CHAPTER IV

1,3-ANIONIC CYCLOADDITIONS OF 1,3-DIPHENYL-2-AZAALLYL AND ETHYL (BENZYLIDENEAMINO)ACETATE ANIONS WITH α-OXOKETENE DITHIOACETALS.

IV.1. INTRODUCTION

The α-oxoketene dithioacetals possess 1,3-electrophilic centres with differing electrophilicity and undergo chemoselective addition-elimination reactions with various carbon and nitrogen nucleophiles. Generally the hard carbon nucleophiles undergo exclusive 1,2-addition while the bulkier and stabilized carbanions undergo 1,4-addition, sometimes followed by 1,2-addition\(^1-^4\). On the otherhand the nitrogen nucleophiles generally undergo 1,4-addition-elimination, though 1,2-addition sequence with hydroxylamine under basic conditions has also been
reported\textsuperscript{5}. As an extension of these studies various allyl\textsuperscript{1,6} and 1-azaallyl\textsuperscript{7} anions have been shown to undergo exclusive 1,2-addition followed by Lewis acid assisted cycloaromatization to yield the corresponding aromatic and heteroaromatic compounds in high yields. In the Chapter III the reactivity of 1-azaallyl anion was demonstrated by reacting 2-picolyllithium with oxoketene dithioacetals to yield the corresponding carbinol acetals in nearly quantitative yields which on boron trifluoride etherate assisted cyclization yielded the corresponding quinolizininium tetrafluoroborates in excellent yields.\textsuperscript{7} The double bond reactivity of the oxoketene dithioacetals towards 1,3-dipolar species such as sodium azide has also been reported from this laboratory to yield triazoles.\textsuperscript{8}

In the course of these studies it was considered of interest to examine the reactivity of 2-azaallyl anions, which are known to undergo 1,3-anionic cycloaddition with activated double bonds in a concerted and stereoselective manner to give a number of five membered heterocycles\textsuperscript{10}. The regiocontrol in these cycloaddition reactions has also shown to be remarkably selective and generally only one regioisomer is formed wherever alternative possibilities existed. The structural features of 2-azaallyl anions have been examined which are shown to exist in different configurations at different reaction conditions. Thus, 1,3-diphenyl-2-azaallyllithium in the \textit{cis,trans} (Z,E) form can be prepared by the conrotatory
ring opening of N-lithio-cis-2,3-diphenylaziridine at 40-60°C, although it rearranges to the thermodynamically more stable trans,trans(E,E) form immediately\(^9\) (Scheme 1). It is therefore possible to utilize these configurational differences by carefully manipulating reaction conditions for the synthesis of stereoselective cycloadducts. In the light of these reactivity profile of 3 towards activated double bonds, it was considered to examine its reactivity with \(\alpha\)-oxoketene dithioacetals which may lead to the corresponding pyrrolidine cycloadducts. The presence of two methylthio groups in these intermediates will further permit the elimination of methylmercaptan in the pyrrolidine adducts and the end product should result in the fully aromatized pyrroles. Such studies may qualify the \(\alpha\)-oxoketene dithioacetals as masked acetylenic compounds. The availability of wide structural variants of \(\alpha\)-oxoketene dithioacetals from abundantly available active methylene ketones will enhance the scope of the methodology for the synthesis of pyrroles and pyrrolidines through 1,3-anionic cycloaddition reaction. The investigations on anionic cycloadditions of 1,3-diphenyl-2-azaallyl and ethyl (benzylideneamino)acetate anions with \(\alpha\)-oxoketene dithioacetals have been presented in this chapter.

The 1,3-anionic cycloaddition of 2-azaallyl anions have been extensively investigated and the results have been reviewed\(^{10}\). Only a selected number of key cycloaddition
reactions have been briefly discussed in this chapter as an introduction to the present investigation. 1,3-Diphenyl-2-azaallyllithium 3 was first reported by Kauffmann by reacting N-benzylidene benzylamine with lithium diisopropylamide\textsuperscript{11}. Subsequently the same group also prepared the anion \( \tilde{3} \) from N-lithio-cis-2,3-diphenylaziridine \( \tilde{1} \) through a thermal conrotatory ring opening process\textsuperscript{9} (Scheme 1). Most of the 1,3-anionic cycloadditions investigated have been shown to be stereospecific. The best studied reaction is that of both \textit{cis,trans} and \textit{trans,trans} 1,3-diphenylazaallyllithium \( 3a \) and \( 3b \) with \textit{trans-} and \textit{cis-}stilbenes\textsuperscript{12}. The anion \( \tilde{3} \) was reacted with \textit{trans-} and \textit{cis-}stilbenes to yield the corresponding pyrrolidines \( 4 \) in a stereospecific manner\textsuperscript{12}. These observations can be most readily interpreted in terms of symmetry-allowed concerted [ \( \pi_4 \delta^+ \pi_2 \delta^* \) ] cycloaddition processes and the reaction was extended to large number of olefins with known geometry to confirm the concertedness of the reaction. The reaction of \( \tilde{3} \) with butadiene yielded the corresponding vinyl pyrrolidines \( 5 \) in high yields\textsuperscript{13}. Also, the reaction of \( \tilde{3} \) with alkynes and nitriles yielded directly the corresponding pyrroles and imidazoles \( 6 \) respectively in good yields\textsuperscript{14} (Scheme 1).

Since the activation of double bond was found to be a prerequisite for cycloaddition reactions, the double bonds activated by groups which can be cleaved
subsequently using appropriate methodology have also been studied. Thus, 3 was reacted with vinyl sulphides, phosphines, selenides, triaryl silanes etc, to yield the corresponding pyrrolidines 7 in high yields and the group G could be removed using appropriate reaction conditions15. A few exceptions of unactivated double bond addition to 3 to yield the corresponding isoindole 8 in moderate yields (Scheme 1).

