약학박사학위논문

Direct Synthesis of *N*-heterocyclic compounds *via* Iron-catalyzed Oxidative Coupling from Alcohol and Methyl Arene

알코올과 메틸아렌으로부터 철-촉매하에 산화 결합을 통한 *N*-헤테로고리 화합물의 직접적인 합성

2023년 8월

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이 석 범의 약학박사 학위논문을 인준함

2023년 8월

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Abstract

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Heterocyclic compounds containing nitrogen are known to have various biological activities and widely found in natural products. Among commercially available small-molecular drugs, the *N*-heterocyclic structure is used as a core scaffold. Due to these characteristics, the study of *N*-heterocyclic compounds is important both in medicinal chemistry and in organic synthesis. Recently, transition metals have been widely applied in the synthetic methods of *N*-heterocyclic compounds. Among transition metals, iron catalysts are inexpensive, eco-friendly, less toxic, and abundant on Earth. These iron catalysts and oxidants are used to oxidize low oxidation level substrates such as alcohols and methyl arenes to aldehydes. The formed aldehydes can be then applied to the synthesis of *N*-heterocyclic compounds.

Generally, *N*-heterocyclic compounds are synthesized through condensation reactions using nucleophiles containing nitrogen and electrophile such as aldehydes. However, the aldehyde is unstable and difficult to obtain diverse structures from commercial source, so it is restricted to expanding substrate scope. In our lab, to improve previously synthetic methods, a synthesis of *N*-heterocyclic compounds has been studied through an oxidative cyclization using iron catalyst and oxidants, from low-oxidation level substrates such as alcohols and methyl arenes. When iron catalysts were used with oxidants, the oxidation process from alcohols and methyl arenes to aldehydes can occur readily in the reaction. The generated aldehyde intermediates could be reacted with 2-aminophenyl ketones or 2-

amino styrenes to complete the synthesis of 4-quinolones and quinolines, respectively, through an oxidative cyclization. This developed synthetic method was applicable to the substrates with various types of functional groups, and a total of 47 types of 4-quinolone derivatives and a total of 58 types of quinoline derivatives were synthesized.

Keyword: *N*-heterocyclic compounds, iron catalysts, oxidants, oxidative cyclization, 4-quinolones, quinolines

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INTRODUCTIONS

1. *N*-Heterocyclic compounds

1.1. Outline of *N*-heterocyclic compounds

N-Heterocycles, heterocyclic compounds containing nitrogen, are widely found in various biological active compounds and natural products. In particular, almost 60% of small-molecule drugs approved by the Food and Drug Administration (FDA) contain *N*-heterocyclic moieties, which occupy a large proportion of components used in medicinal chemistry.[1]

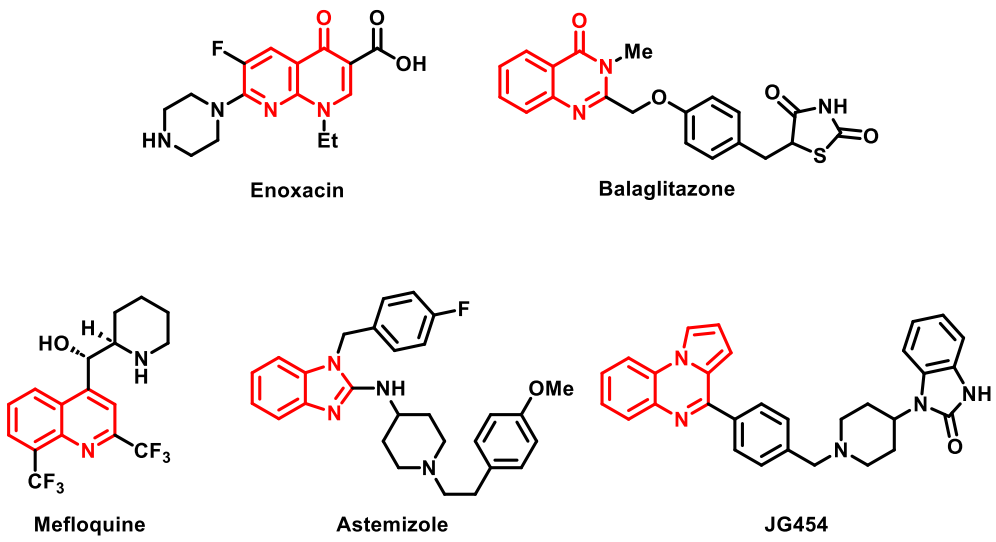


Figure 1. Structure of small-molecule drugs contained *N*-Heterocyclic compounds

Among approved small-molecule drugs, Imatinib is a first-line therapy used to treat Chronic Myelogenous Leukemia (CML) by inhibiting Breakpoint cluster region-Abelson murine Leukemia (Bcr-Abl). Imatinib contains *N*-heterocyclic moieties such as pyridine, pyrimidine, and piperazine, which can bind strongly to amino acids of Bcr-Abl through hydrogen bonds and electrostatic interactions; these binding forces support the idea that the growth and proliferation of CML cells are suppressed by blocking active sites (Figure 2).[2] Because *N*-heterocyclic compounds can control biological activity through various interactions with target proteins, the study of *N*-heterocyclic compounds is encouraged in medicinal chemistry and organic synthesis.

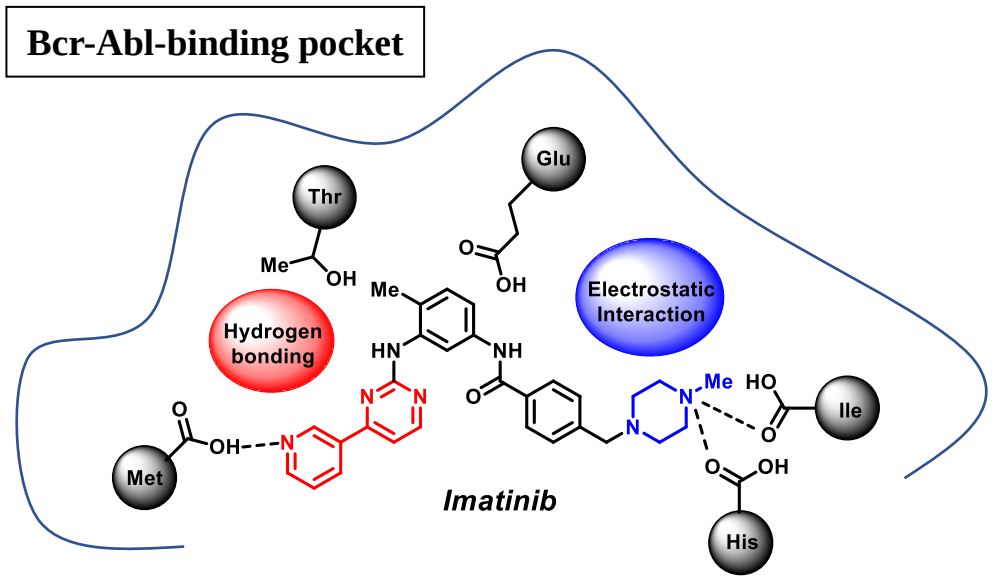


Figure 2. Various interactions between Bcr-Abl and Imatinib

1.2. 4-Quinolones

1.2.1. Diverse characteristics of 4-quinlones

Among *N*-heterocyclic compounds, the structures of 4-quinolones confer various biological and pharmaceutical activities.[3] Indeed, may antibiotics contain 4-quinolones as a privileged scaffold due to their significant antibacterial activity.[4] Additionally, 2-aryl-4-quinolones, aza analogues of flavones, possess potent anticancer effects by inhibiting tubulin polymerization.[5] More recently, certain 2-aryl-4-quinolones and their derivatives have been reported to show potent antiviral,[6] antimalarial,[7] and anti-inflammatory[8] activities, as well as effects on cathepsin inhibition[9] and xanthine oxidase[10] (Figure 3)

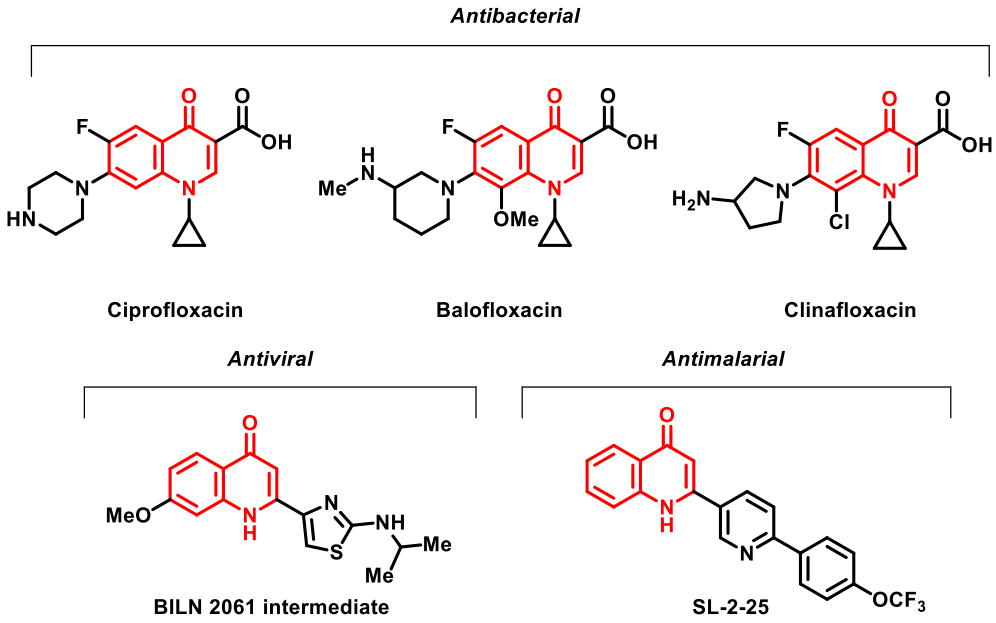


Figure 3. Diverse biological active 4-quinolone derivatives.

4-Quinolone derivatives have been also used as important synthetic building blocks for various biologically active quinolones and quinoline compounds because of the facile functionalization of their reactive centers at positions 1, 3, and 4.[11] The positions 1 and 4 of quinoline can be selectively functionalized with alkyl halide dependent on bases. Additionally, 4-quinolones can be easily converted to quinolines through halogen reagent, and further transformation is possible using the halogenated position (Figure 4).

