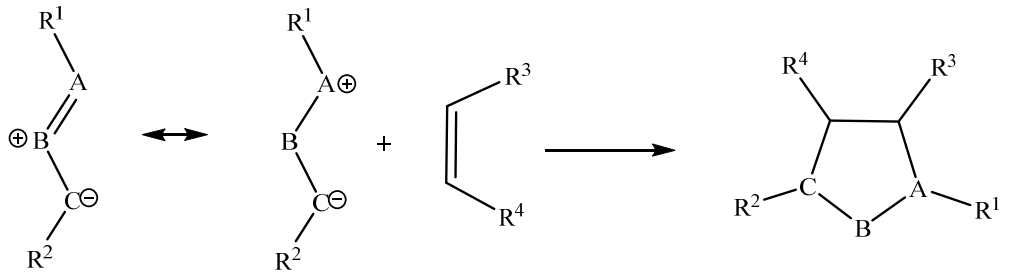
4.1 INTRODUCTION

1,3-Dipolar cycloaddition reactions offers very novel synthetic route for the building of five-membered heterocyclic rings.[167,168] According to Woodward-Hoffmann rules, this thermally allowed [4πs + 2πs] cycloaddition includes the reaction between dipolarophiles with a 1,3-dipole (Scheme 4.1).[169] Smith was the first to perceive the concept of 1,3-dipolar cycloaddition in 1938.[170] but the reaction became widely applicable after Huisgen's generalization in 1960's.[171] 1,3-dipolar cycloadditions have been greatly investigated during past few decades and the diversity of the reaction is utilized starting from material chemistry[172] to drug discovery.[173]



Scheme 4.1. 1,3-Dipolar cycloaddition.

Currently, 1,3-dipoar cycloaddition is an important route to stereo- and regioselective synthesis of the five-membered heterocycles.

4.1.1 1,3-Dipoles

A 1,3-dipole is a three-atom, $4\pi e^-$ containing system in which the centre atom bears a positive charge that counter balances the negative charge dispersed over

two termini. Two major forms of 1,3-dipolar systems can be presented, first is the bent allyl type where the plane of the dipole and 1,3-dipoles having $4\pi e^-$ in three parallel p_z orbitals are perpendicular to each other and second is linear propargyl-allenyl type, which have a triple bond in one canonical form with an additional π-orbital orthogonal to the allyl-anion type molecular orbital and bent allyl-type (Figure 4.1).

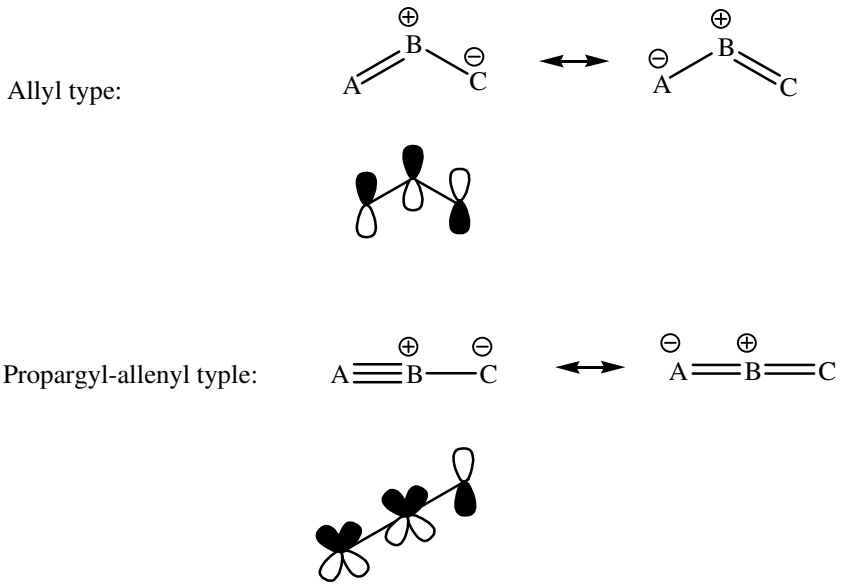


Figure 4.1. Allyl and propargyl-allenyl type 1,3-dipoles.

Various combinations of carbon and heteroatom containing 1,3-dipoles are possible is possible as exemplified in Figure 4.2.

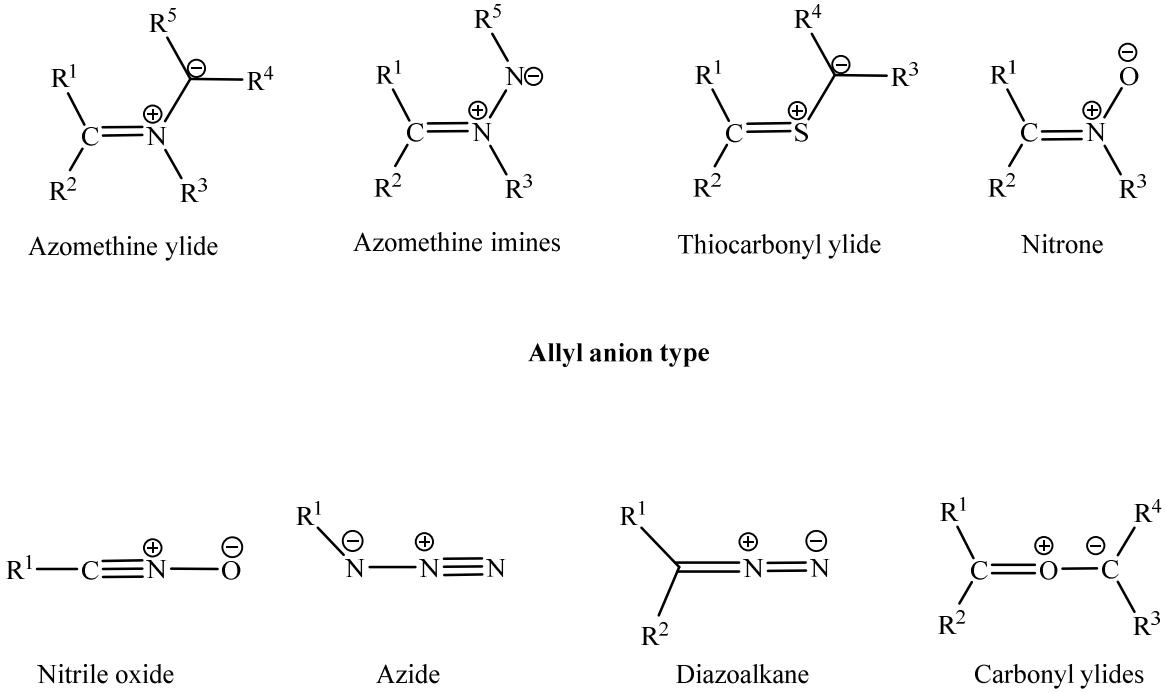


Figure 4.2. Some examples of 1,3-dipoles.

4.1.2 Dipolarophiles

In 1,3-dipolar cycloaddition, dipolarophile is a 2π- component having double or triple bond functionality, such as C=C, C=O, C=S, C≡C, C≡N etc. This π- bond may be conjugated, isolated or can be a part of a cumulene system.[174-178]

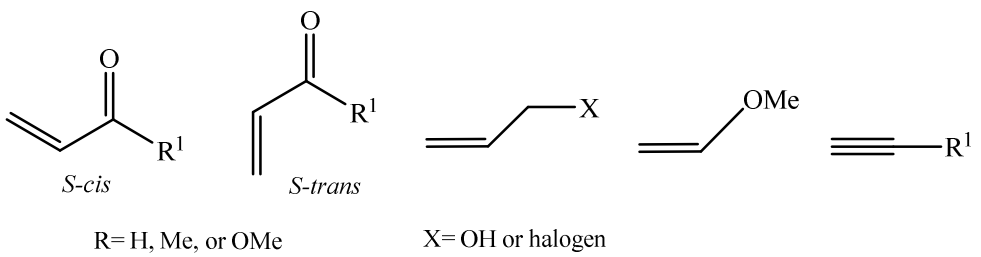
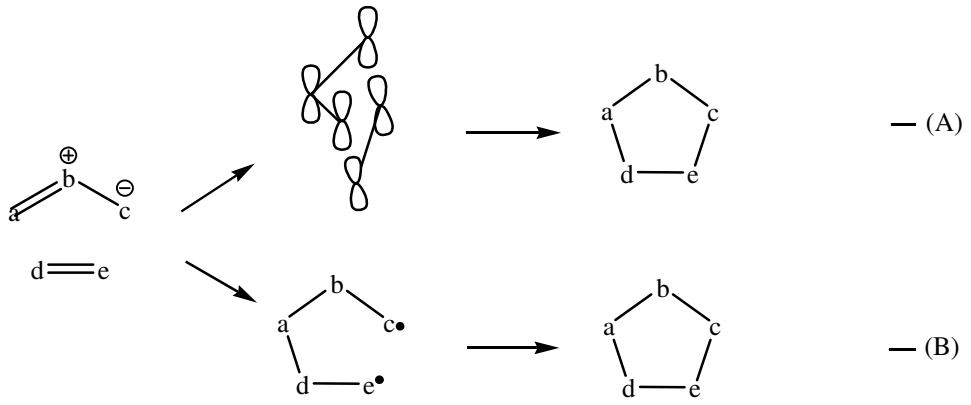


Figure 4.3. Some examples of dipolarophiles.

