_4\) and \( CH_3 \)], 250(44).

3-Methyl-5-methylthio-9-methoxy-6,7-dihydrothiazolo[3,2-a]phenanthroquinolinium tetrafluoroborate (42c) was isolated as yellow solid (ethylacetate), yield 64%; m.p. 278-279°C; \( \nu_{\text{max}} \) 1590, 1577, 1511, 1430, 1412, 1020-1121(br) cm\(^{-1}\); \( S_H \) 2.56(3H, s, \( CH_3 \)), 3.10(2H, t, J=7.0Hz, \( CH_2 \)), 3.29(3H, s, \( SCH_3 \)), 3.60(2H, t, J=7.0Hz, \( CH_2 \)), 4.03(3H, s, \( OCH_3 \)), 6.99-7.23 (2H, m, arom), 7.70(1H, s, arom), 7.97(1H, d, J=8.5Hz, arom), 8.57(1H, s, H-12). (Found: C, 51.91; H, 4.13; N, 3.44. \( C_{18}H_{18}NO_2S_2BF_4 \) requires: C, 52.06; H, 4.37; N, 3.37%); m/z 328(6%, M\(^+\)-BF\(_4\)), 313(100).

3-Methyl-5-methylthio-7,8-dihydro-6H-benzocyclohepta[2,1-d]thiazolo [3,2-a]pyridinium tetrafluoroborate (42d) was isolated as colourless.
crystals (ethylacetate:hexane), yield 60%; m.p. 156-157°C; $\nu_{max}$ 1602, 1588, 1500, 1440, 1412, 1028-1116(br) cm$^{-1}$; $\delta_H$ 2.26-2.78(4H,m,CH$_2$), 2.57(3H,s,CH$_3$ merged with CH$_2$), 2.77-3.36(2H,m,CH$_2$), 3.29(3H,s,SCH$_3$, merged with CH$_2$), 7.25-7.62(4H,m,arom), 7.63(1H,s,arom), 8.13(1H,s, H-13). (Found: C,54.30; H,4.52; N,3.56. C$_{18}$H$_{18}$NS$_2$BF$_4$ requires: C,54.15; H,4.54; N,3.51%); m/z 312(2%,M$^+$/BF$_4$), 311(3), 297(12).

3-Methyl-11-methyl-5-methylthio-6,7-dihydrobenzothiepin[2,1-d]thiazolo[3,2-a]pyridinium tetrafluoroborate (42e) was isolated as yellow solid (ethylacetate), yield 62%; m.p. 239-240°C; $\nu_{max}$ 1598, 1576, 1433, 1411, 1389, 1030-1109(Br) cm$^{-1}$; $\delta_H$ 2.47(3H,s,CH$_3$), 2.57(3H,s, CH$_3$), 3.34(3H,s,SCH$_3$), 2.74-3.40(2H,m,CH$_2$ merged with SCH$_3$), 3.59-4.23(2H,m,CH$_2$), 7.50(2H,brs,arom), 7.59(1H,s,arom), 7.88(1H,brs,arom), 8.29(1H,s,H-13). (Found: C,50.11; H,4.30; N,3.38. C$_{18}$H$_{18}$NS$_3$BF$_4$ requires: C,50.12; H,4.21; N,3.25%); m/z 329[2%,M$^+$/-(BF$_4$ and CH$_3$)], 314(22), 313 (100), 298(85).

3-[5-(2-methyl-4-phenyl)thiazolo]-S-methylthiocinnamate (49) was isolated as yellow crystals (CH$_2$Cl$_2$;hexane), yield 32%; m.p. 115-116°C; $\nu_{max}$ 1655, 1589 cm$^{-1}$; $\delta_H$ 2.20(3H,s,CH$_3$), 2.76(3H,s,SCH$_3$), 6.69(1H, s,vinyl), 7.11-7.46(8H,m,ArH), 7.60-7.74(2H,m,ArH). (Found: C,68.19; H,4.76; N,4.09. C$_{20}$H$_{17}$NOS$_2$ requires: C,68.34; H,4.88; N,3.99%); m/z 351(9%,M$^+$).

5-Methylthio-3-phenyl-6,7-dihydrothiazolo[3,2-a]phenanthroquinolinium tetrafluoroborate(53b) was isolated as yellow solid (ethylacetate), yield 43%; m.p. 254-255°C; $\nu_{max}$ 1589, 1510, 1410, 1027-1110(br) cm$^{-1}$; $\delta_H$ 2.15(3H,s,SCH$_3$), 3.06(2H, distorted t, CH$_2$), 3.46(2H,distorted t, CH$_2$), 7.34-7.71(7H,m,ArH), 7.82(1H,s,H-2), 7.90-8.09(2H,m,ArH),
8.70(1H,s,H-12). (Found: C,59.21; H,4.15; N,3.26. C$_{22}$H$_{18}$NS$_2$BF$_4$
requires: C,59.07; H,4.06; N,3.13%).

9-Methoxy-5-methylthio-3-phenyl-6,7-dihydrothiazolo[3,2-a]phenanthro-
quinolinium tetrafluoroborate (53c) was isolated as yellow solid
(ethylacetate), yield 41%; m.p. 226-228°C; $\nu$$_{max}$ 1587, 1509, 1411,
1020-1101(br) cm$^{-1}$; $\delta$$_H$ 2.13(3H,s,SCH$_3$), 3.03(2H,distorted t, CH$_2$),
3.43(2H,distorted t, CH$_2$), 6.88-7.13(2H,m,ArH), 7.33-7.64(5H,m,ArH),
7.74(1H,s,H-2), 7.94(1H,d,J=8.5Hz,ArH), 8.54(1H,s,H-12). (Found:
C,58.02; H,4.38. N, 3.20. C$_{23}$H$_{20}$NOS$_2$BF$_4$ requires: C,57.87; H,4.22;
N,2.93%).
REFERENCES


