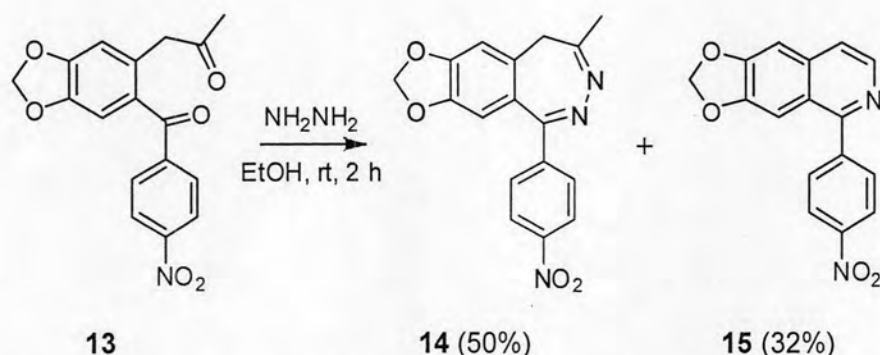


CHAPTER II

LITERATURE REVIEWS AND RETROSYNTHETIC ANALYSIS

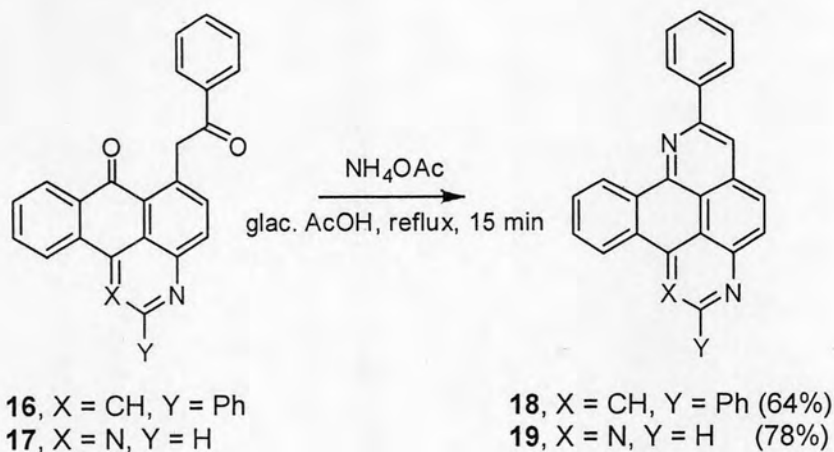
2.1 Literature Reviews

Zappalà and co-workers [15] reported cyclization of diketone **13** with excess hydrazine in ethanol at room temperature for 2 hours to give diazepine **14** as a major product in 50% yield and **15** as a minor product in 32% yield and (Scheme 2-4).



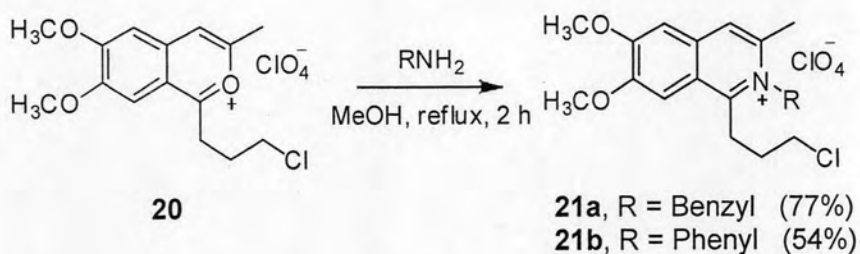
Scheme 2-4. Synthesis of isoquinoline **15** from the reaction of diketone **13** with hydrazine.

Deady and Smith [16] performed a reaction of diketone **16** or **17**, with ammonium acetate in glacial acetic acid at reflux temperature for 15 min to produce the compound **18** or **19** in 64% and 78% yield, respectively (Scheme 2-5).



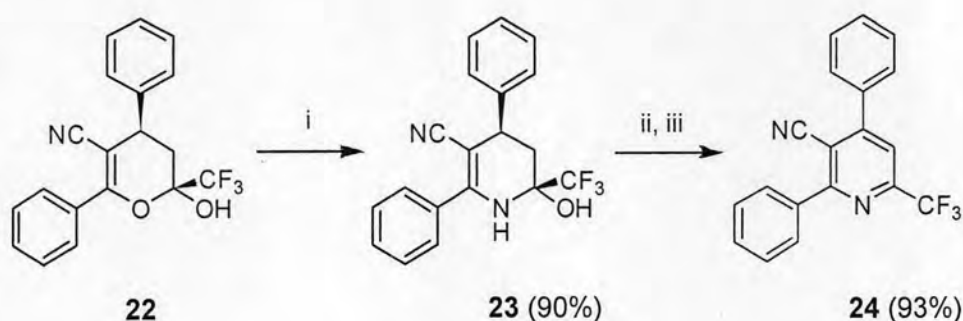
Scheme 2-5. Synthesis of isoquinoline **18** and **19** from the reaction of diketone **16** and **17** with ammonium acetate.

Kibaly and co-workers [17] reported a reaction of pyrylium salt **20** with the suitable primary amine in methanol at reflux temperature for 2 hours to acquire the corresponding isoquinolinium salt **21a** and **21b** in 77 and 54%, respectively (Scheme 2-6).