The reactivity of a dipolarophile increases in the presence of electron- donating or electron- withdrawing group. However, the reactivity is lowered when both electron- donating and withdrawing groups are present within one molecule.

4.1.3 Mechanical aspects of 1,3-dipolar cycloaddition

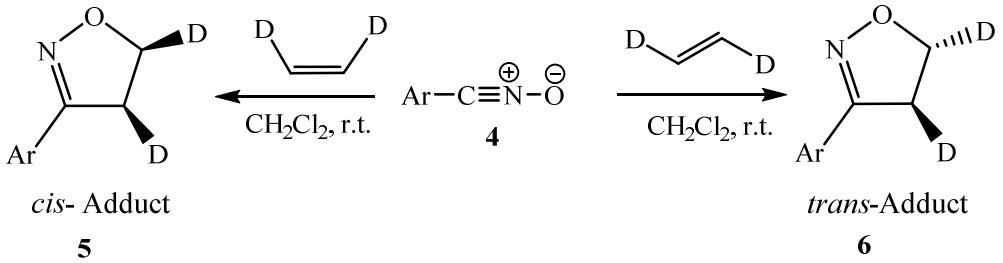
The mechanism of 1,3-dipolar cycloaddition was quite interesting and was a subject of debate during 1960's. Huisgen proposed a synchronous concerted pathway (Scheme 3.2, equation A)[179] whereas Firestone supported a diradical, stepwise pathway (Scheme 4.2, equation B)[180].



Scheme 4.2. Mechanism of 1,3-dipolar cycloaddition.

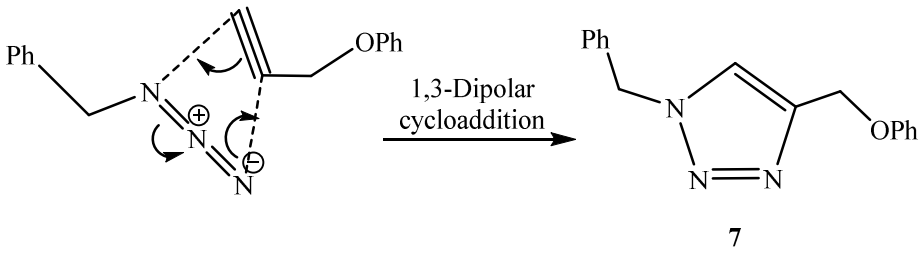
The strongest evidence in the favour of Huisgen's concerted pathway was syn-addition, where the geometrical relationships between substituents on both the reactants are retained in the final product. The 1,3-dipolar addition is stereo-conservative (suprafacial), therefore, the reaction holds similarity to Diels-Alder reaction i.e. [4πs + 2πs] cycloaddition. Firestone, however, stated that the rotation around the single bond has much high energy barrier than the activation energy barrier required for ring closure in the intermediate diradical. It also explains the

cis-stereospecificity in the product. On the basis of the reaction of bezonitrileoxide (**4**) with trans-dideuterated ethylene, the dispute was settled in the favor of the concerted pathway as the reaction gave stereospecific isooxazoline **5** exclusively (Scheme 4.3).[179,181]



Scheme 4.3. 1,3-Dipolar cycloaddition of bezonitrileoxide with *trans*-dideuterated ethylene.

It may be noted that a concerted reaction does not always follow the synchronous pathway. At present, asynchronous concerted pathway is widely accepted which includes the formation of a new σ-bond that is more advanced as compared to the other one (Scheme 4.4).



Scheme 4.4. Asynchronous concerted pathway in 1,3-dipolar cycloaddition.

Depending on the nature of the dipole and dipolarophile, the 1,3-dipolar cycloaddition reaction is controlled either by $HOMO_{(dipole)}$-$LUMO_{(dipolarophile)}$ or

$LUMO_{(dipole)}$-$HOMO_{(dipolarophile)}$ interections, but in some cases, combination of both interactions may be involved.[182]

On the basis of the nature of substituents on the dipole and dipolarophiles, 1,3-dipolar cycloadditions have been classified in three categories by Sustmann.[17] In Type I, the HOMO of dipole interacts with the LUMO of the dipolarophile (commonly in electron-deficient dipolarophiles). Type III includes the interaction of the LUMO of dipole (common for electron-rich dipolarophile) with HOMO of dipolarophile. Type-II includes the interactions between the HOMO and LUMO of almost similar energy levels. In this case both Type I and Type III interactions are possible (Figure 4.4).

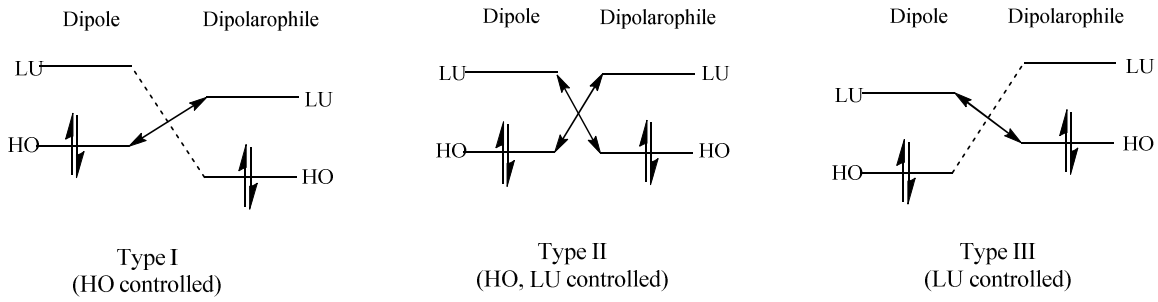


Figure 4.4. Different types of HOMO-LUMO interactions classified by Sustmann.

The presence of electron-withdrawing groups, either on dipole or dipolarophile lowers the energy of the HOMO as well as the LUMO but have much greater effect on energy of the LUMO. In the similar manner, electron-releasing groups increase the energy of the LUMO as well as the HOMO but shows greater impact on the HOMO energy. The coefficient on the unsubstituted atom is larger in comparison to that on the substituted atom. Substituents having conjugation

elevate the energy of the HOMO and lower the energy of LUMO. The coefficients are larger at the unsubstituted centers in both molecular orbitals. The effect of the substituent on dipole energies and coefficients is predictable to be a function of magnitude of the coefficient at the site of the attachment on the parent dipole. Therefore, the effect of substituent for the HOMO of the dipole has been found to follow the order with maximum effect at anionic terminus, then at neutral terminus and least effect is at the central atom. Likewise in the case of LUMO the order is found to be approximately equal on central and neutral terminus and lesser on anionic terminus.[184]

In the case of asymmetrical dipole or dipolarophile, the transition state has more completely formed bond which represents the lowest HOMO-LUMO gap. Thus, by enhancing the electron donating ability on one end (mostly on dipole) and electron withdrawing ability on the other end (mostly in dipolarophile) will push one of the bonds to form faster than the other one (normal demand). Presence of electron donating group on the dipolarophile normally reverts this interaction (inverse demand).