Kauffmann has reported that carbonyl groups of proven value in Diels-Alder reactions and 1,3-dipolar cycloadditions are unsuitable for anionic 1,3-cycloadditions owing to the pronounced nucleophilic character of the anionic reagents15. However, a few examples of this structural feature have been examined, where the carbonyl functionality does not interfere in the formation of the cycloadduct. Thus, the anion 3 when reacted with phenylpropiolic acid N,N-dimethylamide 9 affords the pyrroline 10 which is readily oxidized by air to the pyrrole 1116 (Scheme 2). Similarly the doubly activated methyl α-cyano-β-phenylcinnamate 12 reacted with 3 to yield the corresponding pyrrolidines 13 and 14. The adduct 13 when heated in refluxing toluene under nitrogen atmosphere for 24 hours, underwent retro-cycloaddition to yield azomethine ylide 15 which on reaction with methyl maleate and methyl fumarate yielded the corresponding pyrrolidines 17 and 18 stereospecifically17 (Scheme 3).
Scheme 2
An interesting example showing a two step mechanism for 1,3-anionic cycloadditions has been reported by Grigg and co-workers\textsuperscript{18}. They have selected the potentially ambident imine anions derived from\textsuperscript{19} which are good Michael donors and reacted them with acrylonitrile and methyl acrylate to yield the corresponding Michael adducts\textsuperscript{20} with complete regiocontrol. These Michael adducts are of particular interest because they are structurally suitable for geometrically disfavoured 5-endo-trig ring closure and are shown to undergo cyclisation in the presence of appropriate base and solvent to yield the pyrrolidines\textsuperscript{21-23}. However, the stereochemistry of the pyrrolidines varies with the base and solvent composition. Similarly the imines of \( \alpha \)-amino acid esters\textsuperscript{24} undergo cycloadditions probably via their azomethine ylides\textsuperscript{25} to give the pyrrolidines\textsuperscript{26} in good yields\textsuperscript{19} (Scheme 4).

Tsuge and co-workers have described in a series of papers, the preparation of N-lithiated azomethine ylide 1,3-dipoles by reacting imines with LDA or (LiBr/Et\textsubscript{3}N) and examined their reactivity towards electron deficient olefins\textsuperscript{20,21,24}. These cycloadditions have been found to occur in an exclusively regio- and stereoselective manner. They have also offered explanation of the reactivity of 2-azaallylanions versus azomethine ylides. Although complementary in synthetic application, 2-aza-
allylanions and azomethine ylides are isoelectronic, both carrying 4 conjugation along a carbon-nitrogen-carbon framework. In the case of 2-azaallyl anions, the lone pair of electrons on the nitrogen are free and consequently they should behave like a hard nucleophile rather than a 1,3-dipolar species. However, the lithium cation is known to be associated with the central nitrogen so that these anions behave like soft azomethine ylides and undergo 1,3-cycloaddition reactions. Utilizing these concepts, Tsuge and co-workers have examined the reactivity of azomethine ylides towards activated double bonds as described in the Scheme 5.

The oxoketene dithioacetals with $\beta,\beta$-bis(methylthio) group and an $\alpha$-carbonyl functionality should behave like push-pull ethylenes and consequently their double bond activity as dipolarophile with 2-azaallylanion 3 should yield the corresponding pyrrolidines rather than the 1,2-addition products leading to pyridine 41 (Scheme 6). The results of these studies are presented in the following section.

IV.2 RESULTS AND DISCUSSION

In principle, a large structural variants of the oxoketene dithioacetals can be used in these cycloaddition studies, however only a selected number of these have
Scheme 5

R1 = Ph, R2 = H, Me, i - Pr
R1 = Et, R2 = Ph
R3 = H, R2 = H, Me
R3 = CO2Me, R2 = H
R3 = Me; R2 = H
R3 = Ph, R2 = H

R1 = Ph; R2 = H

R3 = Me02C; R2 = H

- LiCN

R4 LiCN

Me02C

Me02C
been examined in this investigation. Similarly among 2-azaallylanions, 1,3-diphenyl-2-azaallylanion has been selected as a typical example. Also the unsymmetrical azaallylanion derived from Ethyl(benzylideneamino)acetate under very mild conditions have also been used in this study to investigate the reactivity towards oxoketene dithioacetals.

IV.2.1 Reactions of 1,3-Diphenyl-2-azaallyllithium with Oxoketene Dithioacetals.

In a typical reaction, the oxoketene dithioacetal 37a was reacted with 1,3-diphenyl-2-azaallylanion 3 at -78°C derived from deprotonation of N-benzylidene benzylamine using LDA as base to yield after work up the fully aromatized 3-benzoyl-2,5-diphenylpyrrole 39 in 79% yield. Apparently 39 is formed from the corresponding pyrrolidine 38 which in turn is formed via a 1,3-anionic cycloaddition of the 2-azaallylanion 3 with oxoketene dithioacetal, followed by sequential in situ elimination of two MeSLi groups. Thus, the oxoketene S,S-acetals as masked acetylenes are demonstrated through the formation of 39, which could have been obtained from the corresponding β-methylthiobenzoylacetylene 37A and the anion 3. Either the carbinol acetal 40, arising from a possible 1,2-addition or the corresponding cycloaromatized pyridine 41 were not detected in the reaction mixture. The structure of the pyrrole 39 was established by its analytical and spectral data. It showed in its
mass spectrum molecular ion peak at m/z 323(100%) and characteristic fragmentation patterns at m/z 246(72%) which accounted for loss of phenyl group and m/z 218(7%, due to the loss of benzoyl group. The compound was analyzed for C_{23}H_{17}NO and its IR spectrum showed clearly the NH absorption as a broad band at $\gamma_{\text{max}}$ 3200 cm$^{-1}$ and two other prominent bands appeared at 1595 (C=O) and 1572 cm$^{-1}$. The structure of 39a was further confirmed from its $^1$H NMR spectrum (CDCl$_3$). The doublet at $\delta$ 6.75(1H, J=1.5Hz) was assigned to H-4 proton. The 13-aromatic protons appeared as a multiplet between $\delta$ 7.00-7.58, whereas the multiplet between $\delta$ 7.62-7.81 was assigned to the two ortho protons of the benzoyl group. The pyrrole NH proton appeared as broad singlet at $\delta$ 11.93(1H, exchangeable with D$_2$O). The other oxoketene dithioacetals 37b-g similarly reacted with 3 to yield the corresponding 3-acyl pyroles 39b-g in 71-84% overall yields (Scheme 6). Similarly $\alpha$-carbomethoxyketene dithioacetal underwent facile cycloaddition with 3 to afford the corresponding 3-carbomethoxy pyrrole 39h in 71% yield. The structures of the pyrroles 39b-h thus obtained were confirmed by their analytical and spectral data which are described in the experimental section.