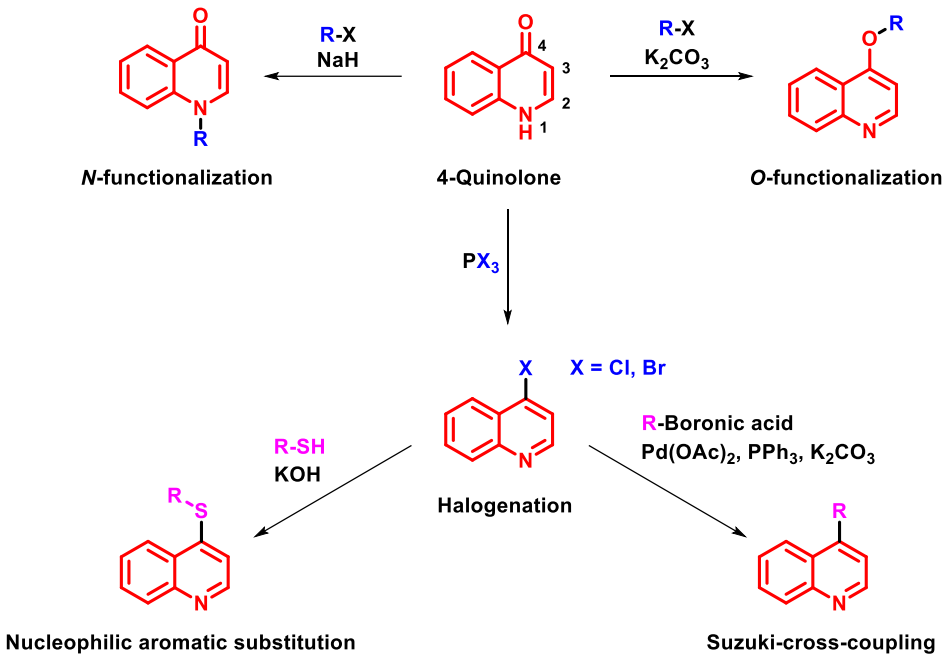
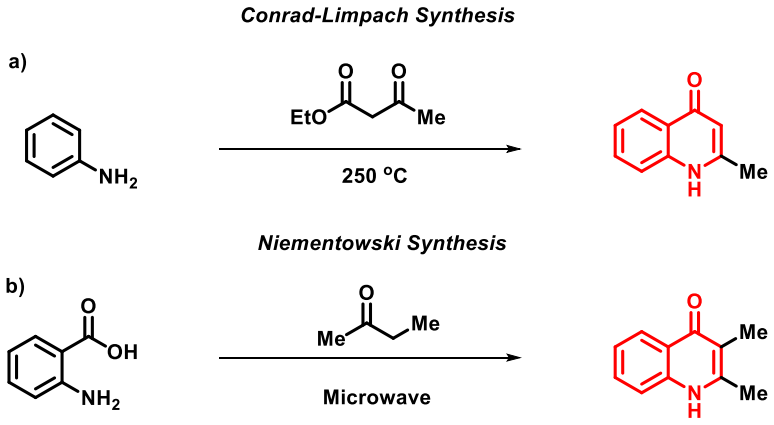


Figure 4. Chemical functionalization using 4-quinolones

1.2.2. Classical synthesis of 4-quinolines

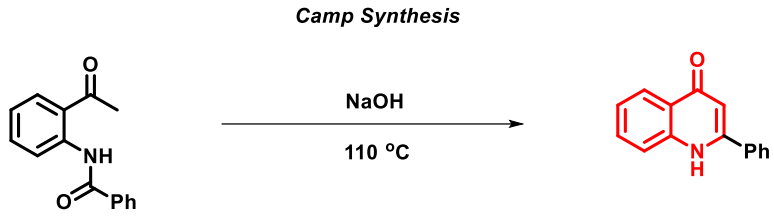
Classical synthesis of 4-quinolones has been reported on the intermolecular cyclocondensation, known as Conrad-Limpach and Niementowski reactions.[12] The Conrad-Limpach reaction proceeds imine condensation of aniline with di-carbonyl substrate, following which, the 4-quinolone structure is formed through Friedel–Crafts type cyclization (Scheme 1a). The Niementowski reaction provides 4-quinolones through imine condensation, which is followed by cyclization using anthranilic acids and ketone substrates. (Scheme 1b). However, these classical methods have the disadvantage of limited substrate range owing to the harsh conditions.



Scheme 1. Classical synthesis of 4-quinolones through intermolecular reactions

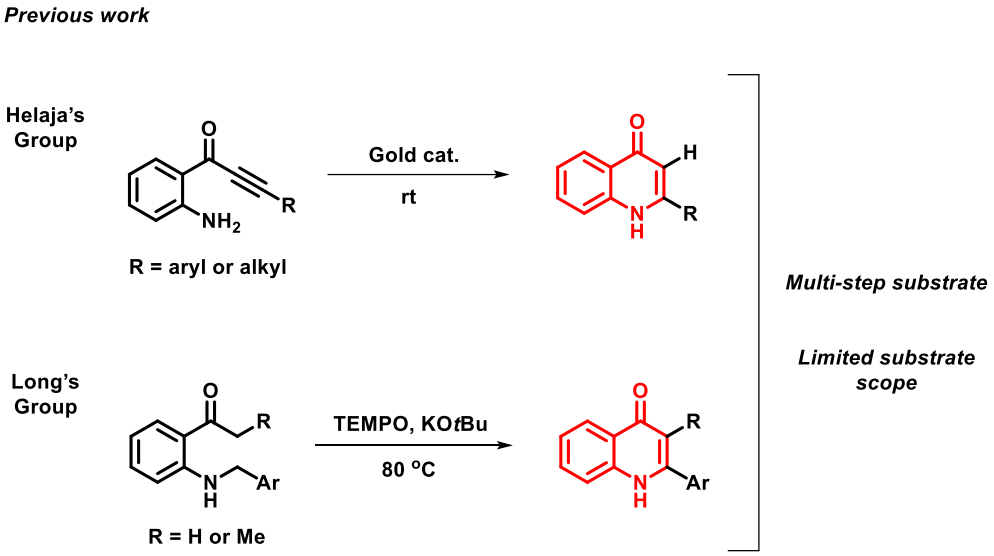
Another classical method is the intramolecular cyclization reaction of *N*-(*o*-ketoaryl) amide, known as Camps cyclization.[13] For this reaction, *N*-acetylated 2-amino acetophenones should be prepared in advance, following which, 4-quinolones are formed through additional intramolecular cyclization using strong bases. Although Camps

cyclization is widely used as the representative synthetic method for 4-quinolones, there are limitations on the substrate scope because a multi-step substrate preparation process and basic conditions are required (Scheme 2).



Scheme 2. Classical synthesis of 4-quinolones through intramolecular reactions

1.2.3. Intramolecular synthesis of 4-quinolones



Scheme 3. Previous intramolecular synthesis of 4-quinolones

In addition to these classical methods, some advanced methods have been developed under mild conditions (Scheme 3). Indeed, Helaja's group designed a method to synthesize 4-quinolones *via* gold-catalyzed intramolecular cyclization using *o*-aminoaryl acetylenic ketones.[14] In the substrate, an acetylene group was introduced at the α-position of the ketone, and the reaction was conducted at room temperature using a cationic gold catalyst. In 2015, Long's group reported a method to synthesize 2-aryl-4-quinolones through the oxidative Mannich reaction.[15] In this method, *N*-benzylated starting materials were oxidized to form imine intermediates, with TEMPO used as an oxidant, before KO*t*Bu such as base activated α-position of carbonyl group to proceed intramolecular cyclization. The intramolecular reactions mentioned above are improved methods to synthesize 4-quinolones, as well as requiring milder conditions compared to those used in the classical methods. However, multiple steps are still required to prepare specific substrates, so there is limited to the extension of the substrate scopes.

1.3. Quinolines

1.3.1. Diverse characteristics of quinolines

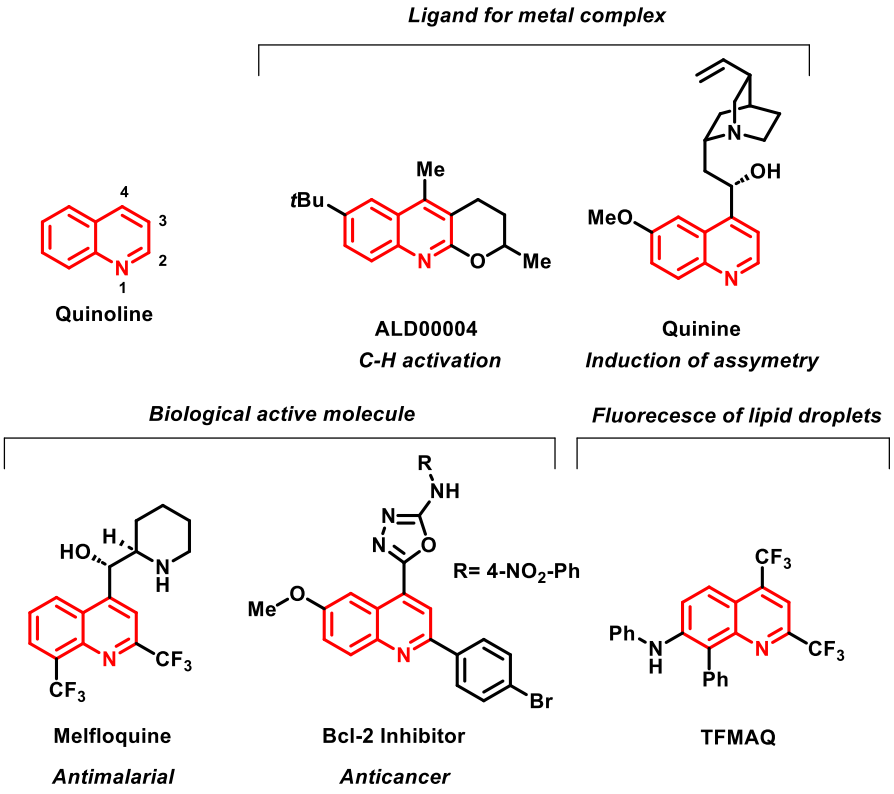
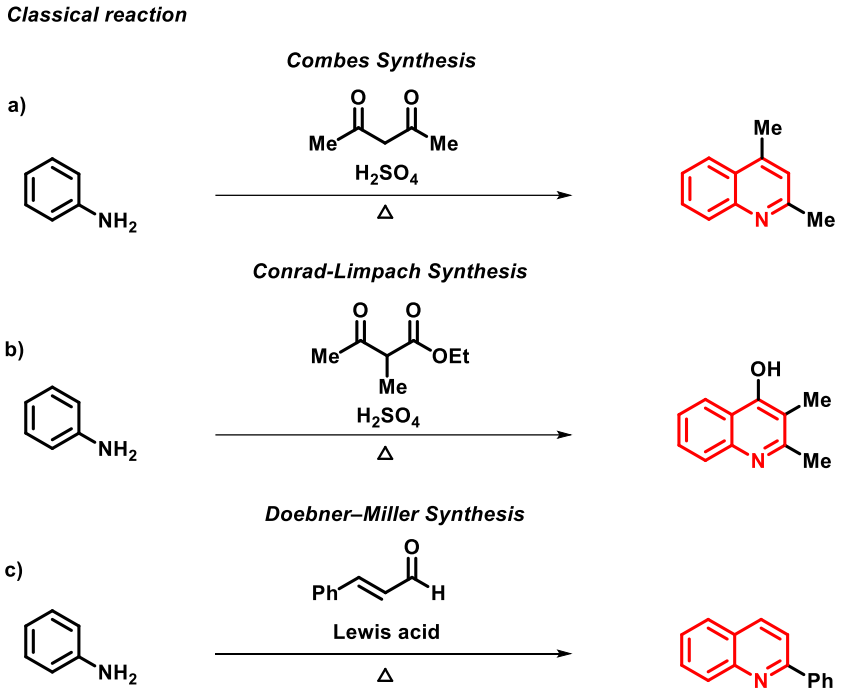