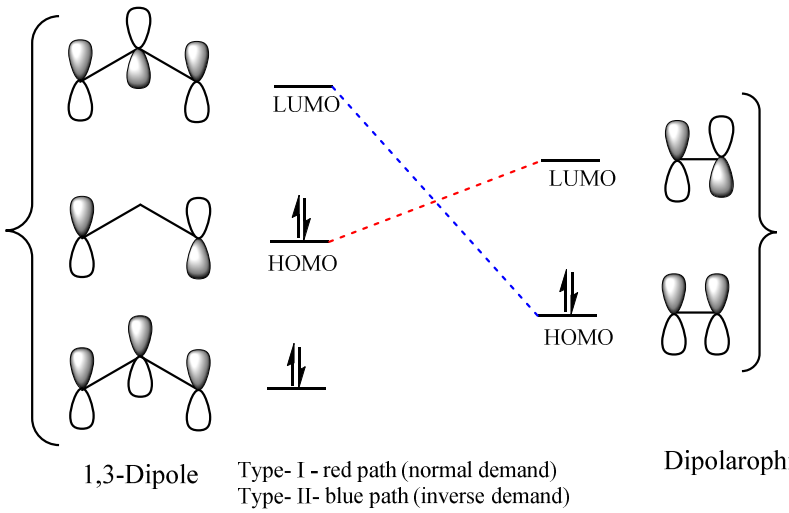
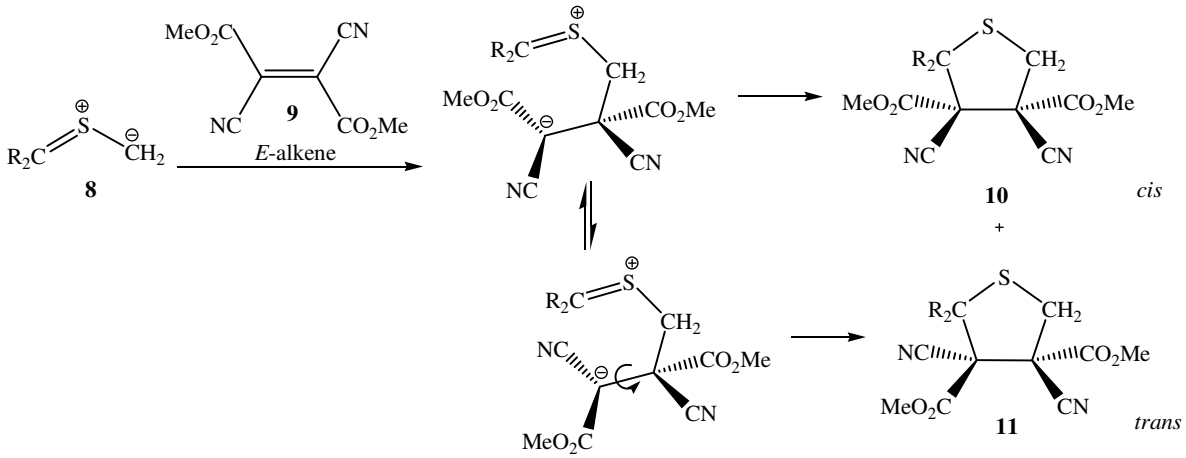


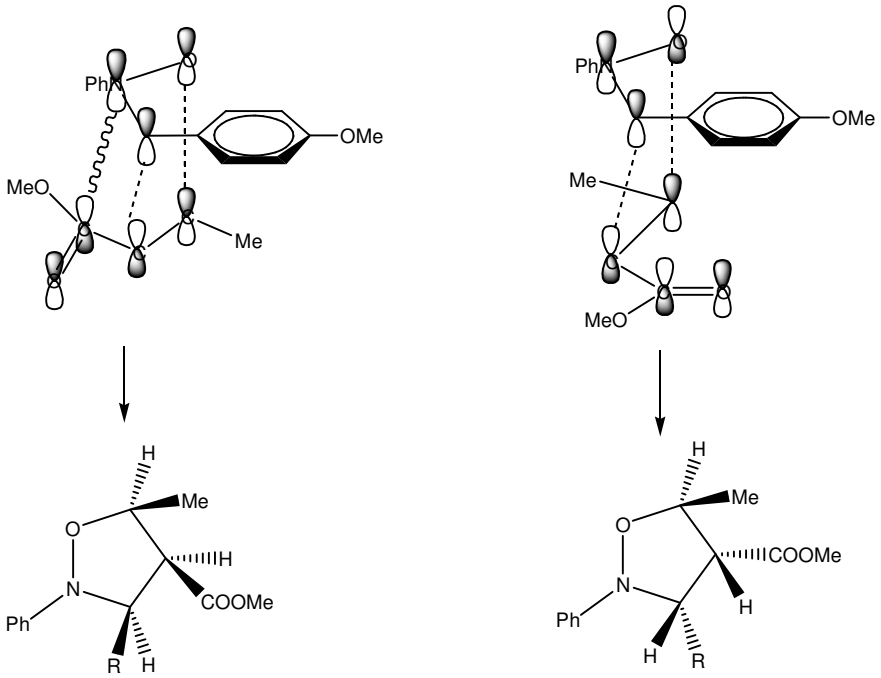
Figure 4.5. HOMO-LUMO interaction diagram for normal and inverse demand 1,3-dipolar cycloaddition

Huisgen et al. later showed that 1,3-dipolar cycloaddition can involve a two-step zwitterionic pathway which scrambled the stereospecificity of the reaction. He proposed that the rotation rate and formation of the second ring closing bond about the zwitterionic σ-bond was in competition. He also found that the stereochemistry could be destroyed by inserting a large difference in electron demand between an electron-rich dipole i.e, thiocarbonyl ylide and electron-poor dipolarophile which is a dicyano-substituted alkene. By these changes, *cis* and *trans* both products were obtained from a single *E*-alkene (Scheme 4.5). [185]



Scheme 4.5. Two-step zwitterionic mechanism of 1,3-dipolar cycloaddition.

As mentioned earlier, the stereochemistry of the original dipolarophile is retained in the cycloadduct as 1,3-dipolar cycloaddition reactions are highly stereoselective. This is due to the concerted mechanism. On the other hand, if the reaction proceeds in a two steps, diastereomers are produced *via* isomerization of the original dipolarophile. With two chiral centres , diastereomeric products **12** and **13** (*cis*- and *trans*-) may be produced adopting *endo* and *exo* transition states ; one is formed from dipole and the other from the dipolarophile.The extent to which each diastereomer will be formed is determined by secondary π-orbital interactions and repulsive van der Waals steric interactions. Secondary interactions have been found to favour an *endo* transition state whereas repulsive interactions favour *exo* transition states with a mixture of diastereomers being obtained in most of the cases. The reaction of methyl and C-*p*-methoxyphenyl-*N*-phenylnitrone clearly supported the above fact (Scheme 4.6).[186]



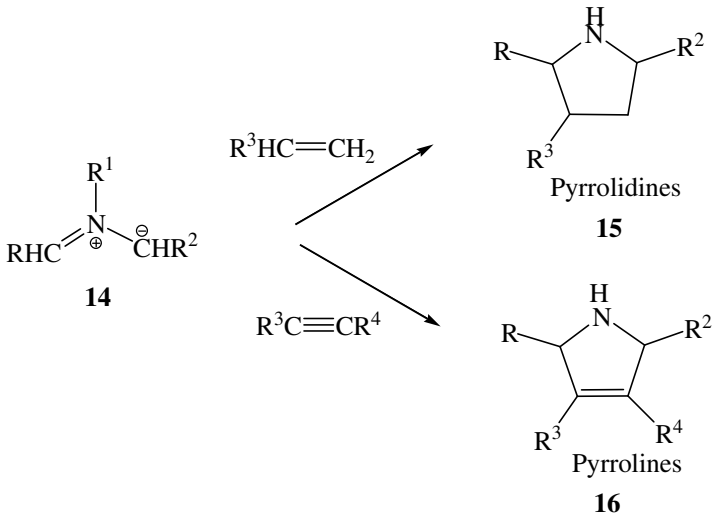
Scheme 4.6. Stereoselectivity in 1,3-dipolar cycloaddition.

