VIETNAM NATIONAL UNIVERSITY HO CHI MINH CITY
UNIVERSITY OF TECHNOLOGY

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TRANSITION METAL-FREE SYNTHESIS AND FUNCTIONALIZATION OF 5- AND 6-MEMBERED HETEROCYCLIC COMPOUNDS

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SUMMARY OF DOCTORAL THESIS

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INTRODUCTION

Heterocyclic compounds are important compounds that exhibit an extensive range of physical, chemical, and biological properties. Heterocyclic compounds have been presented in numerous pharmacological areas, such as anti-cancer, antibiotics, anti-inflammatory, anti-inflammatory and depression, anti-malarial, anti-HIV, antibacterial, antifungal, antiviral, antidiabetic, herbicides, fungicides, and insecticides. In addition, they are considered in pharmaceutical chemistry and agriculture. In fact, heterocyclic frameworks such as quinazolines, quinoxalines, thiocromenones, and *N*-aryl-indoles have become an interesting topic in organic synthesis.

Due to a wide range of applications of heterocyclic compounds in pharmaceutical, cosmetic, and agricultural chemical industries, developing effective processes to synthesize 5- and 6-membered heterocyclic compounds such as quinazoline, quinoxaline, thiocromenone, and *N*-arylindole derivatives have been highly demanding. However, the currently available reactions often require transition metal catalysts and under extreme conditions. Therefore, proposing new methods for the synthesis of heterocyclic compounds without the use of any transition metal catalyst would be considered.

In the progression of studying documents, and investigating many reactions to create heterocyclic compounds, the possible protocols for the synthesis of 4-phenylquinazoline, 2-phenylquinoxaline, 2-arylthiocromenone, and *N*-arylindole derivatives without using transition metal catalysts were detected. On that basis, the reaction conditions for each reaction were screened to maximize yield, conducted survey products to develop plausible reaction mechanisms, and extended the application scope of each response. As a result, the thesis provided effective procedures to synthesize 4-phehylquinazolines, 2-phenylquinoxalines, *N*-arylindoles, and 2-arylthiocromenones, these methods did not overlap with previous publications.

CHAPTER 1 LITERATURE OVERVIEW

1.1 Introduction of quinazoline compounds

1.1.1 Biological activity of the quinazoline compounds

Quinazoline derivatives are the organic compounds, based on the quinazoline framework, which is an aromatic heterocyclic structure containing nitrogen. They are commonly present in nature and also can be synthesized. Most of the quinazoline derivatives are yellow solids and poorly soluble in water. As most of them demonstrate a wide range of biological activities, quinazoline derivatives have attracted more and more attention from researchers.

The pharmacological studies of quinazoline compounds dated back to 1940s. Researchers have identified many biological activities, including anti-cancer, anti-viral, anti-convulsant, anti-inflammatory, analgesic, and anti-oxidation. Several applications of quinazoline derivatives are shown in Figure1.1.

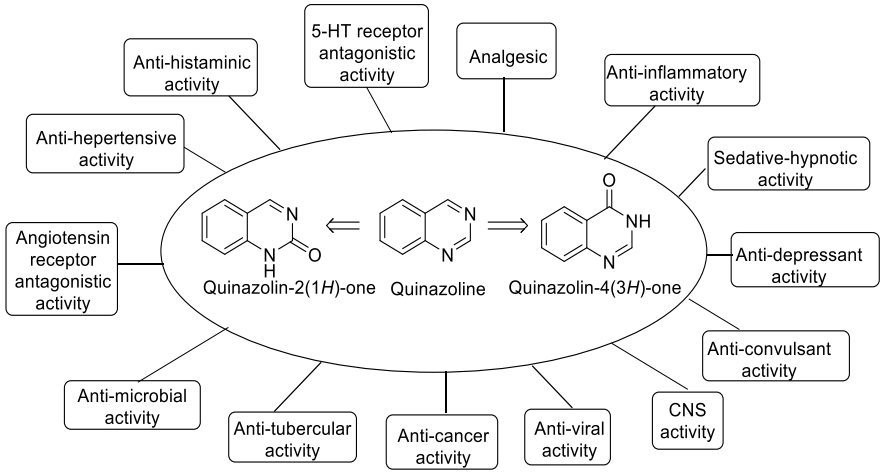
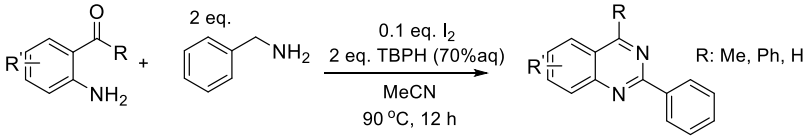


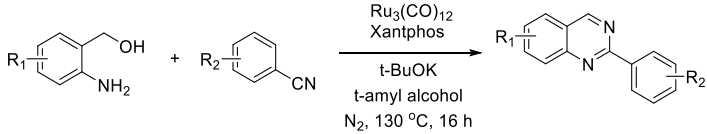
Figure 1.1 Pharmacological significance of quinazolines

1.1.2 Synthetic approaches to quinazoline derivatives

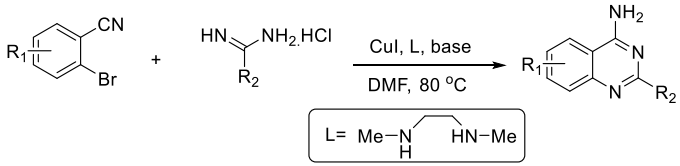
There were many methods to synthesize quinazoline compounds. In this, we would like to epitomize five main methods. First, 2-phenylquinazolines were synthesized via a tandem reaction following sp^3 C-H functionalization between benzylamines and substituted 2-aminobenzophenones (Scheme 1.1). The second one was dehydrocyclization between benzonitrile and 2-amino aryl ketone in the presence of a transition metal-catalyst (Scheme 1.2). The third one was copper-catalyzed *N*-arylation-cyclization via Ullmann-type coupling reactions (Scheme 1.3). In the fourth approach, quinazolines would be synthesized via mediated oxidative C(sp^3)-C(sp^2) bond formation (Scheme 1.4). The last one was the direct oxidative amination of C(sp^3)–H bonds (Scheme 1.5).