Interestingly the nitroketene S,S-acetal 42 reacted with 1,3-diphenyl-2-azaallyl anion 3 to yield the corresponding tetrahydropyrrolidine 43 in 64% yield but the fully aromatized pyrrole 44 could not be detected in
the reaction mixture. The structure of 43 was confirmed from its analytical and spectral data. Thus, in its mass spectrum, it exhibited a signal at m/z 360 (M⁺, 4%) and the compound was analysed for C₁₈H₂₀N₂O₂S₂. In its IR spectrum (KBr) the absorption band at 3342 cm⁻¹ was assigned to the NH group and the strong band at 1600 cm⁻¹ was assigned to the nitro group. The structure was further confirmed from its ¹H NMR spectrum (CDCl₃). The signals at 51.26 (3H) and 2.08 (3H) were assigned to the two methylthio groups. The broad signal at 2.39 (1H, exchangeable with D₂O) stood for the NH proton. The broad singlet at 84.80 was assigned to the H-2 proton while the doublet at 84.69 (J=6Hz) accounted for the H-4 proton. The signal due to H-5 proton appeared at 84.92 (dd, J=6 and 1.5 Hz), while the multiplet between 87.12-7.75 was assigned to the ten aromatic protons. The stereochemical configuration of 43 was tentatively assigned as shown in Scheme 7 on the basis of known literature examples for cycloaddition of 3¹⁰,²⁰.

When the reaction of 3 was extended to the oxoketene dithioacetal 45a derived from tetralone, the corresponding spiropyrrroline 47 was obtained in 74% yield as colourless crystalline solid. Interestingly the other possible structures 48 and 49 (Scheme 7), which might arise from prototopic shift were ruled out and the exclusive structure 47 was confirmed from its spectral data. The mass spectrum of the compound exhibited
molecular ion peak at m/z 397 (M^+, 25%) and was analysed for C_{26}H_{23}NOS. In its IR spectrum (KBr) the absorption band at 1670 and 1605 cm\(^{-1}\) were assigned to C=O and C=N stretching vibrations. The clear absence of peaks due to NH group in the IR spectrum ruled out the possible structure 48. The structure 47 was further confirmed from its \(^1\)H NMR spectrum, which also helped to eliminate the probable structures 48 and 49. The two multiplets (2H each) present at \(\delta\) 1.36-1.59 and 2.25-2.36 were assigned to four methylene protons while the signal due to methylthio group appeared as sharp singlet (3H) at \(\delta\) 1.90. The aromatic protons were present as two multiplets between \(\delta\) 7.00-7.51 (10H) and 8.05-8.25 (3H) respectively. The signals due to the two methine protons H\(_A\) and H\(_B\) were present at \(\delta\) 4.45 and 6.22 respectively as doublets (J=2Hz). The nature of the coupling constant (J=2Hz) point to cis stereochemistry of H\(_A\) and H\(_B\) protons in line with the earlier reported examples in pyrroline systems.\(^{20}\) Similarly the other cyclic oxoketene dithioacetals 45\(_b\) and 45\(_c\) derived from benzothiepinone and pyrazolone reacted with 3 to yield the corresponding spiropyrrroles 50 and 51 in 68 and 71% yields respectively (Scheme 8). The structure and stereochemistry of 50 and 51 were assigned with the help of their spectral and analytical data (experimental).

Interestingly, the cyclic oxoketene dithioacetals 45\(_d\) and 45\(_e\) did not react with 3 in the expected manner of the
\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \quad \text{SMe} \\
\text{H}_5\text{C}_6 & \quad \text{N} \quad \text{C}_6\text{H}_5 \\
\text{Li} & \quad 78^\circ \text{C} \\
\text{H}_3\text{C} & \quad \text{H} \\
\text{H}_5\text{C}_6 & \quad \text{N} \quad \text{C}_6\text{H}_5 \\
\text{Li} & \quad \text{SMe} \quad \text{C}_6\text{H}_5 \\
\text{Ar} \quad \text{N} \quad \text{C}_6\text{H}_5 \\
\text{MeS} & \quad \text{H} \\
\text{Ar} \quad \text{N} \quad \text{C}_6\text{H}_5 \\
\text{MeS} & \quad \text{H} \\
\text{Ar} = 4-\text{MeOC}_6\text{H}_4
\end{align*}
\]
preceeding cycloadditions. When 45d was reacted with 3 under identical reaction conditions, the product isolated in 79% yield was characterized as hexahydroisoquinoline derivative 53a and there was not trace of 1,3-anionic cycloaddition product in the reaction mixture. The structure of the compound 53a was confirmed from its analytical and spectral data. The compound exhibited in its mass spectrum a signal at m/z 379 (M⁺, 96%) and was analysed for C₂₃H₂₅NS₂. Its IR spectrum showed absorption bands at 1605 and 1527 cm⁻¹ which were assigned to C=N and C=C stretching vibrations. In its ¹H NMR spectrum the multiplet between δ1.62-1.82 (4H) was assigned to methylene protons, while the two methylthio protons appeared as sharp singlets (3H each) at δ1.90 and 2.25. The other four methylene protons appeared as multiplet between δ2.50-2.74. The methine proton appeared as a sharp singlet at δ6.88 and the aromatic protons were present as multiplet (10H) between δ7.21-7.50.

The attempts to aromatize the pyridine ring in 53a by elimination of methylmercaptan under different reaction conditions to give 54a however were not successful probably due to steric crowding in 54a. On the other hand, treatment of 53a with HgCl₂ in THF at room temperature, gave a colourless crystalline product which was characterized as tetrahydroisoindole 55a (Scheme 9). The structure of 55a was confirmed from its analytical
and spectral data (experimental section). Similarly 45e reacted with 3, first to yield the annelated dihydropyridine 53b in 76% yield which on treatment with HgCl₂ in THF at room temperature rearranged to the corresponding 3,4-annelated pyrrole 55b (Scheme 10). The structure of both 53b and 55b have been confirmed from its analytical and spectral data which are given in the experimental section.

Apparently the 1,3-diphenyl-2-azaallyl anion 3 did not undergo anionic cycloaddition with the cyclic oxoketene dithioacetals 45d and 45e to give spiropyrrrolines but yielded products by sequential or concerted 1,2- and 1,4-addition-elimination to give 53 and 53b respectively. A plausible mechanism for the formation of 55a and 55b has been described in the Scheme 10. The dihydro-4,5-annelated pyridines 45 appear to suffer an electrocyclic reversion to yield the corresponding azatriene 56 which undergo intramolecular heterotriene cyclization²³ to give the intermediate 57 followed by elimination of MeSH group to yield the imminium intermediate 58 which on hydrolysis give the 3,4-annelated pyrroles 55a and 55b respectively.

IV.2.2 Lithium Bromide-Triethylamine Induced Cycloaddition
Reactions of Ethyl(Benzylideneamino)acetate with Oxoketene Dithioacetals.