The relative reactivity and regioselectivity of 1,3-dipolar cycloaddition can be rationalized by frontier molecular orbital theory, since the transition state is controlled by frontier orbital coefficients.[184,185] It states that only interactions between filled orbitals with unfilled ones direct to an important energy-lowering effect on transition state when two molecules (dipole and dipolarophile) approach each other, particularly the HOMO-LUMO interactions. In spite of the fact that interaction of extra-frontier orbitals, close shell repulsion, and columbic terms also contribute to energy changes, only interactions between frontier orbitals on the 1,3-dipole and dipolarophile have been considered in perturbation expressions to calculate the energy changes.[187]

From these generalizations the stereoselectivity and regioselectivity of most 1,3-dipolar cycloadditions can be rationalized by assuming that the large orbital coefficient of one molecule is interacting with the large orbital coefficient of the other molecule.

4.1.4 1,3- Dipolar cycloaddition of azomethine ylides

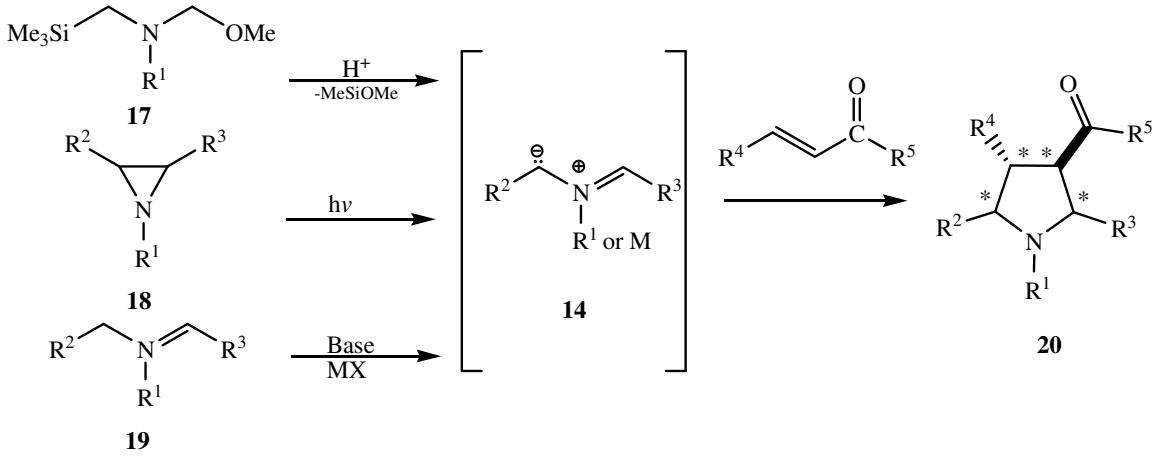
The 1,3-dipolar cycloaddition reaction of azomethine ylides to alkene and alkyne dipolarophiles leads to the formation of pyrrolidines and pyrrolines respectively (Scheme 4.7).



Scheme 4.7. 1,3-Dipolar cycloaddition reaction of azomethine ylide.

Azomethine ylides are 1,3-dipoles belonging to the allyl anion type and are are bent in ground state .They are in general quite reactive, short-lived species which are generated *in situ* from a stable precursor and are afterward trapped by the added dipolarophile. Several methods have been developed for generation of these ylides, including the deprotonation of imine derivatives,[188] thermal isomerisation

of imines of α-amino acids[189] and decarboxylation of iminium ions derived from primary or secondary α-amino acids.[190] Thermolysis or photolysis of the substituted azidirines[191] and desilylation of cynoaminosilanes[192] (Scheme 4.8) are the most common methods used now a days.

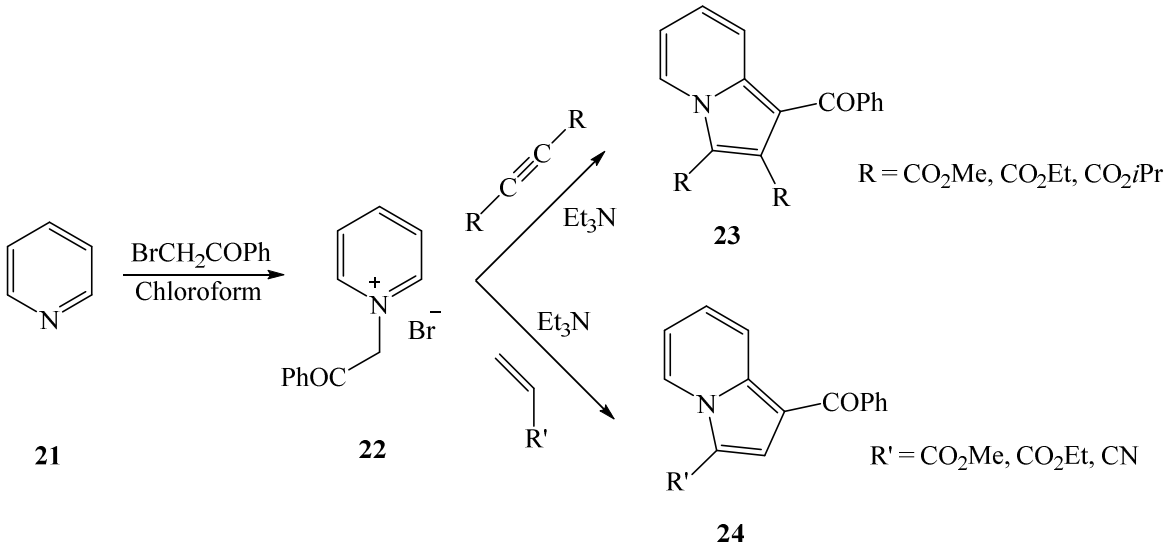


Scheme 4.8. Different pathways for the generation of azomethyne ylide and it's 1,3-dipolar cycloaddition.

The 1,3-dipolar cycloaddition reactions of azomethine ylides with dipolarophiles are in general HOMO- LUMO controlled (Type-I in Figure 4.4).[183] It is generally accepted that cycloaddition follows concerted path which may be sometimes asynchronous to lead the stereospecificity of the reaction and the stereochemistry of dipolarophile is maintained in pyrrolidine product.

Azomethine ylides derived from *N*-substitited pyridinium, quinolinium and isoquinolinium salts are used to generate indolizine, pyrrolo[1,2-*a*]quinolines and pyrrolo[2,1-*a*]isoquinolines, respectively following 1,3-dipolar cycloaddition with electron-deficient acetylenes or alkenes.[193]

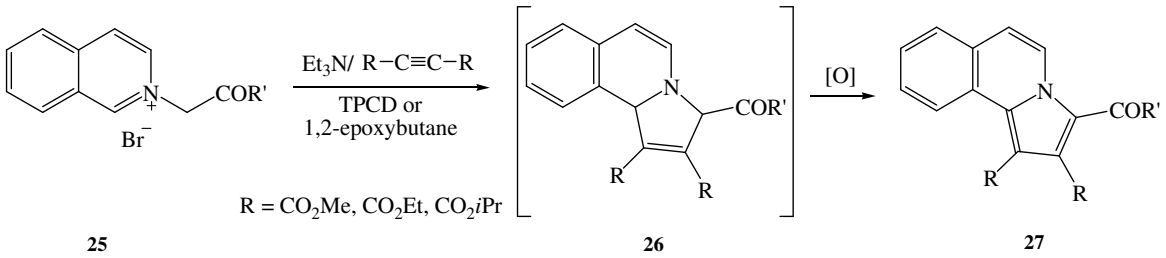
Various substituted indolizines were synthesized via 1,3-dipolar cycloaddition of the pyridinium ylide **22** generated by deprotonation of the pyridinium salt **21** with the acetylene or alkene dipolarophiles in presence of a base such as triethylamine, K_2CO_3, amberlite-IRA-402 (OH) ion exchange resin, etc.[194-198] In the case of the unsymmetrically substituted dipolarophile, adduct (**24**) was formed regiospecifically.[196-198]



Scheme 4.9. 1,3-Dipolar cycloaddition of pyridinium ylide with dipolarophiles.

Similar strategy has been reported for the synthesis of pyrrolo[1,2-*a*]quinolines and pyrrolo[2,1-*a*]isoquinolines.[194-196]

Use of different oxidizing agents such as tetrakispyridinecobalt(II)dichromate (TPCD) or epoxides were also introduced in order to direct the reaction toward the fully oxidized aromatic compounds.[196]



Scheme 4.10. 1,3-Dipolar cycloaddition of isoquinolinium ylide with acetylinic dipolarophile.