Figure 5. Representative quinoline derivatives

Quinolines are important scaffolds used in various fields (Figure 5). The quinoline scaffold is not only found in various biologically active compounds, but also in activating ligands by forming metal complexes. Quinoline derivatives have also been reported to exhibit physiological activities.[16] In particular, 2-substituted quinolines have various

pharmaceutical activities, including antibacterial,[17] antimalarial,[18] and antiviral activities.[19] Additionally, 2-substituted quinolines have also shown potential as anticancer agents due to their Bcl-2 target inhibitory ability.[20] In addition to their various biological activities, aryl-substituted quinolines exhibit excellent fluorescence intensity considering the diversity of their photochemical abilities.[21]

1.3.2 Classical synthetic methods of quinolines

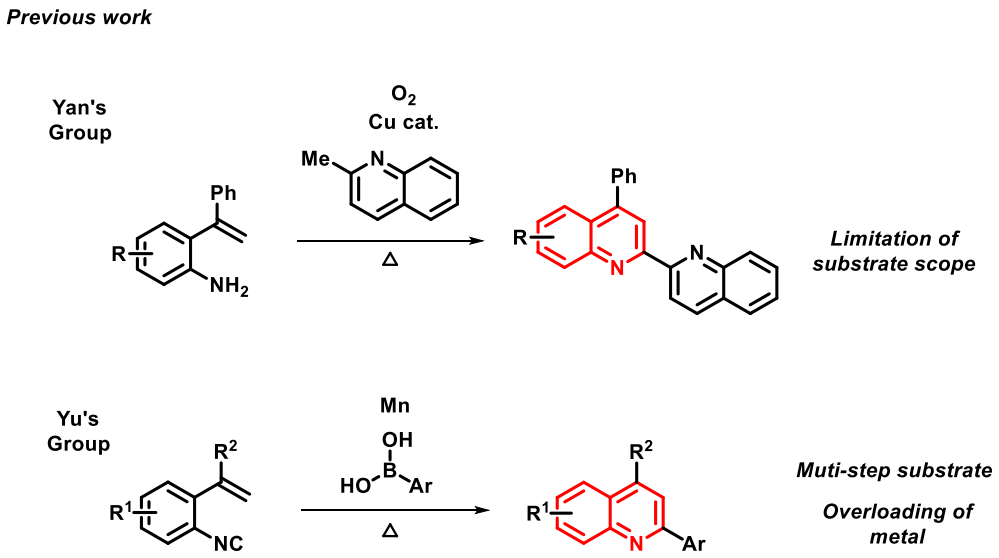


Scheme 4. Classical synthesis of quinolines

The representative named reactions for quinolines include the Combes, Conrad-Limpach, Doebner-Miller, Friedländer, and Skraup reactions (Scheme 4).[22] Quinolines

can also be synthesized using multicomponent reactions including anilines and substrates containing carbonyl groups. However, these reactions usually only proceed with strong acids at high temperatures, which represents a limitation of the direct use of carbonyl substrates, high-oxidation level substrates, to initiate an intermolecular reaction through imine formation.

1.3.3 Previous synthesis of quinolines using styrene substrates



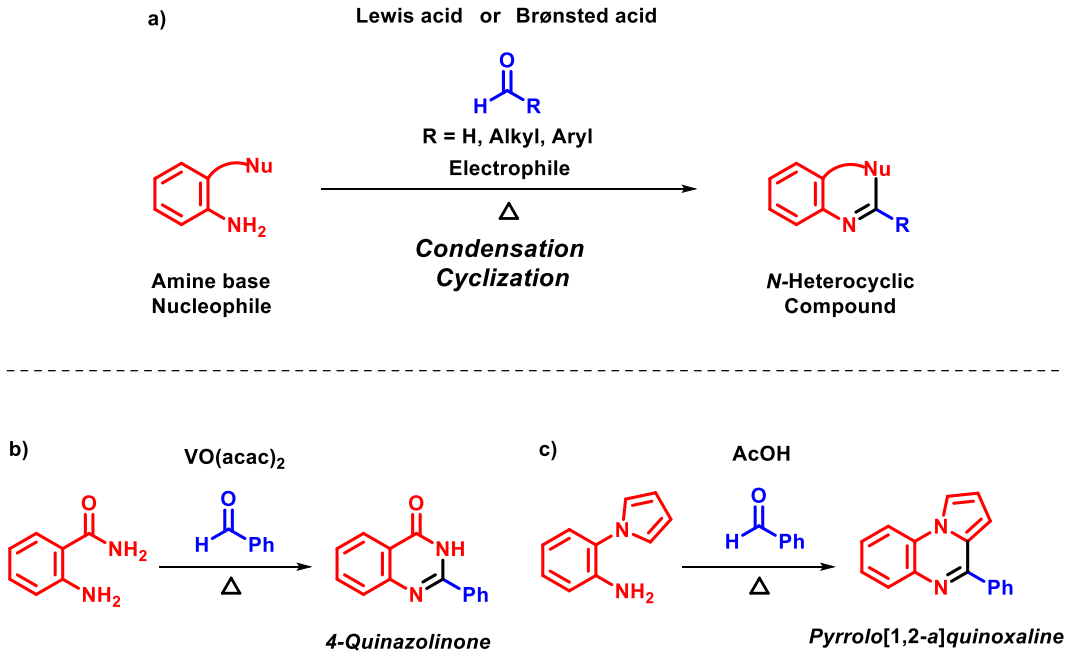
Scheme 5. Previous synthesis of quinolines using styrene substrates

Recently, synthetic methods of quinolines have been developed using styrene-type starting materials through electrocyclization (Scheme 5). Yan's group synthesized 4-phenyl-2,2′-biquinoline using 2-amino styrenes and 2-methylquinolines through oxidative tandem cyclization in the presence of a copper catalysts.[23] Despite this being a good example of low-oxidation level substrate methyl arenes, the substrate range was strictly

limited in 2-methylquinolines. Subsequently, Yu's group reported manganese-mediated radical cyclization using 2-isonitrile styrenes for the synthesis of 2,4-disubstituted quinolines.[24] However, this reaction required an excessive amount of metal, and isonitrile functionality should be installed on the starting materials in advance.

1.4. Synthesis of *N*-heterocyclic compounds

1.4.1 General synthetic approaches for *N*-heterocyclic compounds



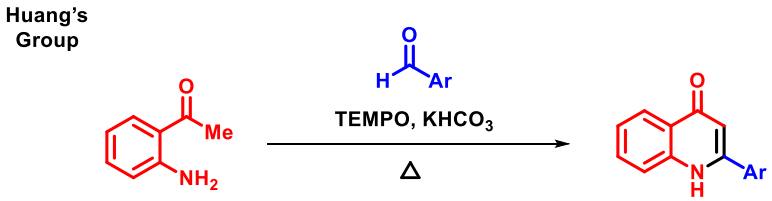
Scheme 6. Presentative synthesis of *N*-heterocyclic compounds using aldehydes

A simple synthetic approach for *N*-heterocyclic compound can be designed with direct intermolecular cyclization between aniline-type nucleophiles possessing 2nd nucleophilic

groups and carbonyl-based electrophiles such as aldehydes. Many *N*-heterocycles have been synthesized following these approaches, in the presence of Lewis acid or Brønsted acid (Scheme 6a). Indeed, 4-quinazolinones have been synthesized by using anthranilamides and aldehydes under Lewis acid (Scheme 6b).[25] Another study reported the synthesis of pyrrolo[1,2-a]quinoxalines following the additional introduction of pyrroles in aniline nucleophiles (Scheme 6c).[26] However, the electrophile substrate scope in these reactions is slightly limited by the need to use aldehyde oxidation level materials.

1.4.2 Recently reported synthesis of 4-quinolones & quinolines

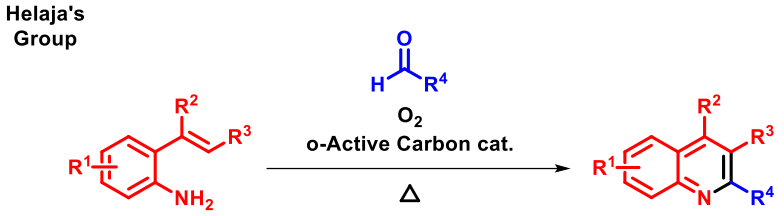
In 2017, Huang's group reported an oxidative cyclization for 2-aryl-4-quinolones from 2-amino-acetophenones and benzaldehydes.[27] This method proceeded through intermolecular cyclization using $KHCO_3$ as a weak base and TEMPO as an oxidant. However, only acetophenone derivatives are applied as starting materials, and aldehyde oxidation level starting materials still limit the substrate scope (Scheme 7).



Scheme 7. Synthesis of 4-quinolones using aldehydes

In 2021, Helaja's group designed a domino reaction protocol to approach poly-substituted quinolines from 2-amino styrenes.[28] Although the reaction was metal-free and

showed various styrene scopes, the catalyst requires to be prepared in advance and still requires aldehyde oxidation level starting materials (Scheme 8).