Tsuge and co-workers have extensively investigated the deprotonation of N-alkylidene-2-amino esters under
varying conditions\textsuperscript{24}. Thus, strong bases such as LDA, n-BuLi, NaH, EtMgBr indeed yielded the corresponding anions, however these species failed to undergo cycloaddition with activated olefins. Tsuge has attributed the failure of these reactions to the facile polymerization of the activated olefins under highly basic reaction conditions. The same authors have successfully attempted the deprotonation of these esters using mild Lewis acid-base combination (LiBr-Triethylamine) to yield the corresponding N-lithiated azomethine ylides in quantitative yields which undergo neat cycloadditions with activated olefins.

When the \( \alpha \)-oxoketene dithioacetal 37a was reacted with N-lithiated azomethine ylide 60 generated under Tsuge's conditions (LiBr-Triethylamine) at room temperature the corresponding pyrrolidine 61a (Scheme 11) was obtained in 72\% yield as a single stereoisomer. The analytical and spectral data of 61a were in confirmity with the assigned structure (experimental). Similarly the corresponding 3-furoylpyrrolidine 61b was obtained in 69\% yield under identical reaction conditions. However, the \( \alpha \)-acetyl ketene dithioacetal 37c failed to give the corresponding pyrrolidine and the bright yellow product (81\%) isolated under similar reaction conditions was characterized as 6-methyl-4-(methylthio)-3-benzylidene aminopyran-2-one 62c on the basis its analytical and spectral data. Thus, in its mass spectrum, it exhibited a signal at m/z 259
Scheme 11
(M+, 59%) and the compound was analyzed for C_{14}H_{13}NO_2S. In its IR spectrum (KBr) the absorption band at 1690 cm\(^{-1}\) was assigned to C=O group and the strong bands at 1622 and 1598 cm\(^{-1}\) were assigned to the C=N and C=C stretching vibrations. The structure was further confirmed from its \(^1\)H NMR spectrum (CDCl\(_3\)). The sharp singlets at \(\delta\)2.28(3H) and \(\delta\)2.43(3H) were assigned to methyl and methylthio protons respectively. The signal at \(\delta\)6.12(s,1H) was assigned to the H-5 proton while the aromatic protons appeared as multiplets between \(\delta\)7.31-7.56(3H) and \(\delta\)7.74-8.08(2H) and the singlet at \(\delta\)9.53(1H) was assigned to the benzylideneamino(C\(_6\)H\(_5\)CH=N-) proton. The \(^{13}\)C NMR(CDC\(_3\)) spectral data was also in full agreement with the assigned structure (experimental). The pyran-2-ones 62a and 62b were also obtained when the oxoketene dithioacetal 37~ and 37b were reacted with 60 under refluxing conditions (16 hr). The analytical and spectral data of the pyran-2-ones 62a and 62b were in agreement with the assigned structures and are given in the experimental section.

The possible mechanism for the formation of pyrrolidine 61 and pyran-2-one 62 from the reaction of the anion 60 with 37 is described in Scheme 12. The pyrrolidine 61 can be formed either through path A involving a concerted endo cycloaddition of the syn N-lithiated azomethine ylide 60A or through a tandem Michael-imine addition of lithium enolate 60B followed by a 5-endo-trig cyclization
of the intermediate 65. The discrimination between the two paths is not possible because of the difficulty in identifying between the two anionic intermediates 60A and 60B. The intermediate 65 at higher temperature equilibrates between the thermodynamically more stable 66 which undergo intramolecular enol lactonization and by loss of methylmercaptan to give the pyran-2-one 62. The formation of only pyran-2-one 62c from α-acetylketene dithioacetal 37c both at room temperature and under refluxing conditions can be rationalized in terms of higher stability of intermediate 66 when R1=Me, than when R1=Ph or furyl, probably due to steric and electronic factors. The exclusive syn and endo selectivity observed in pyrrolidine formation through both the paths presumably is a result of lithium chelation involved in the intermediates 63 and 64 (Scheme 12). Also the high endo selectivity may arise from the attractive secondary orbital interaction, which has many literature precedents25,26,27.

When the α-oxoketene dithioacetal derived from 2-acetyl thiophene 37e and 3-acetyl pyridine 37f were subjected to cycloaddition with 60 under identical conditions either at room temperature or under refluxing conditions, the starting ketene dithioacetal were recovered unreacted. However, when the reaction mixture was refluxed for prolonged time (30 hr) in the absence of nitrogen atmosphere, the product isolated were characterised as
pyrroles 68e and 68f respectively (Scheme 13). Similarly the 3-furoylpyrrole 68d was obtained in 61% yield when 37d was refluxed with 60 in the absence of nitrogen for 30 hr. The intermediate pyrrolidine 67 probably undergo facile dehydrogenation in the presence of oxygen to give the pyrroles 68. The analytical and spectral data of all these compounds are given in the experimental section.

The nitroketene S,S-acetal 42 similarly reacted with 60 at room temperature to give the corresponding pyrrolidine 69 in 55% yield. When the reaction mixture was refluxed for 30 hr in the absence of nitrogen atmosphere the nitropyrrrole 70 was formed in 53% yield. The stereochemistry of the pyrrolidine 69 was tentatively assigned as shown in Scheme 12 with the help of its analytical and spectral data (experimental).

IV.3 CONCLUSION

The 1,3-diphenyl-2-azaallyl lithium have been shown to behave as useful 1,3-anionic species towards oxoketene dithioacetals undergoing [3+2] cycloaddition. The cycloadducts thus formed undergo double MeSH elimination to yield the corresponding pyrroles. The oxoketene dithioacetals can be considered therefore, as masked aroyl or acyl acetylenes. Two exceptions are noted in the case of cyclic oxoketene dithioacetals 45d and 45e, where the 1,2-addition predominates over the cycloaddition. Also it has been shown that ethyl(benzylideneamino)acetate in
presence of lithium bromide and triethylamine undergo highly regio and stereoselective additions with oxoketene dithioacetals to give either pyrrolidine, pyran-2-one or pyrrole depending on the reaction conditions. Thus α-oxoketene dithioacetals have been proved to be acyl or benzoyl acetylene equivalent dipolarophiles as well as push-pull ethylenes and the present study should greatly enhance the synthetic potential of these ketene dithioacetals for the synthesis of pyrroles, spiropyrrrolines, pyrrolidines etc. through a 1,3-anionic cycloaddition reaction with 2-azaallylanions.