A number of pyrrolo- and pyrrolidinophenanthridines were synthesized using similar strategy as discussed in the first chapter.[49-59]

We studied the synthetic routes and found that several moderations were carried out in reaction procedures with time to reduce the reaction time, cost and utility of products. The common method for cycloiminium ylide generation in 1,3-dipolar cycloaddition involves deprotonation of the pre-synthesized N-alkylcycloiminium salt with the base following multistep processes.[199-201] In most of the reactions, polyhaloalkanes were used as solvent which are hazardous to environment as well as human health too. Water has been used as the benign solvent in view of its non-toxicity and abundant availability for many chemical reactions advantageously. However, reactions occur without sacrificing stereo- and regio-selectivities as well as the yields. In fact, more than often, these factors improved in many cases by the use of water as the solvent.[201,202]

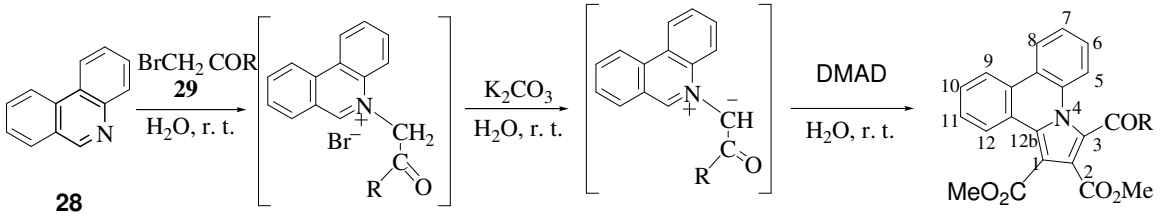
In view of this, we strived to develop a simple eco-friendly method for 1,3-dipolar cycloaddition of phenanthridinium ylides by avoiding the use of polyhaloalkanes as solvents based on the concept of green chemistry.

4.2 RESULTS AND DISCUSSION

We succeeded to develop an environmental friendly 1,3-dipolar cycloaddition of phenaninthridinium ylides generated *in situ* from phenanthridine with different dipolarophiles using water as the solvent for the first time. The results are given here.

4.2.1 Synthesis of pyrrolo[2,1-*f*]phenathridines via 1,3-dipolar cycloaddition

The reaction of phenanthridine (**28**) with α-bromoketone or *tert*-butyl bromoacetate (**29**) in water produces a clear solution at room temperature after stirring for 3-4 days. This clear solution contains cycloiminium bromide salt in soluble form. Addition of potassium carbonate to this solution generates cycloiminium ylide by deprotonation which undergoes 1,3-dipolar cycloaddition with DMAD to afford dimethyl pyrrolo[2,1-*f*]phenanthridine-1,2-dicarboxylates (**30a-e**) in good yields (Scheme 4.12).[203]

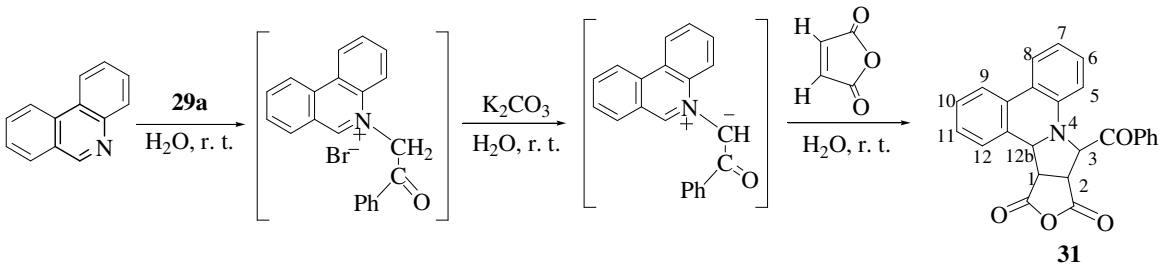


29,30	R
a	Ph
b	*p*- $MeOC_6H_4$
c	*p*-$NO_2C_6H_4$
d	*p*-FC_6H_4
e	$OCMe_3$

Scheme 4.12. One-pot 1,3-dipolar cycloaddition of phenanthridinium ylides with DMAD.

It is noteworthy that in contrast to the earlier reports[196,199,200], no oxidizing reagent is required to oxidize the initially formed dihydropyrrolophenanthridine. Here, auto-oxidation occurs in the presence of air and fully aromatized product is obtained. Aromaticity of the final product is the driving force to lead to the formation of the compounds **30a-e**.

In one case, the initially formed ylide, namely phenanthridinium phenacylide was trapped with maleic anhydride to give tetrahydropyrrolo[2,1-*f*]phenanthridine derivative **31** (Scheme 4.13).



Scheme 4.13. One-pot 1,3-dipolar cycloaddition of phenanthridiniumphenacylide with maleic anhydride.

It is noteworthy that the resulting product **31** does not undergo auto-oxidation. All the compounds obtained are orange to yellow coloured, sharp melting solids (Table 4.1) which are soluble in common organic solvents such as chloroform, dichloromethane etc. The compounds were characterized on the basis of IR, ^{1}H NMR, ^{13}C NMR studies (Table 4.2-4.4) and elemental analysis.[203]

Table 4.1. Physical data of the products obtained from the reaction of phenanthridinium alkoxycarbonylmethyl/phenacylide with DMAD (30a-e) and with maleic anhydride (31).

Compound	R	Molecular Formula	M. P. (°C)	Yield (%)	% calculated (found)		
					C	H	N
30a	C_6H_5	$C_{27}H_{19}O_5N$	155-157 (264-266)[49]	72	74.13 (74.28)	4.38 (4.40)	3.20 (3.21)
30b	*(p-OMe)*C_6H_4	$C_{28}H_{21}O_6N$	95-97	79	71.94 (72.28)	4.53 (4.55)	2.99 (3.00)
30c	*(p-*NO_2*)*C_6H_4	$C_{27}H_{18}O_7N_2$	122-124	68	67.22 (67.38)	3.76 (3.74)	5.81 (5.78)
30d	*(p-F)*C_6H_4	$C_{27}H_{18}O_5NF$	136-138	66	71.20 (71.42)	3.98 (3.06)	3.08 (3.06)
30e	$OCMe_3$	$C_{25}H_{23}O_6N$	162-164	68	69.27 (69.49)	5.35 (5.38)	3.23 (3.24)
31	C_6H_5	$C_{25}H_{17}O_4N$	206-208	61	75.94 (75.71)	4.33 (4.35)	3.54 (3.52)

4.2.2 Spectral characterization of the products

IR

The presence of the >C=O group is confirmed by the sharp absorption band ~1740 and ~1730 cm^{-1} due to symmetric and unsymmetric stretching vibrations. The absorption band due to C-O stretching vibrations appears in the range of 1260-1210 cm^{-1}. A sharp band at 1450 cm^{-1} confirms the C-N stretching vibration in case of **31**. The IR spectrum of one of the representative is given here in figure 4.8.

Table 4.2. IR spectral data of the compounds 30 and 31.

Compound	R	IR (KBr), cm^{-1}
30a	C_6H_5	1730, (s, C=O st.), 1700 (s, C=O, unsymm. st.), 1670 (s, C=O, . st.), 1240 (C-O), 1210 (C-O)
30b	*(p-OMe)*C_6H_4	1740, (s, C=O st.), 1730 (s, C=O, unsymm. st.), 1720 (s, C=O, . st.), 1260 (C-O), 1220 (C-O)
30c	*(p-*NO_2*)*C_6H_4	1740 (s, C=O st.), 1730 (s, C=O, unsymm. st.), 1720 (s, C=O, . st.), 1260 (C-O), 1220 (C-O)
30d	*(p-F)*C_6H_4	1740 (s, C=O st.), 1730 (s, C=O, unsymm. st.), 1720 (s, C=O, . st.), 1230 (C-F st.) 1215 (C-O)
30e	$OC(CH_3)_3$	1735 (s, C=O st.), 1730 (s, C=O, unsymm. st.), 1720 ((s, C=O . st.), 1260 (C-O st.), 1230 (C-O st.)
31	C_6H_5	1710 (s, C=O st.), 1680 (s, C=O, unsymm. st.), 1605 (s, C=O . st.), 1450 (C-N), 1260 (C-O).