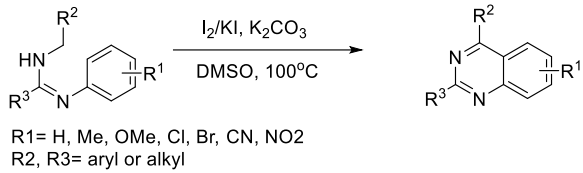
Scheme 1.1 Synthesis of 2-phenylquinazolines via a tandem reaction following sp^3 C-H functionalization



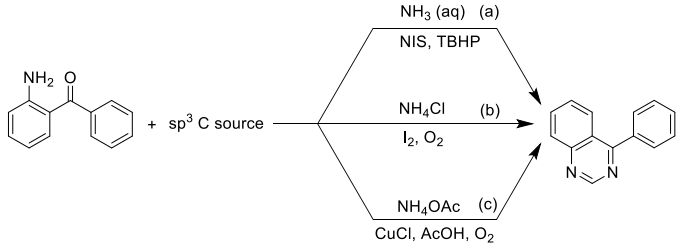
Scheme 1.2 Synthesis of quinazoline derivatives catalyzed by commercial $Ru_3(CO)_{12}$/Xantphos/*t*-BuOK catalyst



Scheme 1.3 Synthesis of quinazoline derivatives via Ullmann-type coupling reactions



Scheme 1.4 Synthesis of quinazoline derivatives via I_2/KI-promoted oxidative C(sp^3)-C(sp^2) bond formation



Scheme 1.5 Synthesis of 4-phenylquinazoline via direct oxidative amination of C(sp3)–H bonds

Because of the fascinating various biological and pharmacological properties of nitrogen-containing molecules, the formation of crucial C-N bond is required. Therefore, the synthesis of quinazoline compounds will be always considered an essential research topic.

1.2 Introduction of quinoxaline compounds

1.2.1 Biological activity of quinoxaline compounds

Among many nitrogen heterocycles, quinoxaline compounds are well-recognized as an essential substances, possessing a wide range of applications in pharmaceutical, agricultural, and material industries. Over the last two decades, quinoxalines have been known to play an important role in medicinal science. Quinoxaline derivatives showed highly significant biological activities such as anti-cancer, anti-HIV, antimicrobial, anti-inflammatory, anti-tumor, anti-tuberculosis, antioxidant, and anti-Alzheimer's. In addition, they

are also used as reagents in organic synthesis and applied in the photovoltaic industry (Figure 1.2).

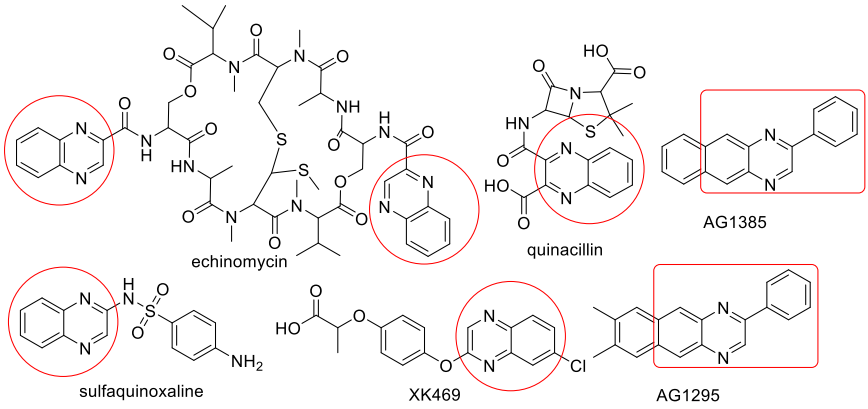
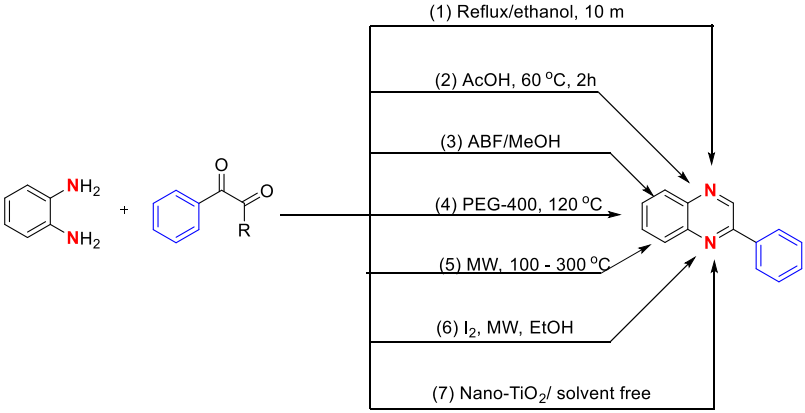


Figure 1.2 Several commercially quinoxaline derivatives.

1.2.2 Synthetic approaches to quinoxaline derivatives

The synthesis of quinoxaline derivatives has been developed for a long time. The most common approach was the condensation reactions of *o*-phenylenediamine with *α*-diketone to form quinoxaline derivatives (Scheme 1.6).



Scheme 1.6 The common approaches for the synthesis of quinoxaline derivatives

In other methods, under transition metal conditions quinoxaline could be synthesized via the reaction between *o*-phenylenediamines with α-hydroxyl ketones or α-haloketones. Aside from *o*-phenylenediamines, a few substrates were used to synthesize quinoxalines, including *o*-nitroanilines, *N*-arylenamines, *o*-diisocyanoarenes… However, all these approaches used transition metal catalysts, toxic solvents and were carried out under extreme conditions so they might not be applied in the pharmaceutical industry.

1.3 Introduction of *N*-arylindole compounds

1.3.1 Biological activity of the *N*-arylindole compounds

N-arylindole is a basic structure found in many biological and pharmaceutical compounds. It is also present in chemical materials and fundamental ligands used in chemical processes. *N*-arylindoles display a lot of valuable activities such as anti-inflammatory, anti-cancer, anti-viral, anti-convulsant, and treatment of schizophrenia (Figure 1.3).