Scheme 8. Synthesis of quinolines using aldehydes

2. Chemical reaction *via* single electron transfer (SET) for diverse bond formations

Single electron transfer (SET) event is found in the formation of free radical species, highly unstable intermediates that contain an unpaired electron. Free radicals are often formed from homolytic cleavage, a process in which the two electrons in a breaking covalent bond. As shown Figure 6a, the chlorine radicals are generated by homolytic cleavage, when chlorine molecule is subjected to heat or light. The formed chlorine radical can be applied to new reactions through radical type addition and hydrogen atom abstract (Figure 6b).[29]

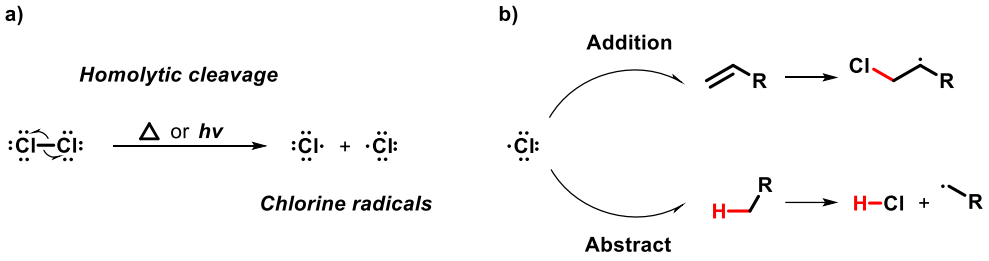


Figure 6. Formation of radical species and radical reactions

2.1. Metal-mediated SET reactions

In recent decades, metal-catalyzed radical reactions have been developed and supported the synthesis of target compounds in various fields.[30] Radical chemistry is considered a potential tool in organic synthesis by forming new bonds through sequential

bond formation or bond rupture. In particular, the generation of carbon-centered radicals is regarded as an important step to form a new bond. As shown in Figure 7, various metals can be applied to generate a carbon-centered radical by inducing electron transfer.

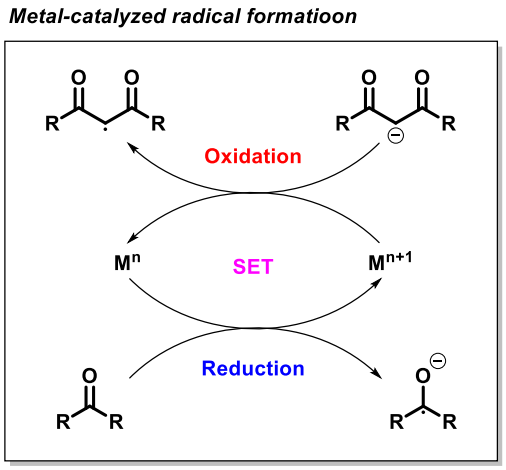
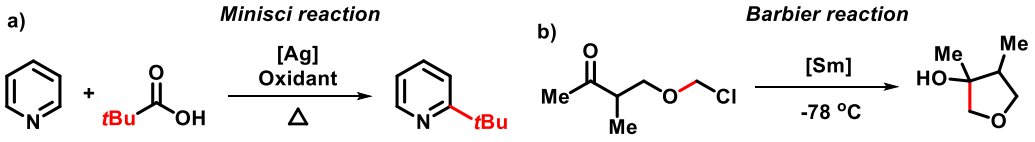


Figure 7. Metal-mediated carbon radical formations

Methods for introducing new C−C bonds have been developed based on the above concept. The Minisci reaction employs a decarboxylation radical process using Ag catalysts and oxidants to form new C−C bonds (Scheme 9a).[31] The Barbier reaction forms new alcohol products by the reaction of the carbonyl groups with the alkyl halides in the presence of SmI_2, which proceeds similarly to the Grignard reaction (Scheme 9b).[32]



Scheme 9. Metal-catalyzed bond formations *via* carbon radicals

2.2. Metal-catalyzed Cross-Dehydrogenative Coupling reactions (CDC)

Many synthetic tools have been developed to introduce C−C bonds. Among them, CDC is the synthetic method of forming a new bond by activating different C−H bonds under oxidative conditions.[33] The CDC reaction can connect various C−H bonds without pre-functionalization in the presence of 1st row base metal catalysts with oxidants (Figure 8). Additionally, the reaction is economical given its use of inexpensive catalysts and the formation of environmentally friendly by-products.

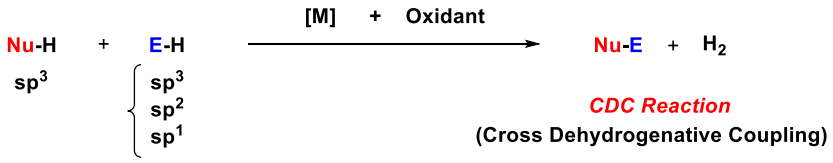
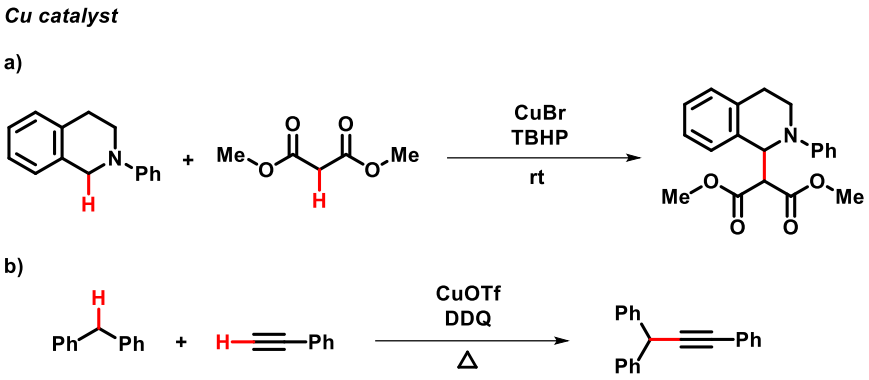


Figure 8. New bond formations through CDC reactions

2.2.1 Presentative CDC reactions using Cu catalysts

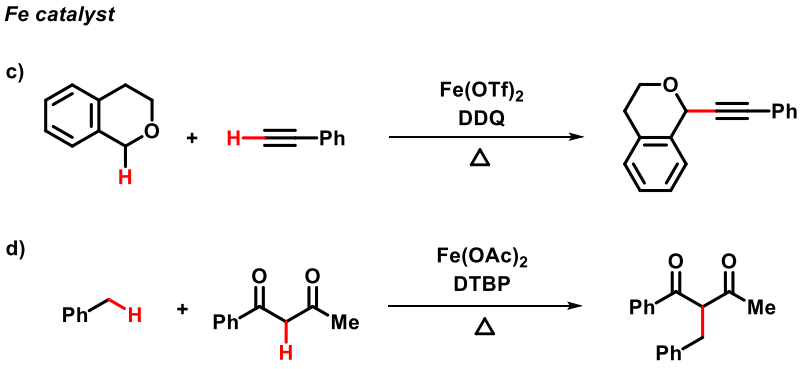
In 2005, Li's and coworkers reported a reaction that activated the C−H bond of malonate to form new bonds with other sp^3 C−H bonds. In general, malonate forms a new bond through a nucleophilic addition using a base and electrophiles, but the developed method formed C−C bond through a CDC reaction using copper catalysts and oxidants (Scheme 10a).[34] The benzylic position smoothly produced carbon radicals by Cu and oxidants, which were then coupled with sequentially-activated malonate to form the product. In 2010, the same group developed a synthetic method that applied CDC

reactions to other substrates. The benzylic position is smoothly activated by Cu and oxidants, and then connected to terminal alkynes containing sp C−H Bonds (Scheme 10b).[35]



Scheme 10. C−C bonds formations *via* Cu-catalyzed CDC reactions

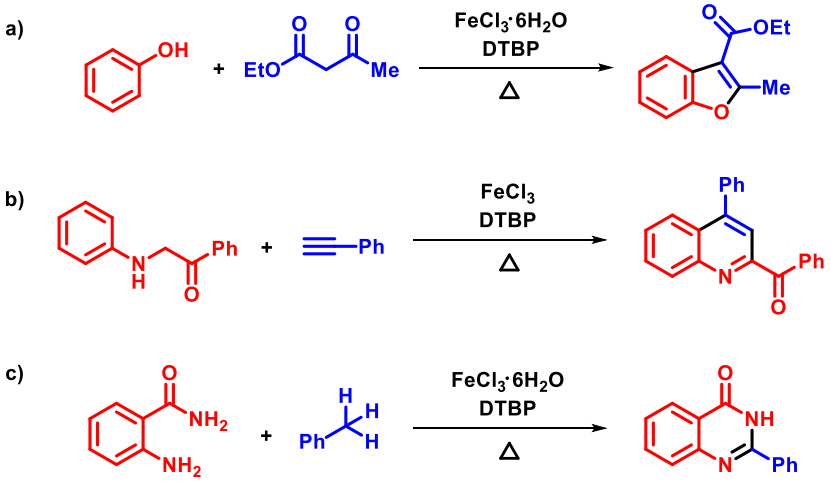
2.2.2 Presentative CDC reactions using Fe catalysts



Scheme 11. C−C bonds formations *via* Fe-catalyzed CDC reactions

In 2011, Jiao's and coworkers showed the formation of new C−C bonds using benzylic ethers and terminal alkynes. The benzylic ethers can easily form carbon radical and react with the activated acetylene substrates. This reaction is high efficiency and atom economy because sp-sp^3 C–C bonds are directly formed without pre-functionalization using cheap iron catalysts and oxidants (Scheme 11a).[36] In 2012, Li's and coworkers developed C–C bonds formation by oxidative activation of benzylic C–H bonds. Toluene is usually difficult to be applied as a reaction substrate because of their low reactivity. However, toluene can be activated through iron catalysts and di-*tert*-butyl peroxide (DTBP) in the reaction and couple with malonates to form new C–C bonds (Scheme 11b).[37]

2.2.3 Synthesis of heterocyclic compounds *via* CDC reactions



Scheme 12. Diverse synthesis of heterocyclic compounds through CDC reactions

CDC reactions have recently been applied to synthesize various heterocyclic compounds. Li's group reported the synthesis of benzofuran scaffold *via* iron-catalyzed Pechmann condensation. After selective oxidative coupling of sp^2 C−H bonds and sp^3 C−H bonds, the synthesis of benzofurans was completed through an intramolecular condensation reaction (Scheme 12a).[38] Hu's group proceeded with the construction of a quinoline structure using glycine derivatives and various alkynes. Glycine derivatives were converted to imine through DTBP and iron catalysts, and then quinoline products are formed through sequential C−C bond formation and cyclization (Scheme 12b).[39] Finally, our group developed an iron-catalyzed synthesis method of 4-quinazolinones through anthranilamides and unreactive methyl arenes. The inactive methyl arenes were oxidized to benzaldehydes under the oxidative conditions, while the formed benzaldehyde intermediates reacted with anthranilamides to synthesize 4-quinazolinones (Scheme 12c).[40]

