5

Summary and Conclusion

The results pertaining to the present investigation on the IEDDA reaction of the diene 2-oxo-2H-pyrido [1, 2-*a*] pyrimidin-3(4*H*)-ylidiene acetic acid is summarized below

- Initially optimization of IEDDA reaction conditions such as catalyst, solvent, time and temperature were done using the diene 2-oxo-2H-pyrido[1,2-*a*] pyrimidin-3(4*H*)-ylidiene acetic acid and the dienophile butyl vinyl ether as model substrates. The results showed that, the reaction was unsuccessful in absence of catalyst and in the presence of catalyst aluminium chloride and zinc chloride.
- The IEDDAR reaction of diene 2-oxo-2H-pyrido[1,2-*a*] pyrimidin-3(4*H*)-ylidiene acetic acid with dienophiles butyl vinyl ether, 1-phenyl-3-methyl-pyrazolone, 1-methyl-1-cyclohexene, 3,4-Dihydro-2H-pyran, 1-morpholinocyclohexene in presence of Lewis acid catalyst indium(III)chloride in DMF medium provided the expected cyclo adducts with moderate to good yields.
- All the synthesized compounds were characterized by spectroscopic methods such as FT-IR, ^{1}H NMR, ^{13}C NMR, and Mass spectral studies.
- The reaction showed endo selectivity. The diastereoisomeric ratio of the adducts were found to be 6:1 for *endo* and *exo* isomers (**9**, **11** and **13**) except for 3-butoxy-9-methyl-2,3,4,5-tetrahydropyrano[2,3-*d*]pyrido[1,2-*a*]pyrimidine-4-carboxylic acid **(5)** and Methyl-2-Oxo-1-Phenyl-1,2,3,3*a*,4,5-hexa hydropyrazolo[1,5-*b*]Pyrido[1',2':1,2]Pyrimido[5,4-*e*][1,2]Oxazine-4-Carboxylic Acid **(7)** which showed 1:1 and 6:4 ratio respectively.
- The IEDDA reaction pathway was proved by the analysis of energies of LUMO and HOMO of diene and dienophiles. The reaction occurred by lowering of LUMO energy of diene by Lewis acid catalyst.
- The computed global reactivity indices, electronic chemical potential (μ), global electrophilicity (ω), and maximum charge transfer (Δ*N* max) also supported the IEDDA mechanism.

- The regioselectivity observed in the IEDDA reaction of diene 2-oxo-2H-pyrido[1,2-*a*] pyrimidin-3(4*H*)-ylidiene acetic acid with dienophiles was explained on the basis of NBO charges calculated by DFT methods.

- Analysis of the transition states and intrinsic reaction coordinates of the reaction of diene 2-oxo-2H-pyrido[1,2-*a*] pyrimidin-3(4*H*)-ylidiene acetic acid with dienophiles butyl vinyl ether and 1-methyl-1-cyclohexene by DFT method explained the observed diastereoisomeric ratio of 1:1 and 6:1 *endo* and *exo* ratio respectively. The synchronous nature of the transition states proved the proposed concerted mechanism of the IEDDA reaction.

- Synthesized compounds were tested for antibacterial activity and all the compounds exhibited moderate activity and the compound 3*a*-methyl-2-oxo-1-phenyl-1,2,3,3*a*,4,5-hexahydropyrazolo[1,5-*b*]pyrido[1',2':1,2]pyrimido[5,4-*e*][1,2]oxazine-4-carboxylic acid (**7a**) was found to be more potent in both *in-silico* and *in-vitro* studies.

To conclude we have demonstrated a successful IEDDA reaction for the synthesis of fused pyrido[1,2-*a*]pyrimidin-2-one by LUMO lowering strategy using Lewis acid catalyst indium chloride. This approach may be used to create highly substituted and functionalized pyrimidine fused heterocyclic scaffolds.