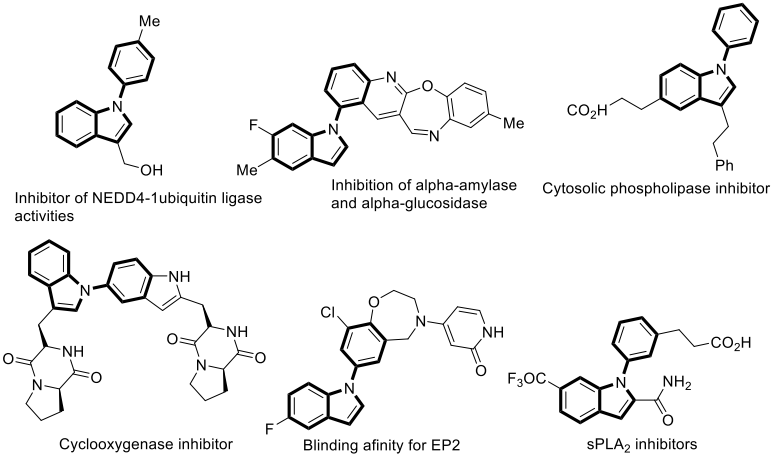
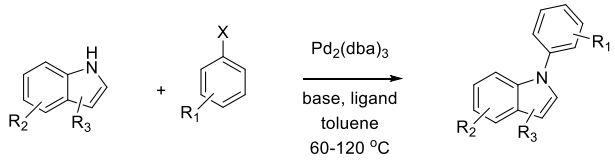


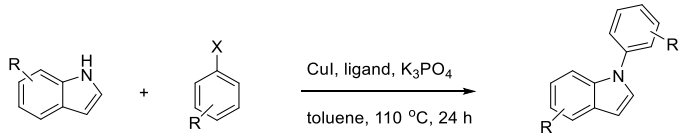
Figure 1.3 *N*-arylindoles and its applications

1.3.2 Synthetic approaches to *N*-arylindole derivatives

Among the methods for synthesizing *N*-arylindoles, the Fisher indole synthesis method is the best known and most widely used. These transition metal-catalyzed reactions traditionally have required ligand, high temperatures, and occurred in extreme conditions.

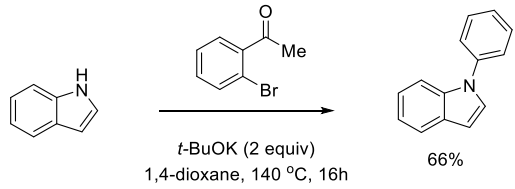


Scheme 1.7 Palladium-catalyzed coupling indoles and halogen-substituted arenes.

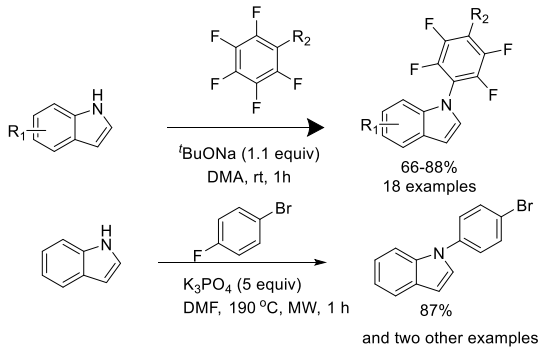


Scheme 1.8 Copper-catalyzed coupling indoles and halogen-substituted arenes.

The direct transitional-metal-free cross-coupling affords an efficient synthetic tool for the selective carbon-carbon and carbon-heteroatom bond formations from simple substrates. The drawbacks of these reactions were high temperature and strong peroxide requirement.



Scheme 1.9 N-arylation of indole using a benzyne intermediate



Scheme 1.10 *N*-arylation of indoles by SNAr of aryl fluorides

Because of their importance, *N*-arylindole derivatives are attracting more attention and there have been numerous strategies reported for the construction of functionalized indoles. Nevertheless, access to *N*-arylated indoles is still extremely limited and highly desirable.

1.4 Introduction of thiocromenone compounds

1.4.1 Biological activities of thiocromenone compounds

Flavones are a class of flavonoids, a joint group of plant polyphenols that is very widespread in nature. 1-thioflavone and its derivatives have been widely investigated as potential drug candidates for diverse pharmacological activities such as anti-bacterial, anti-fungal, anti-carcinogenic, anticancer, etc.

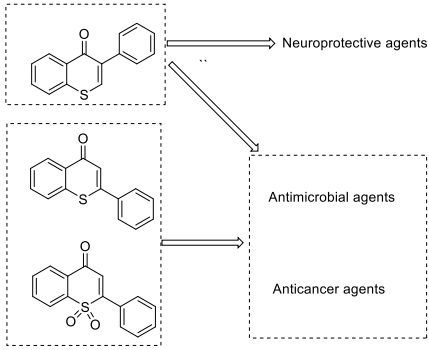
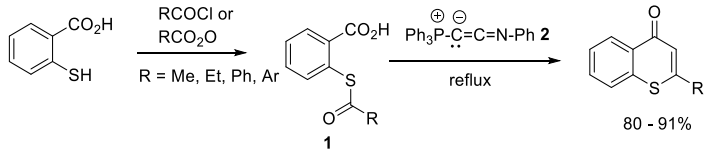


Figure 1.4 Thiocromenones and their applications

Because of its applications, various protocols towards 1-thioflavones and expanded to other 2-substituted thiochromen-4-ones have been developed, which can be separated into multi-step and one-step procedures.

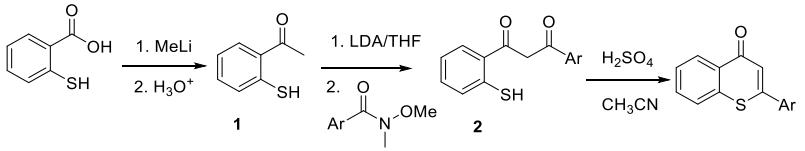
1.4.2 Synthetic approaches to thiocromenone derivatives

By using sulfur-containing reactants as precursors, initially, the strategy to synthesize thiochromen-4-ones used sulfur-containing structural motifs as key reactants. Normally, a one-pot transformation consists of two steps: firstly, converting thiosalicylic acid to various thioesters **1**; secondly, introducing a Wittig reagent **2** under reflux heating (Scheme 1.11).