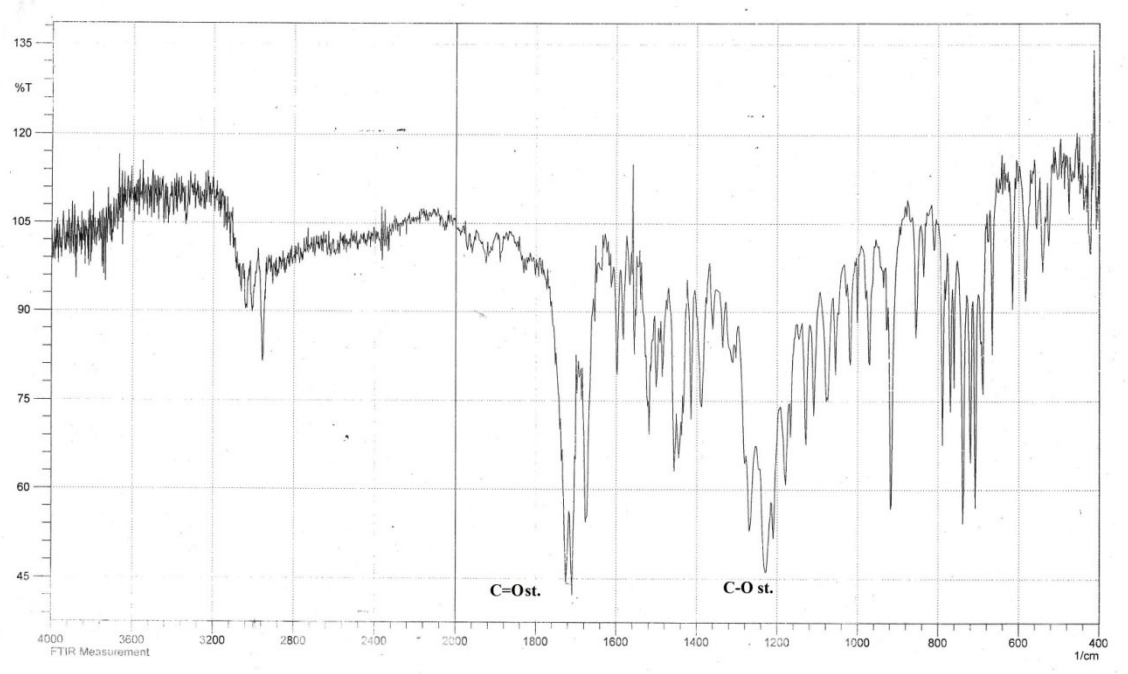
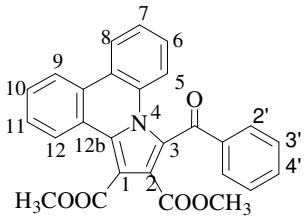


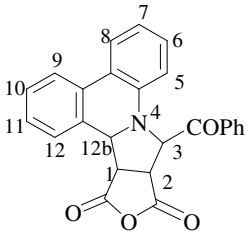
Figure 4.8. IR spectrum of 30a

^{1}H NMR

The ^{1}H NMR chemical shifts are assigned in Table 4.3.



30a



31

Table 4.3. ^{1}H NMR data of the compounds 30a-e and 31.

Compound	R	Solvent	^{1}H NMR δ ppm, *J*(Hz)
30a	C_6H_5	$CDCl_3$	3.55 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 7.28 (t, 2H, $^3J_{HH}$ = 7.5 H-3'), 7.42 (t, 1H, $^3J_{HH}$ = 7.5, H-4'), 7.49 (t, 2H, $^3J_{HH}$ =7.2, H-7, H-11), 7.55 (d 1H, $^3J_{HH}$ = 7.2, H-9), 7.60 (t, 2H, $^3J_{HH}$ = 7.2, H-6, H-10), 7.99 (d, 2H, $^3J_{HH}$ = 7.5, H-2'), 8.17 (d, 1H, $^3J_{HH}$ = 9.3, H-8), 8.34 (d, 1H, $^3J_{HH}$ = 9.3, H-12), 8.37 (d, 1H, $^3J_{HH}$ = 9.3, H-5)
30b	*(p-OMe)*C_6H_4	$CDCl_3$	3.60 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 6.85 (t, 2H, $^3J_{HH}$ = 7.5 H-3'), 7.08 (d, 1H, $^3J_{HH}$ = 7.8, H-9), 7.29 (d, 2H, $^3J_{HH}$ =7.5, H-2'), 7.33 (t, 1H, $^3J_{HH}$ = 7.5, H-11), 7.40 (t, 1H, $^3J_{HH}$ = 7.8, H-7), 7.55 (t, 1H, $^3J_{HH}$ = 7.5, H-10), 7.60 (t, 1H, $^3J_{HH}$ = 8.4, H-6), 7.78 (d, 1H, $^3J_{HH}$ = 7.8, H-8), 7.94 (d, 1H, $^3J_{HH}$ = 8.7, H-12) 8.30 (d, 1H, $^3J_{HH}$ = 8.4, H-5)
30c	*(p-NO$_2$)*C_6H_4	$CDCl_3$	3.61 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 7.29 (t, 2H, $^3J_{HH}$ = 8.7, H-7, H-11), 7.45 (d, 1H, $^3J_{HH}$ = 7.8, H-9), 7.58 (d, 2H, $^3J_{HH}$ = 8.4, H-2'), 7.64 (t, 2H, $^3J_{HH}$ = 8.7, H-6, H-10), 8.15 (t, 2H, $^3J_{HH}$ = 8.4, H-3'), 8.24 (d, 1H, $^3J_{HH}$ = 7.8, H-8), 8.33 (d, 1H, $^3J_{HH}$ = 8.7, H-12) 8.41 (d, 1H, $^3J_{HH}$ = 8.7, H-5)
30d	*(p-F)*C_6H_4	$CDCl_3$	3.59 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 7.15 (t, 1H, $^3J_{HH}$ = 8.7, H-11), 7.29 (d, 1H, $^3J_{HH}$ = 7.2, H-9), 7.42 (t, 1H, $^3J_{HH}$ = 7.5, H-7), 7.52 (d, 2H, $^3J_{HH}$ = 8.4, H-2'), 7.59 (t, 2H, $^3J_{HH}$ = 7.2, H-6, H-10), 8.01 (dd, 2H, $^3J_{HH}$ = 8.4, $^3J_{HF}$ = 5.4, H-3'), 8.21 (d, 1H, $^3J_{HH}$ = 8.7, H-8), 8.33 (d, 1H, $^3J_{HH}$ = 8.7, H-12) 8.37 (d, 1H, $^3J_{HH}$ = 8.7, H-5)
30e	$OC(CH_3)_3$	$CDCl_3$	1.66 (s, 9H, CH_3), 3.92 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 7.50 (t, 2H, $^3J_{HH}$ =7.5, H-7, H-11), 7.54 (d, 1H, $^3J_{HH}$ = 7.5, H-9), 7.58 (t, 1H, $^3J_{HH}$ = 7.5, H-10), 7.60 (t, 1H, $^3J_{HH}$ = 7.5, H-6), 8.33 (d, 1H, $^3J_{HH}$ = 7.5, H-8), 8.38 (d, 1H, $^3J_{HH}$ = 7.5, H-12), 8.41 (d, 1H, $^3J_{HH}$ = 7.2, H-5)
31	C_6H_5	$CDCl_3$	5.23 (unresolved dd, 1H, $^3J_{HH}$ = 8.4, H-1), 5.65 (unresolved dd, 1H, $^3J_{HH}$ = 8.4, H-2), 6.74 (d, 1H, $^3J_{HH}$ = 7.2, H-12b), 6.77 (d, 1H, $^3J_{HH}$ = 7.2, H-3), 7.39 (t, 2H, $^3J_{HH}$ = 7.2, H-3'), 7.61 (t, 1H, $^3J_{HH}$ = 8.4, H-4'), 7.69 (d, 1H, $^3J_{HH}$ = 7.5, H-9), 7.73 (t, 2H, $^3J_{HH}$ = 8.4, H-7, H-11), 7.76 (t, 2H, $^3J_{HH}$ = 8.4, H-6, H-10), 7.79 (d, 2H, $^3J_{HH}$ = 7.2, H-2'), 8.29 (d, 1H, $^3J_{HH}$ = 8.4, H-8), 8.81 (d, 1H, $^3J_{HH}$ = 8.4, H-12), 8.89 (d, 1H, $^3J_{HH}$ = 8.7, H-5)

In the ^{1}H NMR spectra of **30,** H-5 is most deshielded and gives a doublet at δ ~ 8.8 ppm showing three bond coupling of ~8.7 Hz with H-6. Next to the H-5, H-12 gives a doublet in the range of δ 8.8 -7.9 ppm showing three bond coupling of ~ 8.7 Hz with H-11. Other protons appear in the aromatic region anad the peaks are assigned with coupling constants in Table 4.3. The ^{1}H NMR spectrum of a representative compound **30d** is reproduced in Figures 4.7.