3. Our synthesis strategies for *N*-heterocyclic compounds

3.1. Employing low oxidation-level substrates as electrophiles

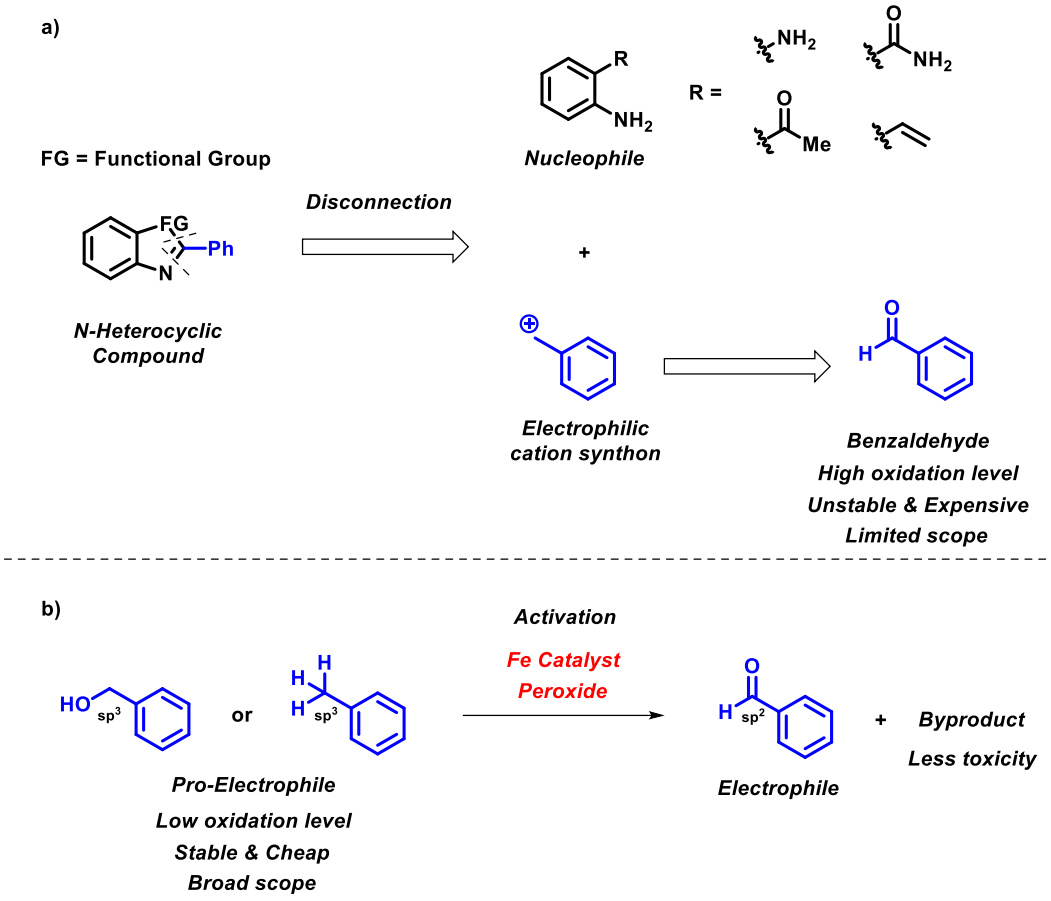


Figure 9. Our strategy to employ low-oxidation level substrates for *N*-heterocyclic compounds

If the *N*-heterocyclic compound is disconnected around the electrophilic carbon, it can be divided into nucleophilic and electrophilic cation synthons. We progressed the research focusing on electrophilic synthons. Aldehyde substrates, as reactive electrophiles, have been widely employed in the synthesis of *N*-heterocyclic compounds. However, in the case of aldehydes, the expansion of the substrate range is limited because it is unstable and difficult to obtain diverse structures from commercial sources (Figure 9a).

To overcome the substrate scope limitation of the previous synthetic methods, alcohols and methyl arenes, both of which are low-oxidation level substrates, were suggested as pro-electrophiles in new synthetic strategy for *N*-heterocyclic compounds. Compared to aldehydes, alcohols and methyl arenes are cheaper, more stable, and readily available from commercial sources. However, as alcohols and methyl arenes are stable enough to be used as solvents, an oxidative activation step is required during the reaction. We planned to employ iron catalysts and peroxides to induce the oxidation of alcohols and methyl arenes.[40-43] Iron, the most abundant transition metal, has low toxicity and is cheap. Given these advantages, iron catalysts will be useful for methodology. Peroxides generate less toxic by-products after the reaction, so there is less concern about environmental pollution. Therefore, the development of a synthetic method using iron catalysts and peroxides will be both economical and eco-friendly (Figure 9b).

3.2. Synthesis of *N*-heterocyclic compounds *via* iron-catalyzed oxidative couplings

Based on the above concept, a new synthetic strategy for *N*-heterocyclic compounds using iron catalysts and peroxides was proposed (Figure 10). First, the peroxides formed an oxygen radical by SET or homolytic cleavage. Alcohols and methyl arenes, which are used as pro-electrophiles, were activated by the generated oxygen radical. The generated oxygen radical activated the alcohols and methyl arenes, which are used as pro-electrophiles. The pro-electrophiles were generated by activating the carbon adjacent of the hydroxyl group or, benzylic carbon. The activated pro-electrophiles can be converted to aldehyde intermediates in situ through a further oxidation process. Then, nucleophiles containing nitrogen react with the electrophilic aldehyde intermediates to synthesize *N*-heterocyclic compounds through imine condensation, cyclization, and final oxidation. We designed appropriate amine-based nucleophiles to synthesize 4-quinolones and quinolines.

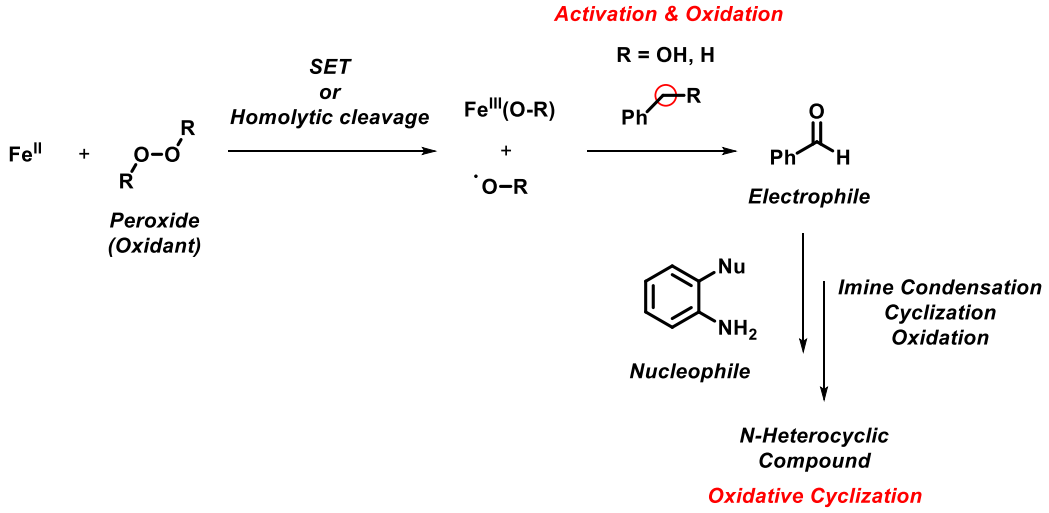
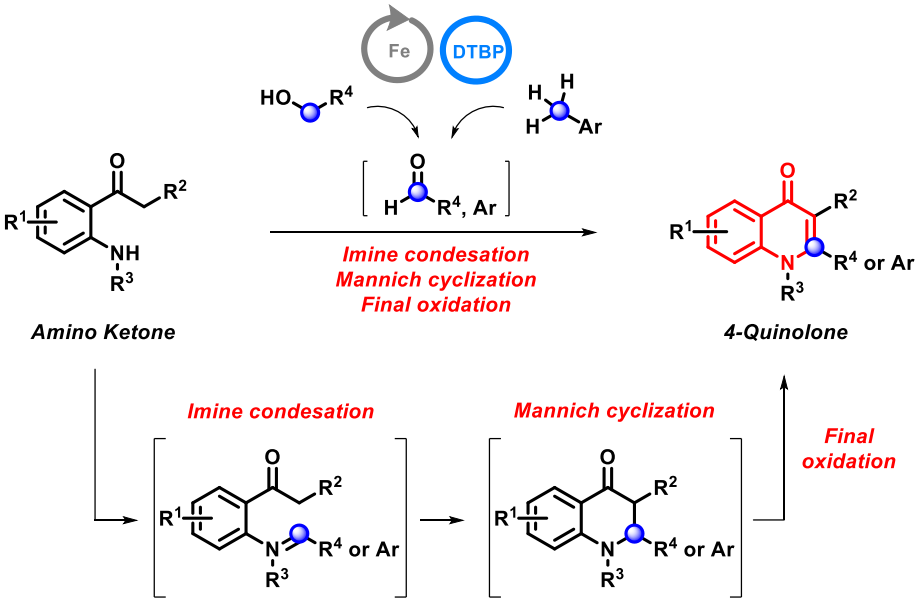


Figure 10. Synthesis of *N*-heterocyclic compounds *via* iron-catalyzed oxidative couplings