Scheme 1.11 Synthesis of 2-substituted thiochromen-4-ones using Wittig reagent

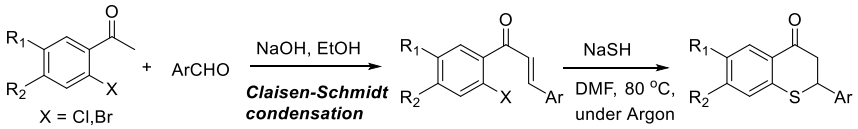
In another approach, the strategy proceeded through the formation of 2'-mercaptoacetophenone **1** from thiosalicylic acid, where 1 would be aroylated at the α-methyl position to furnish **2**. Subsequently, **2** was cyclodehydrated in the presence of sulfuric acid and acetonitrile in a short reaction time to form 2-aryl-thiochromen-4-ones in good yields (Scheme 1.12). Various substituted aroylation agents were compatible with this protocol.



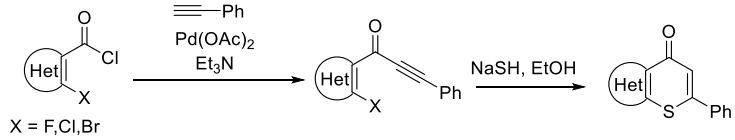
Scheme 1.12 Synthesis of 2-aryl-thiochromen-4-one towards the formation of the 2'-mercaptoacetophenone intermediate

Aside from metal-mediated and metal-catalyzed transformations, a considerable number of one-step synthesis strategies for thiochromones without the aid of any transition metal have also been reported. Various thiochromen-4-ones could also be obtained via dehydrogenation of the corresponding thiochroman-4-ones.

Apart from using sulfur-containing substrates which are not abundant, external sulfur sources such as sodium hydrosulfide, sodium sulfide, or xanthate (KCS_2OEt) can also be used. However, the synthesis studies in the direction of bringing sulfur from an external source to create thiochromenones are still limited and transition metal catalysts appear in all most procedures.



Scheme 1.13 Synthesis of 2-arylthiochroman-4-ones through 2'halochalcones



Scheme 1.14 Using NaSH for the synthesis of
2-substituted thiochromen-4-ones

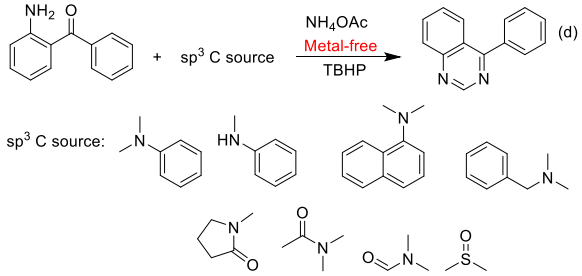
Whereby, according to their importance, 1-thioflavone derivatives are attracting more attention and more studies have been reported to synthesize 1-thioflavone derivatives. With an abundant source of S_8 and the important role of thiocromenone derivatives, there will be many solutions in the direction of using non-toxic elemental sulfur directly to synthesize thiocromenone derivatives.

1.5 Aims of this work

As the literature overview has presented, 5- and 6-membered heterocyclic compounds have a very important role in our life and are widely applied in many fields, specifically the pharmaceutical field. Intending to synthesize heterocyclic

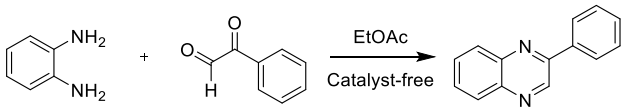
compounds, many tests have been conducted to find the relevant reactions. With the initial results in detecting suitable reactions based on using available reagents and not using transition metal catalysts, the feasible conditions to synthesize 4-phenylquinazoline, 2-phenylquinoxaline, N-arylindole, and 1-thioflavone were revealed. These findings did not overlap with previous studies and were feasible under the current laboratory conditions. Therefore, the thesis aims to complete the synthesis procedures of 4-phenylquinazoline, 2-phenylquinoxaline, *N*-arylindole, and 1-thioflavone, then extend the application range of the reactions and carry out control experiments for proposing the plausible mechanism of each transformation.

For the synthesis of 4-phenylquinazolines, the formation of 4-quinazoline substituents through oxidation was performed in which the organic peroxide is used as an oxidant can readily generate substituents of 4-quinazoline without any additional catalyst. This protocol can be widely applicable to a wide variety of solvents (Scheme 1.15).



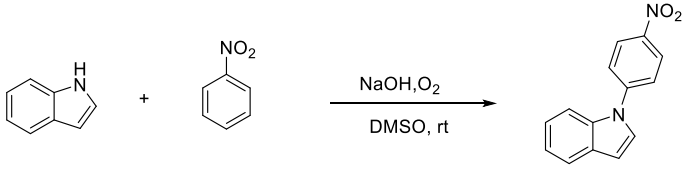
Scheme 1.15 Metal-free synthesis of 4-phenylquinazoline

By studying the synthesis of 2-phenylquinoxaline, a good transformation was proposed, by which the reaction between o-phenylenediamines and phenylglyoxals in ethyl acetate gives excellent performance without any additional catalyst. This reaction suggests an easy pathway for the synthesis of highly bioactive compounds containing the quinoxaline framework through the condensation of *o*-phenylenediamines with phenylglyoxals (Scheme 1.16)



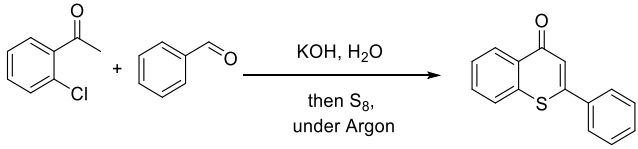
Scheme 1.16 Synthesis of quinoxaline from o-phenylenediamine and phenylglyoxal in ethyl acetate

For the study of 1-(4-nitrophenyl)-1*H*-indole synthesis, in the absence of transition metals, at room temperature, and under simple base conditions, *N*-arylindole is easily obtained from indole and nitrobenzene (Scheme 1.17). The application range of this interesting protocol can be extended to derivatives of 1*H*-pyrrole and 1*H*-pyrazole.



Scheme 1.17 *N*-Arylation of indole and nitrobenzene.

The fourth main part of this work include developing a two-step one-pot synthesis of 2-substituted-thiochromen-4-ones using cheap, and non-toxic elemental sulfur as the sulfur source. The method relies on commercially reagents without using transition metal catalysts. It consists of a condensation of 2'-chloroacetophenone and aryl aldehyde to form a 2'-chlorochalcone intermediate, which is then cyclized to the thiochromen-4-one product by adding elemental sulfur (Scheme .18).