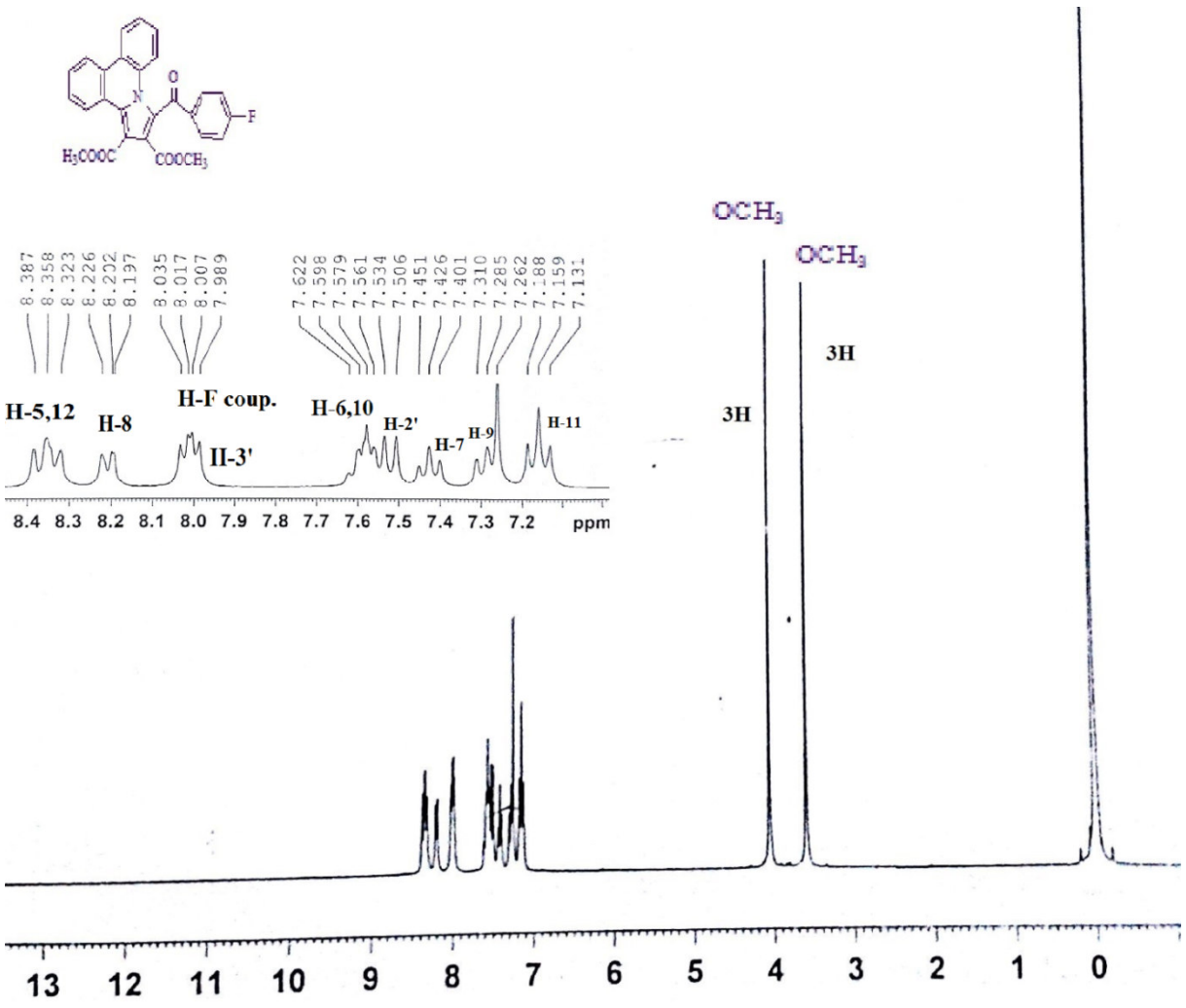


Figure 4.7. ^{1}H NMR spectrum of dimethyl 3-(4'-fluorobenzoyl)pyrrolo[2,1-*f*]phenanthridine-1,2-dicarboxylate (30d) in $CDCl_3$.

^{13}C NMR

The ^{13}C NMR chemical shifts are assigned in Table 4.4. The ^{13}C NMR spectrum of a representative compound **30d** is reproduced in Figure 4.8.

Table 4.4. ^{13}C NMR spectral data of the compounds 30a-e and 31.

Compound	R	Solvent	^{13}C NMR δ ppm, *J*(Hz)
30a	C_6H_5	$CDCl_3$	190.2 (C=O), 167.5 (C=O), 163.4 (C=O), 137.6 (C-12b), 134.1 (C-4a), 131.6 (C-1'), 129.5 (C-4'), 129.0 (C-5), 128.8 (C-8a, 12a), 128.6 (C-10), 128.5 (C-2'), 126.7 (C-6), 125.9 (C-8), 124.3 (C-3, C-2), 124.2 (C-3'), 123.3 (C-12b), 122.6 (C-11, C-7), 119.0 (C-9), 111.6 (C-1), 53.0 (O*C*H$_3$), 51.9 (O*C*H$_3$)
30b	*(p-OMe)*C_6H_4	$CDCl_3$	190.0 (C=O), 165.1 (C=O), 164.6 (C=O), 131.7.6 (C-12b), 129.8 (C-4a), 128.6 (C-1'), 128.5 (C-4'), 128.3 (C-5), 126.9, 126.0, 125.9, 124.2, 124.0, 123.7, 122.5 (aromatic carbons), 121.5 (C-11), 118.9 (C-9), 110.6 (C-1), 83.9 (*p-OCH$_3$*), 52.7 (O*C*H$_3$), 52.2 (O*C*H$_3$)
30c	*(p-NO$_2$)*C_6H_4	$CDCl_3$	189.2 (C=O), 167.8 (C=O), 166.9 (C-4'), 163.4 (C=O), 139. 0 (C-3'), 134.0 (C-12b), 132.3 (C-4a), 132.2 (C-1'), 131.5 (C-8b), 129.2 (C-2'), 128.7 (C-5), 128.5 (C-8a), 126.6 (C-10), 126.0 (C-6), 124.3 (C-12a), 124.1 (C-8), 123.3, 122.7, 120.3, 119.8, 116.4, 116.2, 111.3 (aromaic carbons) 53.1 (O*C*H$_3$), 52.2 (O*C*H$_3$)
30d	*(p-F)*C_6H_4	$CDCl_3$	188.7 (C=O), 167.5 (C=O), 166.4 (C-4', d, $J_{C\text{-}F,}$ = 256.7), 163.3 (C=O), 139. 0 (C-3'), 134.0 (C-12b), 132.3 (C-4a), 132.2 (C-1'), 131.5 (C-8b), 129.2 (C-2'), 128.7 (C-5), 128.5 (C-8a), 126.6 (C-10), 126.0 (C-6), 124.3 (C-12a), 124.1 (C-8), 123.3 (C-3), 122.7 (C-2), 120.1 (C-12), 118.8 (C-11), 116.4 (C-7), 116.1 (C-9), 111.6 (C-1), 53.0 (O*C*H$_3$), 52.0 (O*C*H$_3$)
30e	$OC(CH_3)_3$	$CDCl_3$	166.8 (C=O), 164.2 (C=O), 161.6 (C=O), 131.7 (O-*C*), 129.7 (C-4[a], C-12b), 128.6 (C-1'), 128.5 (C=8b), 128.1 (C-5), 126.9 (C-8a), 124.9 (C-6), 124.1 (C-12a), 124.0 (C-8), 123.7 (C-2, C-3), 123.3 (C-12), 122.5 (C-11), 121.5 (C-7), 118.9 (C-9), 110.6 (C-1), 52.7 (O*C*H$_3$), 52.2 (O*C*H$_3$), 27.8 (*C*H$_3$)
31	C_6H_5	$CDCl_3$	190.87 (C=O), 182.4 (2C=O), 137.50 (C-4a, 12b), 128.01 (C-1'), 125.33 (C-8b), 123.96 (C-4'), 123.23 (C-5), 123.11 (C-8a, 12b), 122.94 (C-6, C-10), 122.08 (C-8), 119.03 (C-3'), 117.47 (C-7, C-11), 113.05 (C-9), 106.55 (C-12b), 55.58 (C-3), 45.86(C-1, C-2)