**IV.4 EXPERIMENTAL**

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were run as KBr discs on a Perkin-Elmer 297 spectrophotometer. $^1$H NMR spectra were recorded on a Varian EM-390 (90 MHz) spectrometer in deuteriochloroform with tetramethylsilane as internal standard unless otherwise stated. Chemical shifts are expressed as $\delta$ (ppm) downfield from TMS. $^{13}$C NMR spectra were recorded on a Brucker WM-400 spectrometer. Mass spectra were obtained using a Jeol JMS D-300 spectrometer. Elemental analysis were carried out on Heraeus CHN-O-RAPID instrument.
Starting Materials

Commercially available ketones were purchased (Aldrich) and were used as supplied. Benzaldehyde and benzylamine were distilled before use. Triethylamine and diisopropylamine were dried over KOH and distilled prior to the reaction. Lithium bromide (SISCO) was used as such without any further purification. Diethyl ether and tetrahydrofuran were dried over sodium wire and distilled prior to use. All α-oxoketene dithioacetals were prepared according to the general procedure described in Chapter II. n-Butyllithium was prepared by reported procedure\textsuperscript{28} in diethyl ether. N-Benzylidenebenzylamine was prepared by the condensation of benzaldehyde with benzylamine and distilled before use\textsuperscript{29}.

Preparation of Ethyl (Benzylideneamino)acetate (59)\textsuperscript{24}

Glycine (7.5 gm, 0.1 mol) was dissolved in 20 ml of 95% ethyl alcohol saturated with dry HCl. This reaction mixture was refluxed (2 hr) and distilled azeotropically with dry benzene (3x50 ml), to give ethylglycinate hydrochloride which was filtered and dried, yield 9g (60%). A solution of the ethylglycinate hydrochloride (7g, 0.05 mol), benzaldehyde (5.3g, 0.05 mol) and triethylamine (5g, 0.05 mol) in benzene (50 ml) was refluxed for 1 hr. The reaction mixture after cooling was washed with water (3x25 ml) and the benzene layer was separated, dried (Na\textsubscript{2}SO\textsubscript{4}) and evaporated in vacuo. The
residue was distilled on a Kugelrohr distilling apparatus to give pure ethyl (benzylidene amino)acetate 8.5g (90%).

General Procedure for the Generation and Reaction of 1,3-Diphenyl-2-azaallyllithium with Oxoketene Dithioacetal:

To a stirred solution of lithium diisopropylamide [(11 mmol) freshly prepared from n-butyllithium (11 mmol) and diisopropylamine (1.10gm, 11 mmol) in dry THF (20 ml)], N-benzylidenebenzylamine (1.95 gm, 10 mmol) in THF (5 ml) was added slowly at -78°C under nitrogen atmosphere. The lithiation was indicated by the appearance of reddish brown colour. The solution was stirred for 1 hr at -78°C and the temperature was raised slowly to room temperature followed by further stirring for 15hr. The reaction mixture was poured into saturated ammonium chloride solution and the organic layer was separated. The aqueous layer was extracted with ether (2x50 ml) and the combined organic layer was washed with water (100 ml), dried (Na₂SO₄) and evaporated to give viscous residue which were purified by column chromatography over silica gel using hexane-ethylacetate as eluent (5:1) to give the corresponding 2,5 diphenyl pyrroles.

3-Benzoyl-2,5-diphenylpyrrole (39a) was isolated as colourless crystals (EtOAc-hexane), yield 79%, m.p. 168-169°C; IR and ¹H NMR data described in text. (Found: C, 85.71,H,5.21;N,4.62; Calc. for C₂₃H₁₇NO: C,85.42; H,5.30; N,4.36%); m/z 323 (M⁺,100%); 246 (72); 218(7).
3-(4-Methoxybenzoyl)-2,5-diphenylpyrrole (39b) was isolated as light yellow crystals (EtOAc-hexane); yield 82% m.p. 183-184°C; IR $\nu_{\text{max}}$ (KBr) 3150, 1605, 1594, 1565 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 3.78 (s, 3H, OCH$_3$); 6.72-6.88 (m, 3H, arom); 7.05-7.58 (m, 10H, arom); 9.10 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 81.78; H, 5.63; N, 3.86; Calc. for C$_{24}$H$_{19}$NO$_2$: C, 81.56; H, 5.42; N, 3.96%); m/z 353 (M$^+$, 100%); 246 (24); 217 (15).

3-Acetyl-2,5-diphenylpyrrole (39c) was isolated as colourless crystals (EtOAc-hexane); yield 74%; m.p. 196°C; IR $\nu_{\text{max}}$ (KBr) 3240, 1605, 1455 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 2.25 (s, 3H, CH$_3$); 6.90 (d, J=1.5 Hz, 1H, H-4); 7.19-7.61 (m, 10H, arom); 9.08 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 82.54; H, 5.82; N, 5.23; Calc. for C$_{18}$H$_{15}$NO: C, 82.73; H, 5.79; N, 5.36%); m/z 261 (M$^+$, 70%); 246 (100); 217 (16).

2,5-Diphenyl-3-(2-furyl)pyrrole (39d) was isolated as yellow crystals (EtOAc-hexane); yield 76%; m.p. 162-163°C. IR $\nu_{\text{max}}$ (KBr) 3240, 1602, 1578, 1560 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 6.31 (dd, J=3 and 1.5 Hz, 1H, H-4' furyl); 6.79-7.56 (m, 13H, arom); 9.60 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 80.68; H, 4.58; N, 4.23; Calc. for C$_{23}$H$_{15}$NO$_2$: C, 80.49; H, 4.83; N, 4.47%); m/z 313 (M$^+$, 100%); 296 (17); 284 (14).
2,5-Diphenyl-3-(2-thienoyl)pyrrole (39e) was isolated as yellow crystals (EtOAc-hexane); yield 78%; m.p. 145-146°C. IR $\nu$ max (KBr) 3200, 1600, 1588 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 6.74-7.58 (m, 14H, arom); 9.51 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 76.69; H, 4.38; N, 4.18; Calc. for C$_{21}$H$_{15}$NOS: C, 76.57; H, 4.59; N, 4.25%); m/z 329 (M$^+$, 100%); 246 (28).

2,5-Diphenyl-3-(3-pyridoyl)pyrrole (39f) was isolated as light yellow crystals (EtOAc-hexane); yield 81%; m.p. 266-267°C IR $\nu$ max (KBr) 3150, 1645, 1600, 1582 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 6.73 (d, J=1.5Hz, 1H, H-4); 6.94-7.99 (m, 12H, arom); 8.38 (d, J=6Hz, 1H, H-6' pyridyl); 8.70 (s, 1H, H-2'pyridyl); 10.61 (brs, 1H, NH, exchangeable with D$_2$O); (Found C, 81.23; H, 4.82, N, 8.73; Calc. for C$_{22}$H$_{16}$N$_2$O: C, 81.46; H, 4.97; N, 8.64%); m/z 324 (M$^+$, 100%); 247 (22), 217 (29).