Scheme 1.18 Using elemental sulfur for the synthesis of 1-thioflavone

CHAPTER 2 EXPERIMENTS

2.1 Materials and Instrumentations

2.1.1 Materials

All chemicals as well as materials used in this study were obtained commercially from Merck (Germany), Sigma (USA), Acros (USA), Chemsol (Vietnam), and Xilong (China) suppliers as listed in Table 2.1, were used without further purification and of an analytical grade.

2.1.2 Instrumentations

Gas chromatography (GC) analyses were performed by a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis held samples at 100 °C for 1 minute, then gradually raised the temperature from 100 °C to 280 °C with an increment of 40 °C /min, which took 4.5 minutes to reach the highest temperature, and finally held them at 280 °C for another 4.5 minutes. Inlet and detector temperatures were set constant at 280 °C. The internal standard used in the calculation of GC yield was diphenyl ether.

Gas chromatography coupled with mass spectrometry (GC-MS) analyses were performed on Shimadzu GCMS-QP2010Ultra with a ZB-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for the GC-MS analysis held samples at 50 °C for 2 minutes, then gradually raised the temperature from 50 °C to 280 °C with an increment of 10 °C /min, which took 23 minutes to complete, and finally held them at 280 °C for another 10 minutes. The inlet temperature was set constant at 280 °C. Mass spectroscopy used the electron ionization (EI) method to convert the samples into ions, and mass spectra were compared with those gathered from the NIST library.

The ^{1}H and ^{13}C NMR have been recorded on Bruker AV 500 spectrometer or AvanceNEO 600MHz spectrometer (600 and 151 MHz, respectively) using residual solvent peak as a reference. HR-MS spectra were recorded by an Agilent HPLC 1200 Series coupled to Bruker micrOTOF-QII.

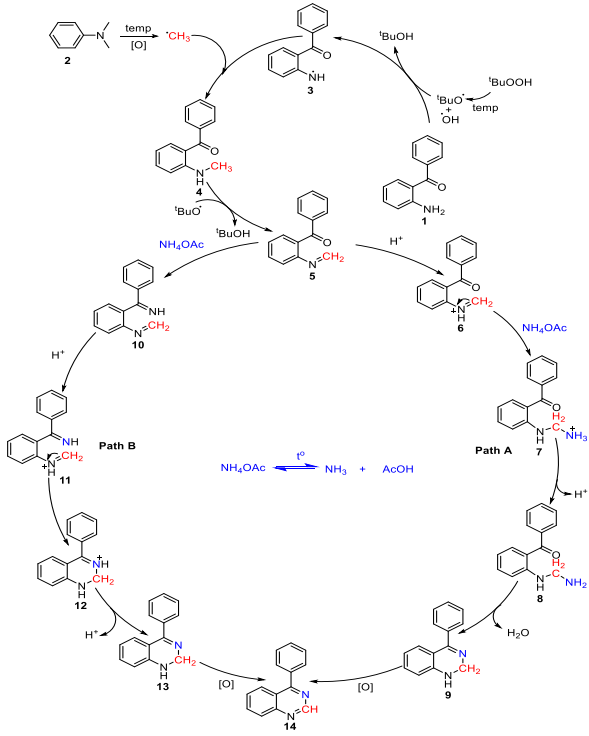
2.2 Experimental procedures

The 0.1 mmol first reagent reactions were repaired according to the target products. Subsequently, the reaction mixture was cooled down to room temperature, diluted with ethyl acetate (5 mL), and washed with saturated $NaHCO_3$ solution (5 mL). The organic layer was dried using anhydrous Na_2SO_4. Reaction yields were recorded from the GC analysis results based on the diphenyl ether internal standard. To isolate the desired product, the solvents were removed via a rotary evaporator, and the residue was purified by flash chromatography. The product specification was additionally verified by GC-MS, ^{1}H NMR, and ^{13}C NMR.

CHAPTER 3 RESULTS AND DISCUSSION

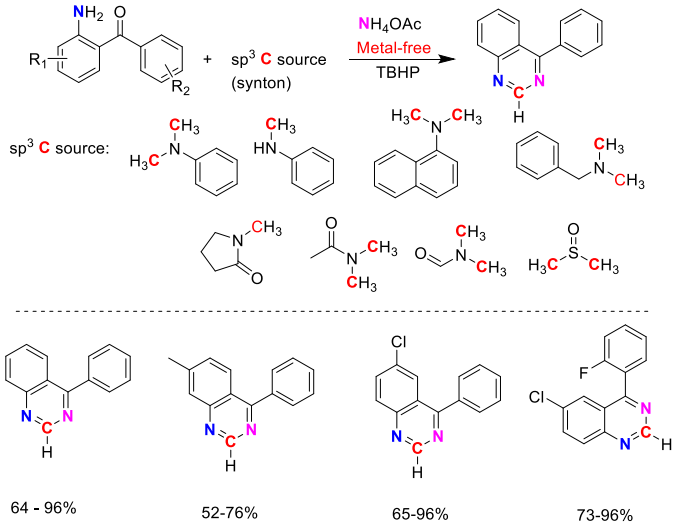
3.1 Synthesis of quinazoline derivatives via peroxide-mediated direct oxidative amination of C(sp^3)-H bonds

Screening of reaction conditions of synthesis of 4-phenylquinazoline via peroxide-mediated direct oxidative amination of C(sp^3)-H bonds, the relevant conditions were proceeded that: 2-aminobenzophenone (0.1 mmol), NH_4OAc (0.2 mmol), TBHP/decane (0.2 mmol), DMA (1 mL), 80 °C; 8 h. Base on the results of control experiment reactions and previous reports, a plausible mechanism has also proposed (Scheme 3.1).



Scheme 3.1 Proposed reaction mechanism for the synthesis of 4-phenylquinazoline via peroxide-mediated direct oxidative amination of C(sp^3)-H bonds

Following the suitable condition of the basic reaction, a series of reactions of different starting materials to produce corresponding 4-phenylquinazolines were investigated. Whereby, 27 products were obtained in yields ranging from 52 to 96%.