3.2.1 Synthesis of 4-quinolones *via* iron-catalyzed oxidative couplings

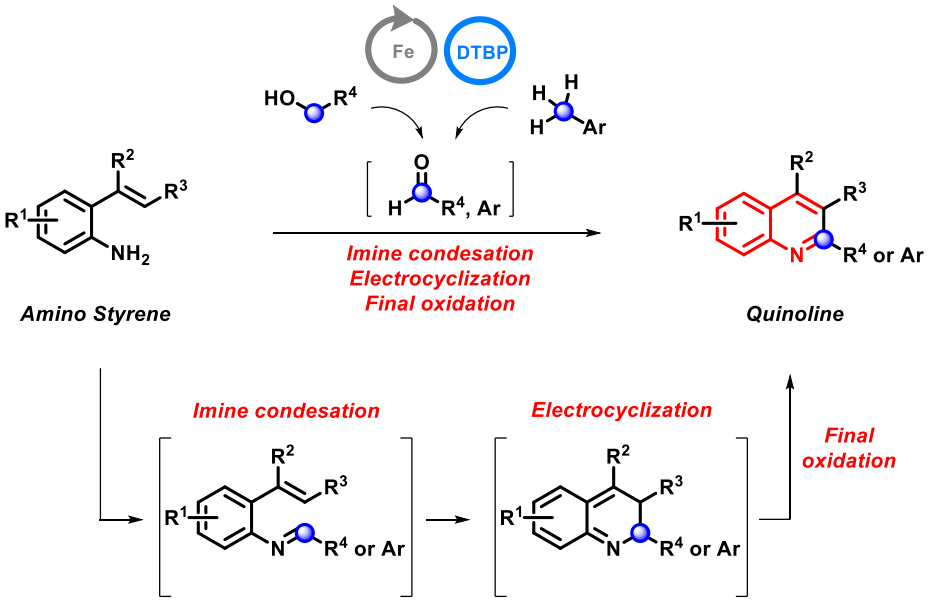
We designed a synthetic scheme of 4-quinolones using iron-catalyzed oxidative coupling as shown in Scheme 13. Ketone groups were introduced on the *o*-position of aniline as another nucleophilic group, and 2-aminophenyl ketone substrates were conceived as a nucleophile. Various substituents on 2-aminophenyl ketones could expand the nucleophilic substrate scope. The iron catalysts and DTBP oxidized alcohols and methyl arenas to form an electrophilic aldehyde intermediate during the reaction. Then the aldehyde intermediates reacted with 2-aminophenyl ketones to form 4-quinolones through imine condensation, Mannich-type cyclization and final oxidation. This method could propose the direct synthesis of 4-quinolones between low-oxidation level substrate and amine based nucleophiles through intermolecular reactions.[42]



Scheme 13. Design of synthesis 4-quinolones *via* iron-catalyzed oxidative couplings

3.2.2 Synthesis of quinolines *via* iron-catalyzed oxidative couplings

To develop a new synthetic route for quinolines, we designed 2-amino styrenes as a nucleophile, which has olefin on *o*-position of aniline (Scheme 14). As with the synthetic scheme of 4-quinolones shown above, alcohols and methyl arenes were employed as a pro-electrophile, and iron catalysts and DTBP were selected for oxidative activation of these low-oxidation level substrates. The generated aldehyde intermediates reacted with 2-amino styrenes to construct a quinoline structure through imine condensation, electrocyclization, and final oxidation.[43]



Scheme 14. Design of synthesis quinolines *via* iron-catalyzed oxidative couplings

RESULTS AND DISCUSSIONS

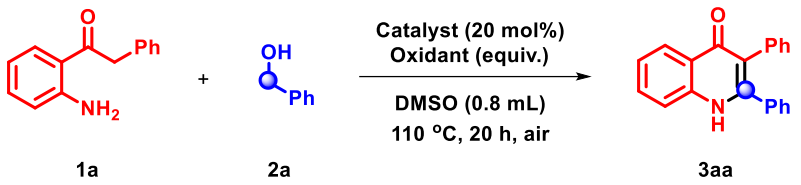
1. Synthesis of 4-quinolones

1.1. Optimization of reaction condition using alcohol substrates

The optimization process was based on our previous synthesis of 4-quinazolinones[40]. As shown in Table 1, we began by optimizing various reaction parameters in the reaction of 1-(2-aminophenyl)-2-phenylethanone (**1a**) with benzyl alcohol (**2a**). Using 20 mol% $Fe(OTf)_3$ and 2 equiv. of di-*tert*-butyl peroxide (DTBP) in DMSO at 100°C under air, the desired quinolone product **3aa** was obtained, with a 12% yield (entry 1). Theoretically, 2 equiv. of oxidant is required in the reaction; 1 equiv. for the oxidation of alcohol and 1 equiv. for the final oxidation after cyclization. However, the final oxidation proceeded well and the yield of **3aa** was improved when the amount of DTBP was increased to 3 equiv. (entry 2). Moreover, when the temperature was increased to 110°C, full conversion of **1a** was achieved and a significantly increased yield of **3aa** was observed (entries 3 and 4). Based on these results, we considered that temperature was the critical factor; however, a small amount of unoxidized cyclized product was detected in the reaction with 2 equiv. of DTBP (entry 3). Only trace amounts of **3aa** were observed in the DMF solvent (entry 5). Next, various types of oxidants and catalysts were tested in the reaction system. *tert*-Butyl hydroperoxide (TBHP) showed low efficiency, and H_2O_2 gave a yield of **3aa** that was similar to that of DTBP (entries 6 and 7, respectively). Among the explored catalysts, $Fe(OTs)_3 \cdot 6H_2O$ was the best catalyst (entries 8−13). To further optimize the conditions, we applied O_2 or N_2 gas to the reaction system (entry 14 or 15, respectively). Interestingly,

the N_2-charged reaction system gave the best yield with clean conversion, while exposure of the reaction mixture to O_2 resulted in a lower yield. We supposed that O_2 accelerated a side reaction that originated from the oxidative cleavage of **1a**. In the absence of a catalyst, the reaction was very slow and was not completed (entry 16). This result demonstrates the important role of iron catalysts in the oxidation process.

Table 1. Optimization for the Reaction between 1-(2-Aminophenyl)-2-phenylethanone (**1a**) and Benzyl Alcohol (**2a**) [a]

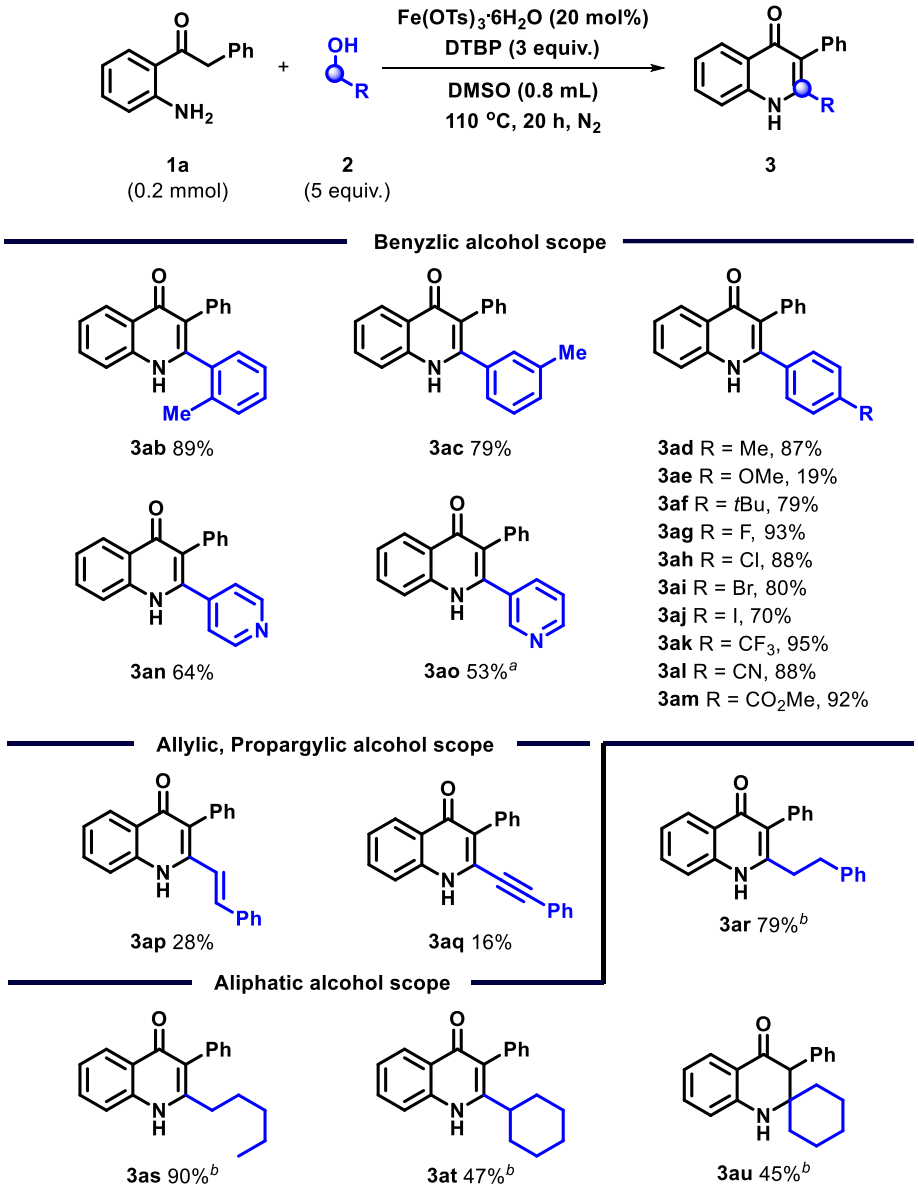


1a **2a** **3aa**

Entry	Catalyst	Oxidant (equiv.)	Yield [b] (%)
1 [c]	$Fe(OTf)_3$	DTBP (2.0)	12
2 [c]	$Fe(OTf)_3$	DTBP (3.0)	42
3	$Fe(OTf)_3$	DTBP (2.0)	61
4	$Fe(OTf)_3$	DTBP (3.0)	74
5 [d]	$Fe(OTf)_3$	DTBP (3.0)	Trace
6	$Fe(OTf)_3$	TBHP (3.0)	50
7	$Fe(OTf)_3$	H_2O_2 (3.0)	73
8	$Cu(OTf)_2$	DTBP (3.0)	Trace
9	I_2	DTBP (3.0)	5
10	$Mn(OAc)_2$	DTBP (3.0)	4
11	$Fe(OAc)_2$	DTBP (3.0)	13
12	$FeCl_3{\cdot}6H_2O$	DTBP (3.0)	Trace
13	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	81
14 [e]	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	49
15 [f]	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	92
16	None	DTBP (3.0)	28

[a] Reaction condition: **1a** (0.2 mmol), **2a** (1.0 mmol), catalyst (20 mol%), oxidant (0.6 mmol) in DMSO (0.8 mL) at 110 ℃ for 20 h under Air. [b] Isolated yield. [c] Reaction temperature 100 ℃. [d] DMF solvent. [e] O_2 balloon. [f] N_2 balloon.