Scheme 2-6. Synthesis of isoquinolinium **21a-b** from the reaction of pyrylium **20** with aniline and benzylamine.

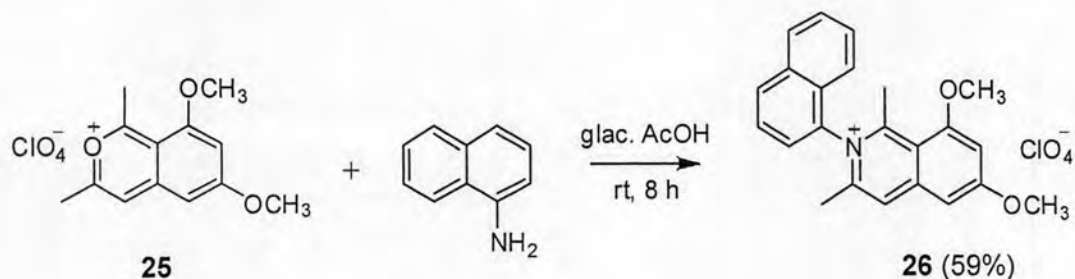
Nenajdenko and co-workers [18] described condensation of hemi-acetal **22** with ammonium acetate in ethanol at reflux temperature for several hours until the reaction was completed to give compound **23** in 90% yield. Subsequently, compound **23** was dehydrated by *p*-toluenesulfonic acid as acidic catalyst in toluene at reflux temperature for several hours too, and then further reacted with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane at room temperature to obtain pyridine **24** in 93% yield (Scheme 2-7).



conditions: i) NH_4OAc , EtOH, reflux; ii) *p*-TsOH, toluene, reflux; iii) DDQ, CH_2Cl_2 , rt.

Scheme 2-7. Synthesis of pyridine **24** from the reaction of hemi-acetal **22**.

Ponte-Sucre and co-workers [19] reported the use of benzopyrylium salt **25** to react with 1-aminonaphthalene in glacial acetic acid as solvent at room temperature for 8 hours to produce isoquinolinium salt **26** in 59% yield (Scheme 2-8).



Scheme 2-8. Synthesis of isoquinolinium **26** from the reaction of pyrylium **25** with 1-aminonaphthalene.

2.2 Retrosynthetic Analysis

According to above mentioned literature reviews, in this work, the retrosynthesis of compounds **4** and **5** is directed to conversion of pyrylium ring of compound **3** into pyridine ring, and cyclization of 1,5-diketone **27** in the presence of appropriate amine precursor, such as ammonium salt or primary amine. Both retrosynthetic approaches are schematically illustrated in Chart 2-2. Compound **3** is generated by acid-catalyzed dehydration of **1** [8], while compound **27** is prepared from base-catalyzed hemi-acetal cleavage of **1** [8].

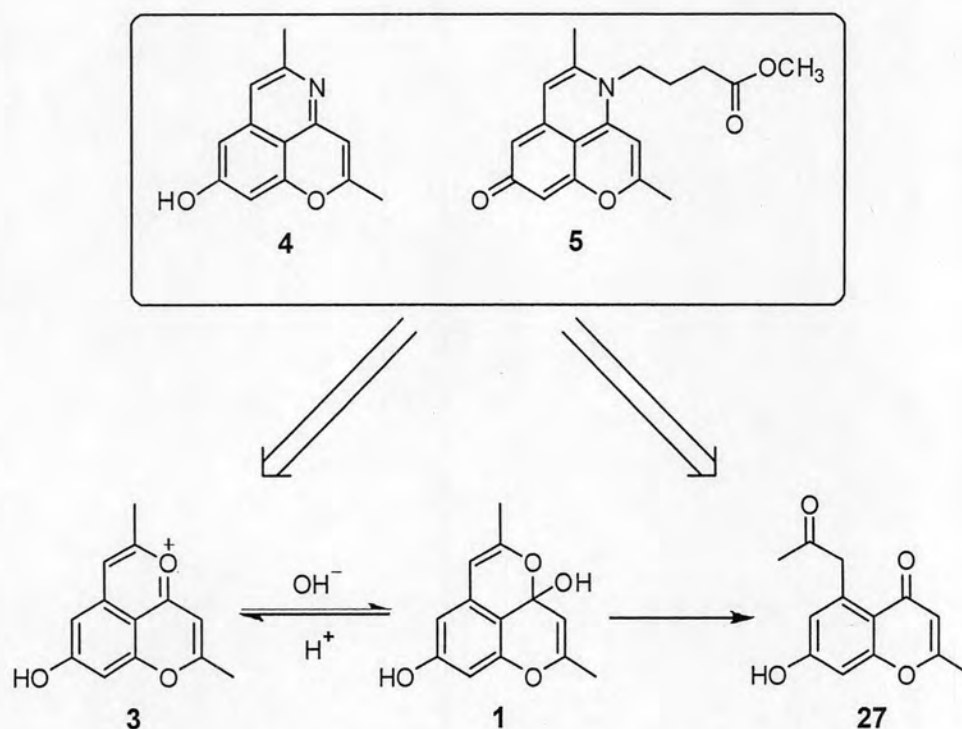


Chart 2-2. Retrosynthesis of **4** and **5**.