The most deshielded signal in the ^{13}C NMR spectra of the compounds **30a-e** corresponds to the benzoylic carbonyl group. Next two less intense signals correspond to the two ester carbonyl groups and most upfield signals correspond to the alkoxy carbon atoms. In case of the compound **30e,** an intense signal at δ 27.8 ppm corresponds to the methyl carbons. C-4'. The C-4' of **30d** gives signal at δ 166.4 ppm showing C-F coupling of ~256.7 Hz with fluorine atom. The ^{13}C NMR spectrum of the compound **30d** is reproduced in Figure 4.7.

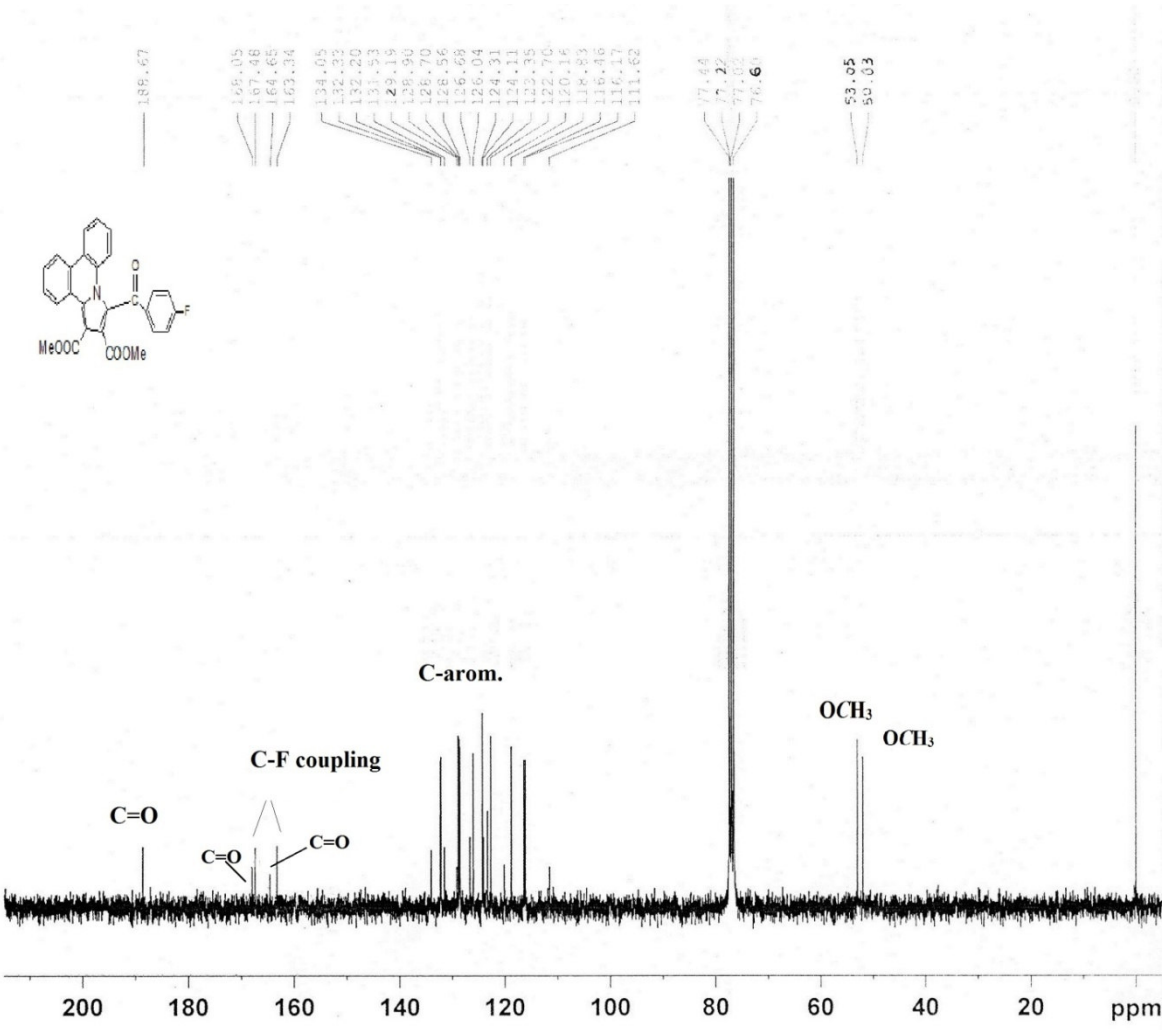


Figure 4.9. ^{13}C NMR spectrum of dimethyl 3-(4'-fluorobenzoyl)pyrrolo[2,1-*f*]phenanthridine-1,2-dicarboxylate (30d).

4.3 EXPERIMENTAL DETAILS

4.3.1 Materials

All the reactions were carried out in one-pot using distilled water as a solvent. Alkyl bromoacetate or phenacyl bromide, ethanol and ethyl acetate were of commercial grade, purchased from Sigma-Aldrich and used without further purification. Prepared compounds were washed with distilled water again, dried and recrystallized from ethanol or ethyl acetate under normal environmental conditions.

4.3.2 Instrumentation

IR spectra were recorded on Shimadzu IR spectrophotometer using KBr pellets in the range between 4000-500 cm^{-1}.

^{1}H Nuclear magnetic resonance spectra were recorded on Bruker-DPX-300 at frequency 300.13MHz spectrometer in $CDCl_3$ using TMS as an internal standard in a 5mm tube.

^{13}C Nuclear magnetic resonance spectra were recorded on Bruker-DPX-300 at a frequency of 100.52 MHz in DMSO- d_6 or $CDCl_3$ using TMS as an internal standard in 5mm tube.

The C, H, N element analyses were done on CHNS Analyzer Perkin Elmer Ser.Second 2400.

4.3.3 Synthetic procedure

Phenthridine (1 mmol, 182 mg) and α-bromoketone (1 mmol) or t-butyl bromoacetate (1mmol, 190 mg, 0.15 mL) were added to water (20 mL) taken in a 100 mL R.B. flask. A turbid aquous mixture appeared which turned to almost a clear solution on stirring at room temperature for 2-3 days. The resulting solution was transferred to a 250 mL beaker and DMAD (1 mmol, 142 mg, 0.12 mL) was added, followed by slow addition of an aqueous solution of potassium carbonate (2 mmol, 276 mg in 10 mL water) with vigorous stirring with a glass rod. An instant visible reaction occurred by showing formation of pink coloured ylide, which disappeared immediately and an orangish to yellow coloured compound precipitated out. After leaving it at room temperature overnight, the solid was collected by decanting off the aqueous phase. The collected solid was washed with water (3x20 mL), dried and recrystallized from ethanol, except **3b**, which was recrystallized from ethyl acetate.

4.4 CONCLUSION

Water can be used as the solvent for 1,3-dipolar cycloaddition of the cycloiminium ylides generated in situ. N-Alkylation of the azine with an α-bromoketone or –ester produces (substituted methyl) azinium bromide in aqueous phase which on reacting with a base, such as potassium carbonate generates ylide in situ. The latter can be trapped with a dipolarophile, namely DMAD or maleic anhydride to furnish pyrrolo[2,1-*f*]phenanthridines in good yields.