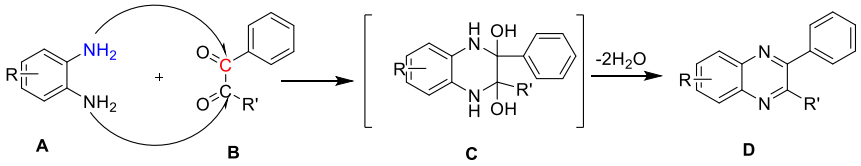


Scheme 3.2 Synthesis of 4-phenylquinazolines.

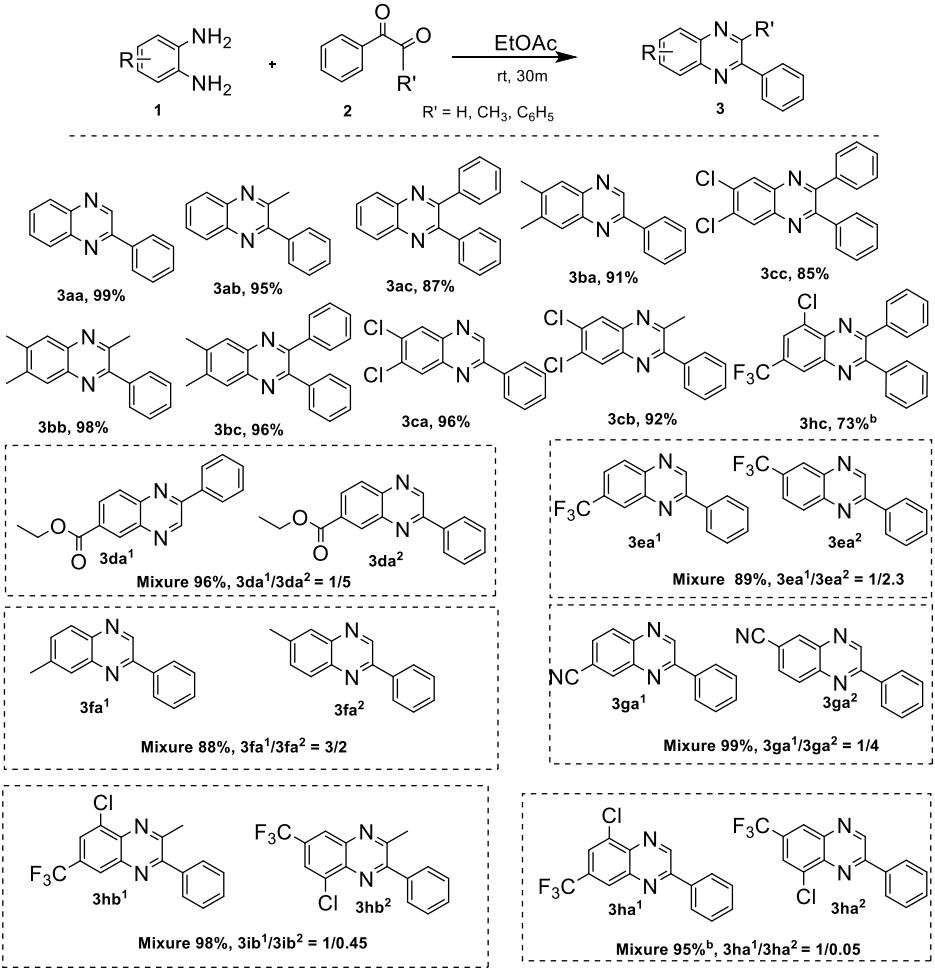
3.2 Condensation of 1,2-phenylenediamines and dicarbonyl compounds in ethyl acetate toward quinoxalines

Screening reaction conditions of condensation of 1,2-phenylenediamine and phenylglyoxal toward 2-phenylquinoxaline, the appropriate conditions were obtained that *o*-phenylenediamine (0.1 mmol), phenylglyoxal (0.11 mmol), 1.5 mL EtOAc, room temperature, under air, 30 minutes. A possible reaction pathway is proposed in Scheme 3.3.

Under the relevant conditions, the scope of the reaction was subsequently extended to the synthesis of many 2-arylquinoxalines. As result, 16 substitutes of 2-arylquinoxaline were obtained in yields ranging from 73 to 99% (Scheme 3.4).



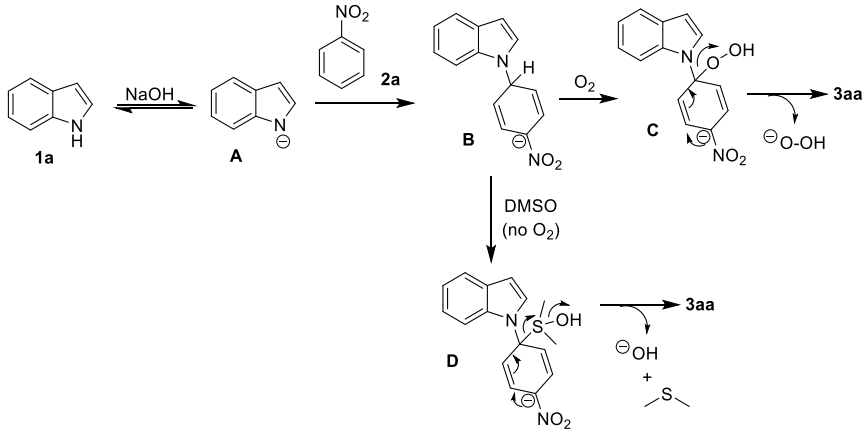
Scheme 3.3 Proposed reaction mechanism for the synthesis of 2-phenylquinoxalines