2,5-Diphenyl-3-(2-naphthoyl)pyrrole (39g) was isolated as light yellow crystals (EtOAc-hexane); yield 84% m.p. 181°C, IR $\nu$ max (KBr) 3255, 1601, 1570 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 6.81 (d, J=1.5Hz, 1H, H-4); 7.02-7.98 (m, 16H, arom); 8.31 (s, 1H, H-1' naphthyl); 9.30 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 86.58; H, 5.24; N, 3.86; Calc. for C$_{27}$H$_{19}$NO$_2$: C, 86.84; H, 5.13; N, 3.75%); m/z 373 (M$^+$, 100%); 344 (5).

Methyl-2,5-diphenylpyrrole-3-carboxylate (39h) was isolated colourless crystals (EtOAc-hexane); yield 71% m.p.
162°C; IR$_{\text{max}}$(KBr) 3310,1670, 1606, 1591 cm$^{-1}$, $^1$H NMR (CDCl$_3$): 3.70 (s, 3H, OCH$_3$); 6.96 (d, J=1.5 Hz, 1H, H-4); 7.15-7.72 (m, 10H, arom); 8.69 (brs, 1H, NH, exchangeable with D$_2$O); (Found: C, 77.78; H, 5.68; N, 5.25; Calc. for C$_{18}$H$_{15}$NO$_2$: C, 77.96; H, 5.45; N, 5.05%); m/z 277 (M$^+$, 100%), 246 (58); 217(15).

3,3-Bis(methylthio)-2,5-diphenyl-4-nitropyrrolidine (43) was isolated as colourless crystals (EtOAc-hexane); yield 64%; m.p. 118°C, IR and $^1$H NMR data given in the text. (Found:C, 59.81; H, 5.48; N, 3.63; Calc. for C$_{18}$H$_{20}$N$_2$O$_2$: C, 59.97, H, 5.59; N, 3.89%); m/z 360 (M$^+$, 4% 266(37).

Spiro[(3,4-dihydronaphth-1-one)-2,3'-(2',5'-diphenyl-4'- (methylthio)-1'-pyrroline)] (47) was isolated as colourless crystals (EtOAc-hexane); yield 74%, m.p. 163°C. IR and $^1$H NMR data are given in the text. (Found: C, 78.26; H, 5.89; N, 3.68; Calc. for C$_{26}$H$_{23}$ONS: C, 78.55; H, 5.83; N, 3.52%); m/z 397 (M$^+$, 25%); 350(100).

Spiro[(2,3-dihydro-8-methyl-[1]-benzthiepin-5-one)-4,3'-(2',5'-diphenyl-4'-(methylthio)-1'-pyrroline)] (50) was isolated as colourless crystals (EtOAc-hexane); yield 68%; m.p. 173-174°C. IR$_{\text{max}}$ 1659,1616,1600 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 1.82 (s, 3H, CH$_3$); 2.34 (s, 3H, SCH$_3$); 2.48-2.95 (m, 4H, -CH$_2$-); 5.05 (d, J=1.5Hz, 1H, H-4'); 5.90 (d, J=1.5Hz, 1H, H-2'); 7.05-7.88 (m, 12H, arom); 8.09 (d, J=9 Hz, H-6); (Found: C, 72.94; H, 5.74; N, 3.28; Calc. for
Spiro[3-(4-methoxyphenyl)-1-phenyl-pyrazolo-2-one]-3,3'-
(2',5'-diphenyl-4'-(methylthio)-1'-pyrroline)] (51) was
isolated as yellow crystals (EtOAc-hexane); yield 71%; IR
\[\nu_{\text{max}} \ 1710, 1625, 1608, 1598 \ \text{cm}^{-1}\]; $^1$H NMR (CDCl$_3$):
2.18 (s, 3H, SCH$_3$); 3.69 (s, 3H, OCH$_3$); 5.00 (d, $J=1.5$ Hz, 1H, H-4');
6.02 (d, $J=1.5$ Hz, H-2'); 6.56-6.74 (m, 2H, arom); 7.02-7.65 (m, 13H, arom);
Found: C, 74.38; H, 5.16; N, 8.32; Calc. for C$_{32}$H$_{27}$O$_2$N$_3$S: C,
74.25, H, 5.26; N, 8.12%).

4,4-Bis(methylthio)-1,3-diphenyl-5,6,7,8-tetrahydro-3H-
isoquinoline (53a) was isolated as colourless crystals
(EtOAc-hexane); yield 77%; m.p. 155°C, IR $\nu_{\text{max}}$(KBr) 1605,
1571, 1520 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 1.62-1.82 (m, 4H, -CH$_2$-);
1.90 (s, 3H, SCH$_3$); 2.15 (s, 3H, SCH$_3$); 2.50-2.74 (m, 4H,
-CH$_2$-); 6.38 (s, 1H, H-3); 7.21-7.50 (m, 10H, arom);
(Found: C, 72.53; H, 6.82; N, 3.43; Calc. for C$_{23}$H$_{25}$N$_2$: C,
72.78; H, 6.64; N, 3.69%); m/z 379 (M$^+$, 96%); 332(40).

3,3-Bis(methylthio)-2,9-diphenyl-5,6,7,8-tetrahydro-4H-
cyclohepta[d]pyridine (53b) was isolated as colourless
crystals (EtOAc-hexane); yield 76%; m.p. 157°C; IR $\nu_{\text{max}}$
(KBr) 1600,1488,1463 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 1.30-1.76 (m,
6H,CH$_2$); 1.87 (s,3H,SCH$_3$);2.07 (s,3H,SCH$_3$); 2.28-2.90 (m,
4H,CH$_2$); 6.38 (s, 1H,H-2); 7.13-7.55 (m,10H,arom);
(Found: C,73.0; H,6.81; N,3.28; Calc. for C$_{24}$H$_{27}$NS$_2$: C,
Mercuric Chloride Catalyzed Ring contraction of 53a and 53b: General Procedure:— A suspension of dihydro-pyridine 53a or 53b (1 mmol) and HgCl₂ (0.27g, 1 mmol) in dry THF (10 ml) was stirred at room temperature for 6 hr. The reaction mixture was filtered through a G-4 sintered funnel to remove traces of mercuric chloride and the filtrate diluted with chloroform (25 ml) washed with saturated sodium bicarbonate solution and evaporated to give the crude products which were purified by column chromatography over silica gel. Elution with hexane-ethyl acetate (20:1) gave pure products 55a and 55b respectively.