1.2. Scope of alcohol substrates



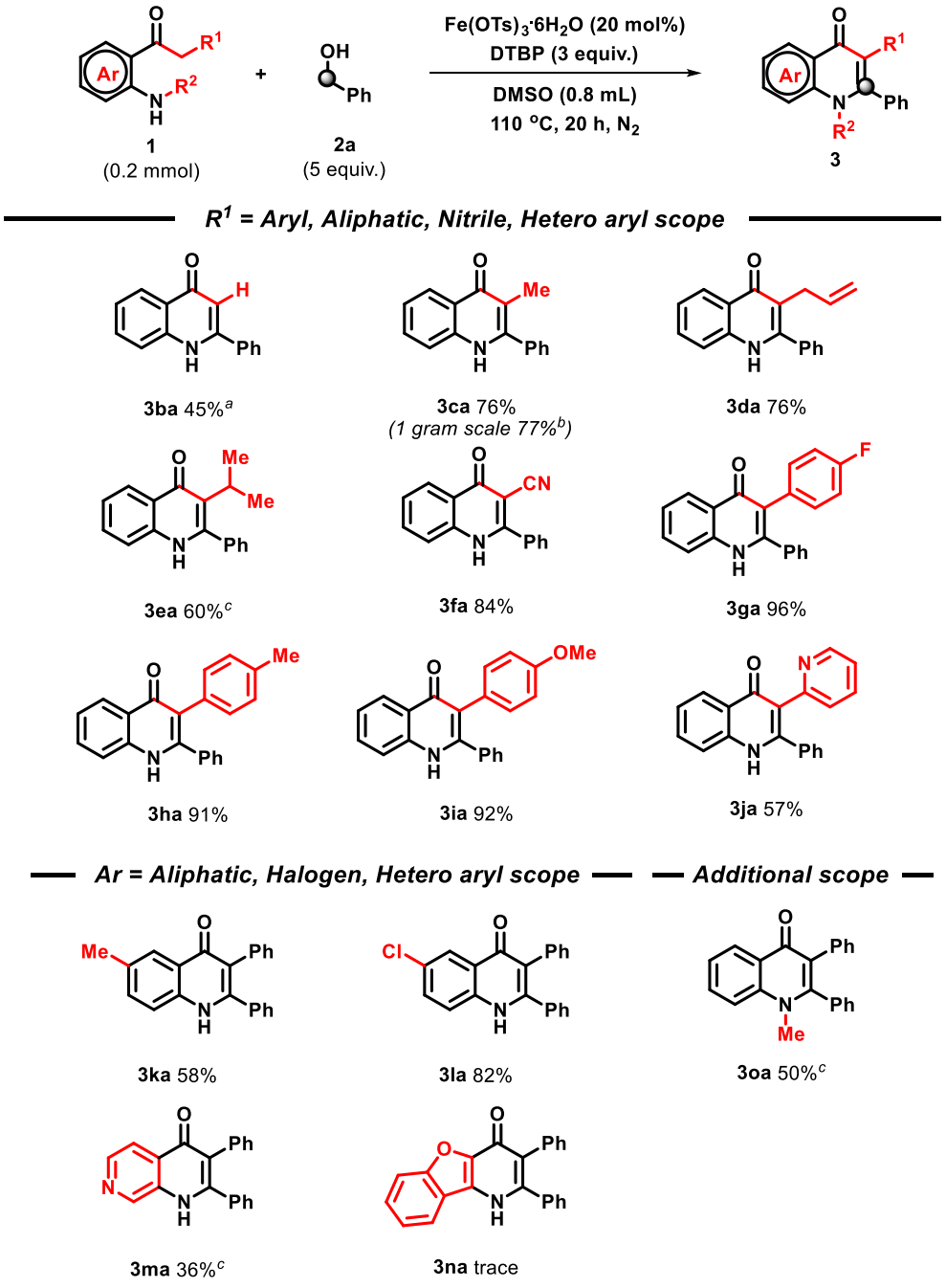
[a] 40 h. [b] 20 equiv. of alcohol, 28 h.

Scheme 15. Synthesis of 4-quinolones using alcohol derivatives

To evaluate the substrate scope of the reaction, various alcohols **2** reacted with **1a** under the optimized reaction conditions (Scheme 15). Benzylic alcohols with various substituents were smoothly reacted with **1a** to afford the corresponding 4-quinolone products **3ab**−**3am** in good yield, except for the methoxy group (**3ae**). In the case of 4-methoxy benzyl alcohol, a complex product mixture was observed. Other substituents, such as *tert*-butyl, halogen, nitrile, and ester, were well tolerated under the reaction conditions. The pyridine group was employed at position 2 of the 4-quinolone products in moderate yields (**3an** and **3ao**). Allylic, propargylic, and aliphatic alcohols were also explored for further expansion of the alcohol scope. Cinnamyl and 3-phenylpropargyl alcohol could participate in the reaction, but only a low yield of **3ap** and **3aq** products were obtained. Aliphatic alcohols also afforded the desired products **3ar**−**3at**, even though an excess amount of alcohol was required. For the secondary alcohol, a moderate yield of the expected 2,3-dihydro-4-quinolone product **3au** was formed.

1.3. Scope of 2-aminophenyl ketone substrates

Next, we employed a series of 2-aminophneyl ketones **1** for further extension of the substrate scope (Scheme 16). A moderate yield of the desired product **3ba** was obtained from the most simple methyl ketone **1b**. In addition to methyl ketone, various substituted ketone substrates could be successfully applied for 4-quinolone formation (**3ca**–**3ia**). For the isopropyl group, the reaction was slow due to steric effects, thus a longer reaction time was required for a satisfactory yield (**3ea**). The 5-methyl substituent on the phenyl group of substrate **1k** showed a negative result compared to the chloride substituent (**3ka** and **3la**). The introduction of a pyridine instead of a phenyl group resulted in a lower yield of the desired products (**3ja** and **3ma**), and a small amount of unoxidized dihydroquinoline intermediates remained. In the case of 2-amino benzofuran-3-ketone **1n**, the tricyclic product **3na** was obtained in trace amounts. *N*-methyl substituted **1o** could also participate in oxidative cyclization, affording an *N*-methyl-4-quinolone product **3oa**. The broad range of substrates explored demonstrates the synthetic potential of this method for the synthesis of 4-quinolones. Furthermore, the practical utility of the developed method was demonstrated on a gram scale (6.7 mmol scale) reaction for **3ca** (77%).



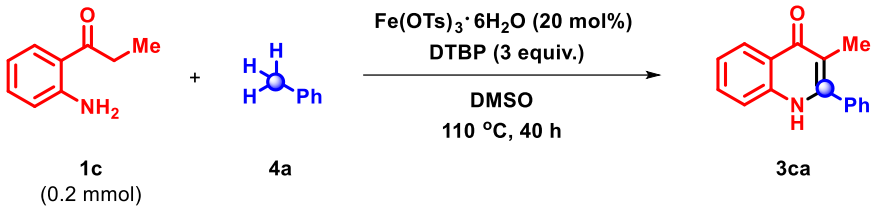
[a] 10 equiv. of alcohol. [b] 24 h. [c] 40 h.

Scheme 16. Synthesis of 4-quinolones using 2-aminophneyl ketone derivatives

1.4. Optimization of reaction condition using methyl arene substrates

After the successful synthesis of 4-quinolones using alcohols, our interest moved to a methyl arenes as a coupling partner. We envisioned that methyl arenes could also be oxidized to aldehydes under the developed conditions. As shown in Table 2, a preliminary study was conducted with the cyclization between 2-aminopropiophenone (**1c**) and toluene (**4a**). Considering the lower reactivity of methyl arene, excess **4a** was used as a cosolvent. Fortunately, **4a** was also readily applied in the annulation and provided the **3ca** product at a 52% yield (entry 1). On the basis of our experience and that of a previous study,[40, 41] we expected that O_2 gas would assist with the oxidation of methyl arene. As expected, when the reaction mixture was exposed to air, an improved yield was obtained with clean conversion (entry 2). After the **4a**/solvent ratio had been controlled, the optimized condition was selected as entry 4 (72%).

Table 2. Optimization for the Reaction between 2-Aminopropiophenone (**1c**) and Toluene (**4a**) [a]



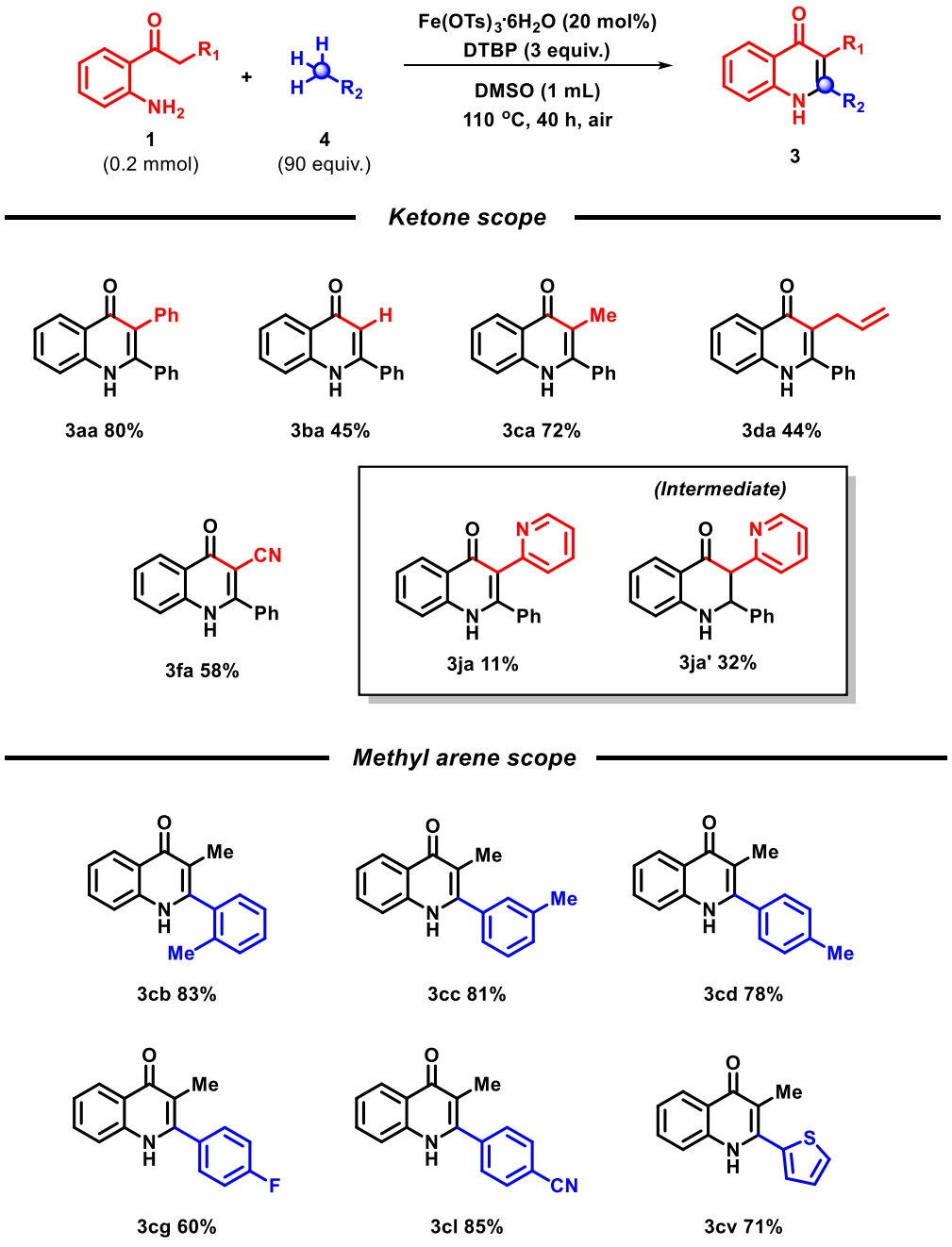
Entry	**4a**	Atmosphere	DMSO (mL)	Yield [b] (%)
1	1.2 mL (60 equiv.)	N_2	0.8	52
2	1.2 mL (60 equiv.)	Air	0.8	57
3	1.9 mL (90 equiv.)	Air	0.8	67
4	**1.9 mL (90 equiv.)**	**Air**	**1.0**	**72**
5	1.9 mL (90 equiv.)	Air	1.2	64