Scheme 3.4 Synthesis of 2-phenylquinoxalines

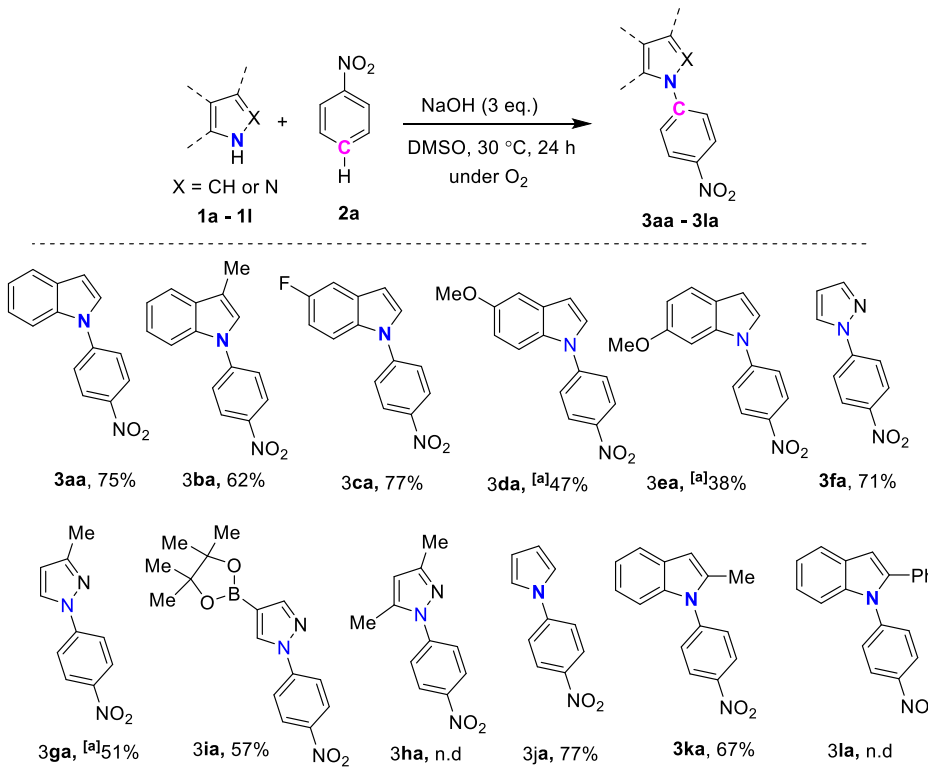
3.3 Oxidative nucleophilic functionalization of nitrobenzene with N-H bond to the synthesis of 1-(4-nitrophenyl)-1*H*-indoles

Screening reaction conditions of synthesis of 1-(4-nitrophenyl)-1H-indole, the consistent conditions were improved that indole (1 mmol), nitrobenzene (4 mmol), NaOH (3 mmol), DMSO (3.3 mL), under O_2, 30 °C, 24 h. Based on the previous report, a possible mechanism has been proposed (Scheme 3.5).



Scheme 3.5 Possible mechanism for oxidative amination of nitrobenzene with *N*-heterocycles

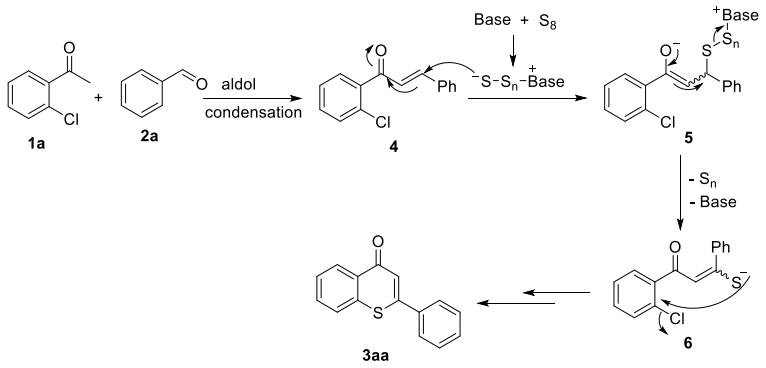
Encouraged by the results achieved above, the scope of the reaction was further examined with the derivatives of indole and nitrobenzene to obtain more valuable N-heterocycles. Whereby, 10 N-heterocycle products were obtained in yields ranging from in 38 to 77% (Scheme 3.6).



Scheme 3.6 Synthesis of *N*-arylindole derivatives

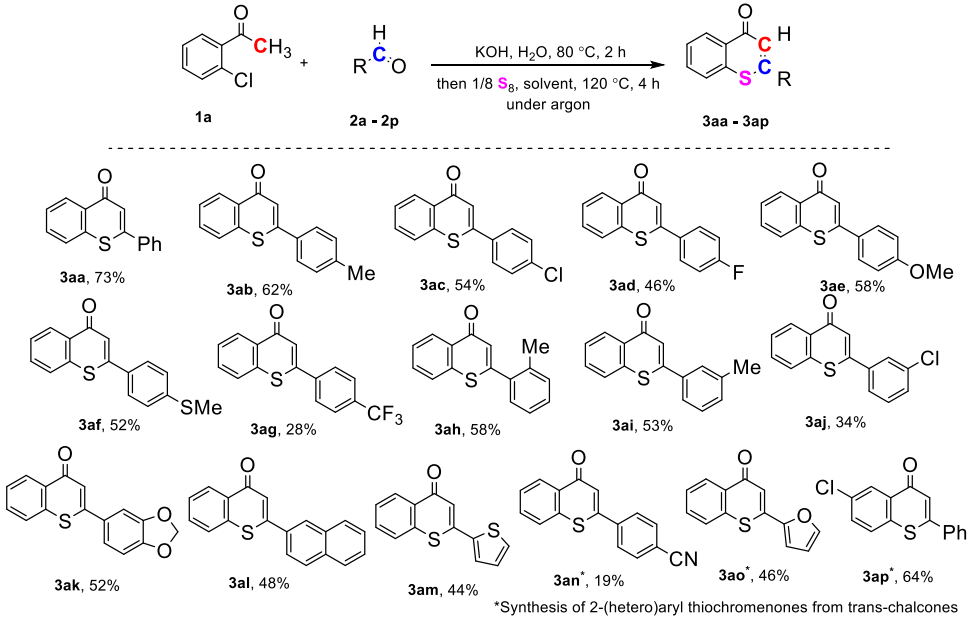
3.4 Elemental sulfur for the synthesis of 2-arylthiochromenones

The main reaction was carried out under relevant conditions in a two-step one-pot fashion. For the first step, a mixture consisting of 0.1 mmol of 2-chloroacetophenone, 2 equivalents of benzaldehyde, 2 equivalents of KOH, and 0.1 mL of water was heated at 80 °C for 2 hours under an argon atmosphere. For the second step, the resulting mixture from step 1 was added to 2 equivalents of elemental sulfur and 0.5 mL of DMF, then heated at 120 °C for 4 hours under an argon atmosphere. Based on previous reports, a possible mechanism was proposed as that shown in Scheme 3.7.