1-(Methylthio)-3-phenyl-4,5,6,7-tetrahydroisoindole (55a) was isolated as colourless crystals (EtOAc-hexane); yield 73%; m.p. 91-92°C; IRν max (KBr) 3320, 1600, 1585, 1512 cm⁻¹; ¹H NMR (CDCl₃); 1.71-1.92 (m, 4H, CH₂); 2.19 (s, 3H, SCH₃); 2.48-2.72 (m, 4H, CH₂); 7.21-7.54 (m, 3H, arom); 7.61-7.82 (m, 2H, arom); 8.01 (brs, 1H, NH exchangeable with D₂O); (Found: C, 74.12; H, 7.28; N, 5.54 Calc. for C₁₅H₁₇NS: C, 74.03, H, 7.04; N, 5.76%); m/z 243 (M⁺, 100%) 228(41).

2-(Methylthio)-8-phenyl-4,5,6,7-tetrahydro[3H]cyclohepta[c] pyrrole (55b) was isolated as colourless crystals (EtOAc-hexane); yield 68%, m.p. 90-91°C; IR
\(\nu_{\text{max}}(\text{KBr}),3325, 1605, 1598 \text{ cm}^{-1}\),\(\text{H NMR (CCL}_4\)): 1.45-1.82 (m, 6H, CH\(_2\)); 1.99 (s, 3H, SCH\(_3\)); 2.38-2.79 (m, 4H, CH\(_2\)); 7.01-7.35 (m, 3H, arom); 7.42-7.64 (m, 2H, arom); 7.74 (brs, 1H, NH exchangeble with \(\text{D}_2\text{O}\)); (Found: C, 74.40; H, 7.53; N, 5.23 Calc. for C\(_{16}\)H\(_{19}\)NS: C, 74.66; H, 7.44; N, 5.44%); m/z 257 (M\(^+\), 100%); 242(25).

**General Procedure for the Reaction of N-Lithioethyl-(benzylideneamino)acetate with Oxoketene Dithioacetals:**

To a solution of ethyl (benzylideneamino)acetate (2.10g, 11 mmol) and oxoketene dithioacetal (10 mmol) in dry THF (25 ml) was added lithium bromide (1.30g, 15 mmol in THF (10 ml) and then triethylamine (1.21g, 12 mmol in THF (5 ml) with the help of a syringe. The mixture was stirred at room temperature for 14-16 hr under nitrogen (checked by TLC) and poured into concentrated aqueous ammonium chloride (50 ml), extracted with chloroform (50mlx3), dried over sodium sulphate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane-ethylacetate (5:1) as eluent to give the corresponding pyrrolidines, 61a and 61b.

Pyran-2-ones 62a and 62b were obtained when the reaction mixture after an initial 3 hr stirring at room temperature was refluxed for 16 hr at 70°C under an efficient atmosphere of nitrogen. While pyran-2-one 66c
was obtained by stirring the reaction mixture at room temperature only (16 hr).

Pyrroles 64d, 64e and 64f were obtained when the same reaction mixture after an initial 3 hr stirring at room temperature was refluxed for 30 hr at 70°C in the absence of nitrogen.

Ethyl 4-benzoyl-3,3-bis(methylthio)-5-phenyl pyrrolidine-2-carboxylate (61a) was isolated as colourless crystals (EtOAc-hexane); yield 72%, m.p. 154°C; IR$\nu_{\text{max}}$ (KBr) 3300, 1750, 1680, 1600 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 1.39 (t, J=7 Hz, 3H, CH$_3$); 1.98 (s, 3H, SCH$_3$); 2.21 (s, 3H, SCH$_3$); 2.59-2.71 (brs 1H, NH, exchangeable with D$_2$O) 4.31 (q, J=7 Hz, 2H, OCH$_2$); 4.68 (d, J=5 Hz, 1H, H-4); 4.96 (brs, 1H, H-2); 5.41 (d, J=6.5 Hz, 1H, H-5); 6.98-7.69 (m, 10H, arom); $^{13}$C NMR (CDCl$_3$) 12.95 (CH$_3$); 13.81, 14.04 (SCH$_3$); 61.29 (OCH$_2$); 61.78, 63.78, 70.13 (CH, C-2, C-4, C-5); 70.69, (C-3); 126.93, 127.26, 127.63, 128.21, 132.61 (CH-phenyl) 139.60, 139.61 (quaternary Ar) 170.81 (C=OEt); 197.44 (C$_6$H$_5$C=): (Found: C, 63.39; H, 6.01, N, 3.22; Calc. for C$_{22}$H$_{25}$NO$_3$S$_2$: C, 63.58; H, 6.06; N, 3.37%); m/z 368 (M$^+$-47, 100%); 225(59).

Ethyl 4-furoyl-3,3-bis(methylthio)-5-phenylpyrrolidine-2-carboxylate (61b) was isolated as colourless crystals (EtOAc-hexane); yield 69%; m.p. 135-136°C; IR$\nu_{\text{max}}$ (KBr) 3340, 1723, 1660, 1565 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 1.49 (t, J=7 Hz, 3H, CH$_3$); 2.02 (s, 3H, SCH$_3$); 2.21 (s, 3H, SCH$_3$); 3.05-3.20 (brs, 1H, NH); 4.25 (q, J=7 Hz, 2H, OCH$_2$); 4.49 (d,
J=6.5Hz, 1H, H-4); 4.89 (s, 1H, H-3); 5.38 (d, J=6.5Hz, 1H, H-5); 6.48 (dd, J=3 and 1.5Hz, H-4'furyl); 6.87-7.49 (m, 7H, arom and furyl); (Found: C, 59.12; H, 5.61; N, 3.48; Calc. for C_{20}H_{23}NO_{4}S_{2}: C, 59.23; H, 5.72; N, 3.45%); m/z 358 (M^+-47, 14%); 312 (4).

3-Benzylideneamino-4-(methylthio)-6-phenylpyran-2-one (62a) was isolated as yellow crystals (EtOAc-hexane); yield 69%; m.p.164-165°C; IR \( \nu_{\text{max}}(\text{KBr}) \) 1701, 1618, 1575 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 2.46 (s, 3H, SCH\(_3\)); 6.68 (s, 1H, H-5); 7.30-7.59 (m, 6H, arom); 7.78-8.02 (m, 4H, arom); 9.49 (s, 1H, CH=N-); (Found: C, 71.18; H, 4.79; N, 4.46; Calc. for C\(_{19}\)H\(_{15}\)N\(_2\)O\(_2\)S: C, 71.00; H, 4.70; N, 4.36%); m/z 321 (M^+, 61%); 306 (100).