Scheme 3.7 Plausible mechanism for synthesis of 2-arylthiocromenone

Following the appropriate conditions outlined, the scope of the substrates was next investigated. The outcomes are presented in Scheme 3.8. In total, 16 substitutes of thiocromenone were obtained in yields ranging from 19 to 73%.



Scheme 3.8 Synthesis of thiocromenone derivatives

CONCLUSIONS

This thesis has successfully developed the synthesis of 4-substituted quinazoline derivatives via direct oxidative amination of C(sp^3)-H bonds. The transformation proceeded readily in the presence of an organic peroxide without any added catalyst. The nature of the oxidant significantly affected the reaction, in which tert-butyl hydroperoxide in decane emerged as the peroxide of choice. Several nitrogen sources were explored, and ammonium acetate exhibited the best performance. A plausible reaction mechanism was proposed, in which acetic acid originating from ammonium acetate was essential for the formation of the 4-substituted quinazoline product. A variety of sp^3 carbon sources could be utilized for the reaction, including *N*,*N*-dimethylaniline, *N*-methylaniline, *N*,*N*-dimethylacetamide, *N*,*N*-dimethylformamide, *N*-methyl-2-pyrrolidone, dimethyl sulfoxide, and *N*,*N*-dimethyl-1-phenylmethanamine. Several 4-substituted quinazoline derivatives were synthesized via this approach in good yields. The fact that 4-substituted quinazolines derivatives were achieved via peroxide-mediated direct oxidative amination of C(sp^3)-H bonds without any added catalyst would offer a complementary synthetic pathway to previous protocols.

For the synthesis of 2-phenylquinoxalines, this thesis has reported a new pathway, in which 2-phenylquinoxalines were obtained via the condensations between o-phenylenediamines and phenylglyoxals in ethyl acetate without any added catalyst. The relevant conditions of reaction were exposed and a possible mechanism has been composed. A wide range of substituents could be utilized for the reaction. All quinoxaline derivatives were synthesized via this pathway in good and excellent yields. The significant points of this protocol are (1) metal-free, (2) green solvent, (3) short duration, (4) in room temperature, (5) excellent yields, and (6) wide range of applications. With these advantages, the procedure of synthesizing 2-phenylquinoxaline derivatives of the thesis will be applied in the field of organic synthesis and pharmaceuticals.

The third success in this thesis is the successful synthesis of N-arylindole derivatives. This study took advantage of nitroarene's oxidizing-substituent nucleophilic ability on the hydrogen atom to pair with a nitrogen atom containing an N-H bond without using a transition metal catalyst. Simple base NaOH and DMSO solvents were combined to mediate the amination of para C−H bond in nitrobenzene with N−H heterocycles. In addition, a plausible mechanism was also proposed. The substrate's scope included indoles, pyrazoles, and pyrroles had been investigated. By the transition metal-free; room temperature, and simple base conditions, this strategy promises to tackle the previously mentioned disadvantages and become an efficient methodology in chemical fields.

The fourth point of the thesis is the successful development of a two-step one-pot procedure using elemental sulfur directly to synthesize thiocromenone derivatives. Whereby 2-arylthiocromenone derivatives were formed through the sulfurization of the 2'-chlorochalcones that were produced in the previous step between 2'-chloroacetophenones and aromatic aldehydes. A possible mechanism has been also offered and a large range of substrates have been investigated. The significances of this protocol are (1) direct use of elemental sulfur; (2) transition metal-free; (3) simple base, and (4) tolerance of many functionalities. Based on these advantages, this protocol would be mentioned in organic synthesis.

In summary, 5- and 6-membered heterocyclic compounds have very important roles in the fields of biology, chemistry, and biomedicine. In addition to being extracted from nature, heterocyclic compounds have become very attractive in organic synthesis. Previous reports normally required a transtition metal catalyst to obtain heterocyclic compounds. This thesis was successful in developing green pathways for the synthesis and functionalization of 5-, 6-membered heterocyclic compounds containing quinoxaline, quinazoline, N-indole, thiocromenone frameworks from common and abundant materials. All these protocols were taken place under simple conditions and especially without any added transition metal catalysts. These methodologies would be complementary to previous

synthetic protocols and would be of interest to the pharmaceutical and chemical industries.

Suggestions for future work

Continuing to study improving the reaction efficiency by using green solvents to replace toxic solvents such as *N*,*N*-dimethylaniline, *N*-methylaniline…in the synthesis of 4-phenylquinoxalines. Modeling the procedure of the synthesis of 2-phenylquinazolines so that these derivatives could be obtained continuously. Continues to improve performance and minimize co-products in the synthesis of N-arylindoles and 2-arylthiocromenones. From the obtained products 4-phenylquinoxalines, 2-phenylquinazolines, N-arylindoles, and 2-arylthiocromenones, continue to study their biological activities and take these derivatives as starting reagents to synthesize further compounds.

LIST OF PUBLICATIONS

1. Tan N. Huynh, Tien V. Huynh, Thuy T Ca, Dat T. Tran, Hai H. Pham, Tung T. Nguyen, and Nam T. S. Phan, *Annulation of 2'-chlorochalcones and Elemental Sulfur toward the Synthesis of 2-Aryl Thiochromenones*, ChemistrySelect, 2022, 7, e202201732, 1-3

2. Duy T. M. Chung, Phuc Q. Le, Huy X. Le, Tien V. Huynh, Anh N. Q. Phan, Tung T. Nguyen, and Nam T. S. Phan, *Oxidative Nucleophilic Functionalization of Nitrobenzene and 3-Nitroacetophenones with N -H bonds*, ChemistrySelect 2021, 6, 8971 –8973

3. Tien V. Huynh, Son H. Doan, Khang H. Trinh, Trang H. Ly, Anh L. T. Phan, Tung T. Nguyen, Anh N. Q. Phan* and Nam T. S. Phan*, *Metal-Free One-Pot Three-Component Synthesis of Quinazoline Derivatives via Peroxide-Mediated Direct Oxidative Amination of C(sp3)–H Bonds*, ChemistrySelect 2019, 4, 11808–11814