3-Benzylideneamino-6-(2-furyl)-4-(methylthio)pyran-2-one (62b) was isolated as yellow crystals (EtOAc-hexane); yield 61%, m.p.119-120°C; IR \( \nu_{\text{max}}(\text{KBr}) \) 1705, 1625, 1562 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 2.56 (s, 3H, SCH\(_3\)); 6.58 (dd, J=3.0 and 1.5Hz, H-4'furyl); 6.73 (s, 1H, H-5); 7.10 (d, J=3Hz, H-3'furyl); 7.31-7.53 (m, 4H, arom); 7.81-8.04 (m, 2H, arom); 8.52 (s, 1H, C\(_6\)H\(_5\)CH=N-); (Found: C, 65.32; H, 4.38; N, 4.68; Calc. for C\(_{17}\)H\(_{13}\)N\(_2\)O\(_3\)S: C, 65.58; H, 4.21; N, 4.68%); m/z 311 (M^+, 3%); 296 (4); 214 (22).

3-Benzylideneamino-6-methyl-4-(methylthio)pyran-2-one (62c) was isolated as yellow crystals (EtOAc-hexane); yield 81%; m.p.139-140°C; IR \( \nu_{\text{max}}(\text{KBr}) \) 1690, 1622, 1598 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 2.28 (s, 3H, CH\(_3\)); 2.43 (s, 3H, SCH\(_3\)); 6.12 (s, 1H, H-5); 7.31-7.56 (m, 3H, arom); 7.74-8.08
Ethyl-4-(2-furoyl)-3-(methylthio)-5-phenylpyrrole-2-carboxylate (68d) was isolated as colourless crystals (EtOAc-hexane); yield 73%; m.p. 117-118°C; IRνmax(KBr) 3310,1680, 1668,1565 cm⁻¹; ¹H NMR (CDCl₃); 1.38 (t, J=7Hz, 3H, CH₃); 2.35 (s, 3H, SCH₃); 4.30 (q, J=7Hz, 2H, OCH₂); 6.36 (dd, 3 and 1.5Hz, 1H, H-4’furyl); 6.91 (d, J=3Hz, 1H, H-3’furyl); 7.14-7.52 (m, 6H, arom and 5’furyl); 10.01 (brs, 1H, NH exchangeable with D₂O); (Found: C, 64.02; H, 4.96; N, 3.83; Calc. for C₁₉H₁₇NO₄S: C, 64.21; H, 4.82; N, 3.94%); m/z 356 (M⁺,100%); 309(17); 280(18).

Ethyl-3-(methylthio)-5-phenyl-4-(2-thienyl)pyrrole-2-carboxylate (68e) was isolated as colourless crystals (EtOAc-hexane); yield 69%; m.p. 128-129°C; IRνmax(KBr) 3260,1680,1620, 1550 cm⁻¹; ¹H NMR (CDCl₃); 1.35 (t, J=7Hz, 3H, CH₃); 2.45 (s, 3H, SCH₃); 4.31 (q, J=7.00Hz, 2H, OCH₂); 7.05-7.49 (m, 6H, arom and thieryl); 7.50-7.98 (m, 2H, arom); 10.11 (brs, 1H, NH, exchangeable with D₂O) (Found: C, 61.48; H, 4.58; N, 3.71; Calc. for C₁₉H₁₇NO₃S₂: C, 61.43; H, 4.60; N, 3.77%).
Ethyl-3-(methylthio)-5-phenyl-4-(3-pyridoyl)pyrrole-2-carboxylate (68f) was isolated as colourless crystals (EtOAc-hexane); yield 79%; m.p. 141-142°C; IR \( \nu \text{max} \) (KBr) 3410, 1718, 1640 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 1.32 (t, J=7Hz, 3H, CH\(_3\)); 2.31 (s, 3H, SCH\(_3\)); 4.31 (q, J=7Hz, 2H, OCH\(_2\)); 7.21-7.49 (m, 4H, arom); 8.08 (m, 1H, H-4' pyridyl); 8.65 (dd, J=6 and 1.5Hz, 1H, H-6'pyridyl); 8.98 (d, J=1.5Hz, H-2'pyridyl); 10.61 (brs, 1H, NH, exchangeable with D\(_2\)O); (Found: C, 65.32; H, 4.91; N, 7.72; Calc. for C\(_{20}\)H\(_{18}\)N\(_2\)O\(_3\)S: C, 65.55; H, 4.95; N, 7.65%); m/z 366 (M\(^+\), 100%); 320 (34).

Ethyl-3,3-bis(methylthio)-4-nitro-5-phenylpyrrolidine-2-carboxylate (69) was isolated as colourless crystals (EtOAc-hexane); yield 58%; m.p. 160-161°C; IR \( \nu \text{max} \) (KBr) 3330, 1728, 1550, 1450 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 1.28 (t, J=7Hz, 3H, CH\(_3\)); 2.11 (s, 3H, SCH\(_3\)); 2.21 (s, 3H, SCH\(_3\)); 2.60-2.65 (brs, 1H, NH exchangeable with D\(_2\)O); 4.22 (q, J=6.5Hz, 2H, OCH\(_2\)); 4.69 (brs, 1H, H-2); 5.29 (m, 2H, H-4 and H-5); 7.05-7.56 (m, 5H, arom); (Found: C, 50.50; H, 5.68; N, 7.72; Calc. for C\(_{15}\)H\(_{20}\)N\(_2\)O\(_4\)S\(_2\): C, 50.54; H, 5.66; N, 7.86%); m/z 262 (M\(^+\)-94, 15%); 216(6); 209(100).

Ethyl-3-nitro-2-phenylpyrrole-4-carboxylate (70) was isolated as colourless crystals (EtOAc-hexane); yield 56%; m.p. 128-129°C; IR \( \nu \text{max} \) (KBr) 3250, 1700, 1580, 1510cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): 1.22 (t, J=7Hz, 3H, CH\(_3\)); 4.12 (q, J=7Hz, 2H, OCH\(_2\)); 7.08-8.02 (m, 6H, arom); 10.35 (brs, 1H, NH, exchangeable with D\(_2\)O); (Found: C, 59.10; H, 4.59; N, 10.78; Calc. for C\(_{13}\)H\(_{12}\)N\(_2\)O\(_4\): C, 59.99; H, 4.65; N, 10.84%).
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