[a] Reaction conditions: **1c** (0.2 mmol), **4a**, $Fe(OTs)_3·6H_2O$ (20 mol%), and DTBP (0.6 mmol) in DMSO at 110 °C for 40 h under Air. [b] Isolated yield.

1.5. Substrate scope in the reaction between 2-aminophneyl ketone substrates and methyl arene substrates

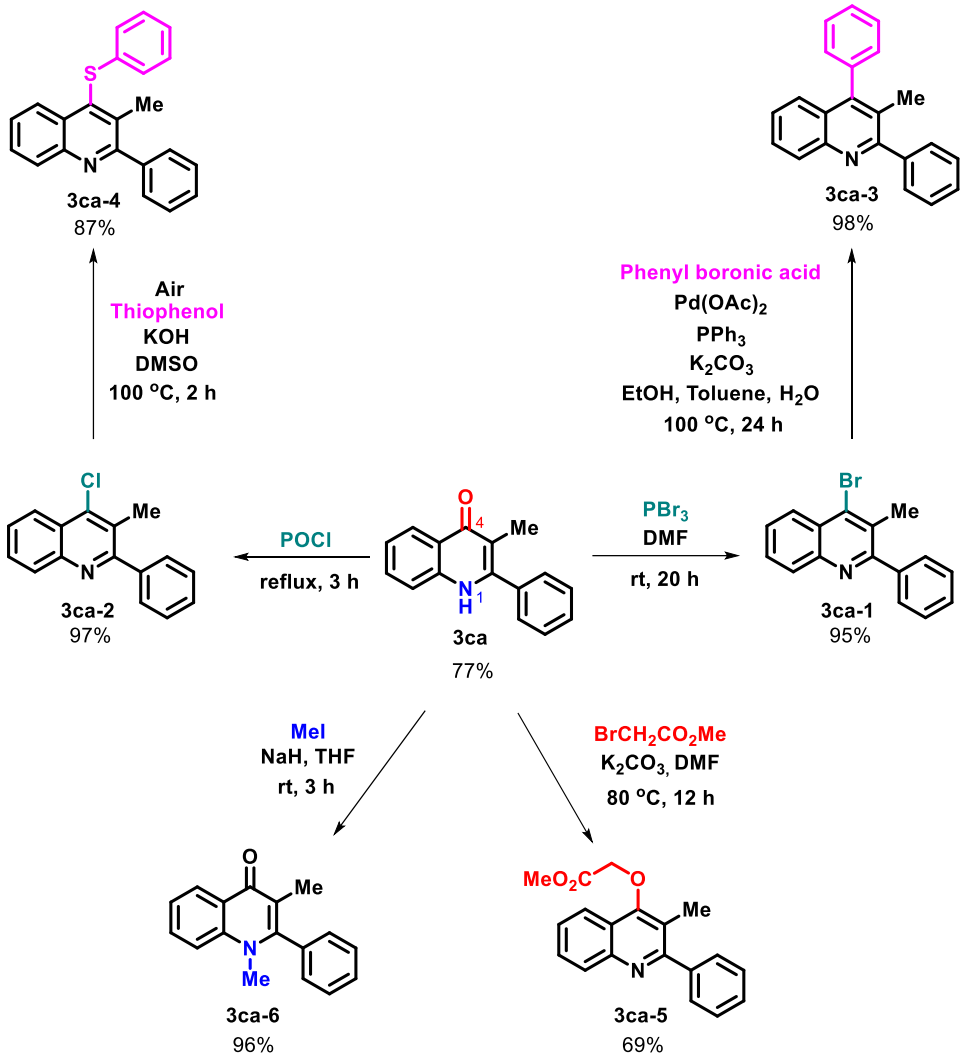
We next investigated the substrate scope for the synthesis of 4-quinolones using methyl arenes (Scheme 17). Under the optimized conditions, various ketone-substituted starting materials **1** reacted with toluene **4a** and afforded the desired 4-quinolone products in moderate to good yield (**3aa**–**3da** and **3fa**). Similar to the reaction using an alcohol substrate, a low yield of the 3-pyridyl quinolone product **3ja** was obtained along with the unoxidized dihydroquinolone intermediate **3ja′**. Initially, we had expected the pyridine group to be oxidized in the reaction, but no oxidation products were detected. Thus, we

proposed another possibility that Lewis basic pyridine captures Lewis acidic iron salt and disrupts iron-mediated oxidation from the dihydroquinolone intermediate to the quinolone product. The phenylethanone substrate (**1a**, R_1 = Ph) smoothly reacted with toluene, resulting in a good yield of **3aa**. However, some inseparable mixture was obtained in the reaction with other methyl arene partners, which is presumed to originate from the oxidative cleavage of **1a**. On the contrary, propiophenone substrate (**1c**, R_1 = Me) could react with various methyl arenes, and the desired products **3cb**−**3cd**, **3cg**, and **3cl** were readily synthesized without side products. Thiophene was also applied to position 2 of the 4-quinolone product (**3cv**) under the developed conditions.



Scheme 17. Synthesis of 4-quinolones using methyl arenes and 2-aminophneyl ketone derivatives

1.6. Synthetic applications



Scheme 18. Diverse chemical conversions of 4-quinolone **3ca**

To demonstrate the synthetic potential of the developed method, we next attempted to convert 4-quinolone product **3ca** to various quinoline compounds *via* functionalization of

the carbonyl moiety at position 4 (Scheme 19). Halogenation with PBr_3 and $POCl_3$ provided the corresponding 4-haloquinolines **3ca-1** and **3ca-2,** respectively. Subsequent Suzuki coupling introduced a phenyl group at position 4 of **3ca-1,** which led to the synthesis of 4-phenyl quinoline **3ca-3**. Furthermore, direct nucleophilic substitution of **3ca-2** with thiophenol afforded 4-sulfide quinoline **3ca-4**.[44] *O*-Alkylation could also be achieved directly from **3ca** using alkyl halide and K_2CO_3, leading to the generation of quinoline product **3ca-5,** which has an ether linkage at position 4.[45] In addition to the ketone group at position 4, the *N*-position 1 could be directly substituted with iodomethane in the presence of NaH as a base.[46] Under these conditions, high yields of *N*-methylated quinolone **3ca-6** was synthesized selectively.

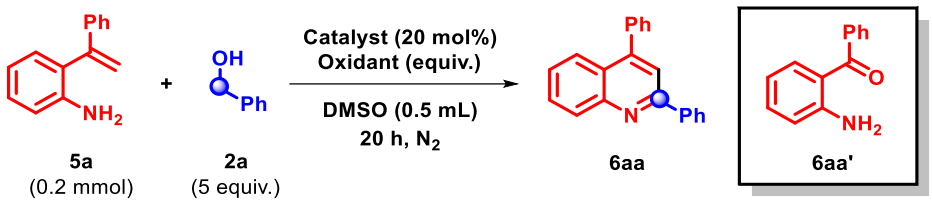
2. Synthesis of quinolines

2.1. Optimization of reaction condition using alcohol substrates

Next, we attempted to extend the developed iron-catalyzed oxidative coupling system to the synthesis of quinolines. As shown in Table 3, we began by optimizing various factors in the reaction of 2-(1-phenylvinyl)aniline **5a** with benzyl alcohol **2a**. Using 20 mol% of $Fe(OTs)_3 \cdot 6H_2O$ and 3 equiv. of DTBP in DMSO at 100°C under a N_2 atmosphere, the desired quinoline product **6aa** was obtained with a yield of 64% (entry 1). Interestingly, when the reaction was conducted under air conditions, **6aa′** was generated as a side product, and the yield of **6aa** decreased (entry 2). We hypothesized that the olefin of **5a** underwent oxidative cleavage in the presence of O_2. Thus, we adjusted the reaction conditions under N_2 gas and then screened various factors. Using TBHP, H_2O_2, BPO, and oxone as oxidants led to unknown side reactions (entries 3−6). To identify mild reaction conditions, we gradually decreased the reaction temperature. Although the yield of **6aa** was similar at 90°C and 100°C, the aldehydes and imine intermediates were significantly observed at 80°C (entries 7−8). We assumed that the cyclization step was retarded at 80°C. Additionally, when the amount of DTBP was reduced to 2 equiv., the cyclization process slowed (entries 7 and 9). A temperature of at least 90°C and 3.0 equiv. of DTBP were required for sufficient conversion (entries 7−9). $Fe(OTs)_3 \cdot 6H_2O$ was confirmed as the optimal catalyst after screening the catalysts (7, 10−13 entries). The yield was enhanced to 71% and 84%, respectively, by increasing the amount of benzyl alcohol to 1.5 mmol and 2.0 mmol (14−15 entries). The only trace amount of the desired product was observed in the absence of either the catalyst or the peroxide (16−17 entries).

This result demonstrates that both iron catalysts and DTBP are important factors in the reaction process.

Table 3. Optimization for the Reaction between 2-(1-Phenylvinyl)aniline (**5a**) and Benzyl Alcohol (**2a**) [a]



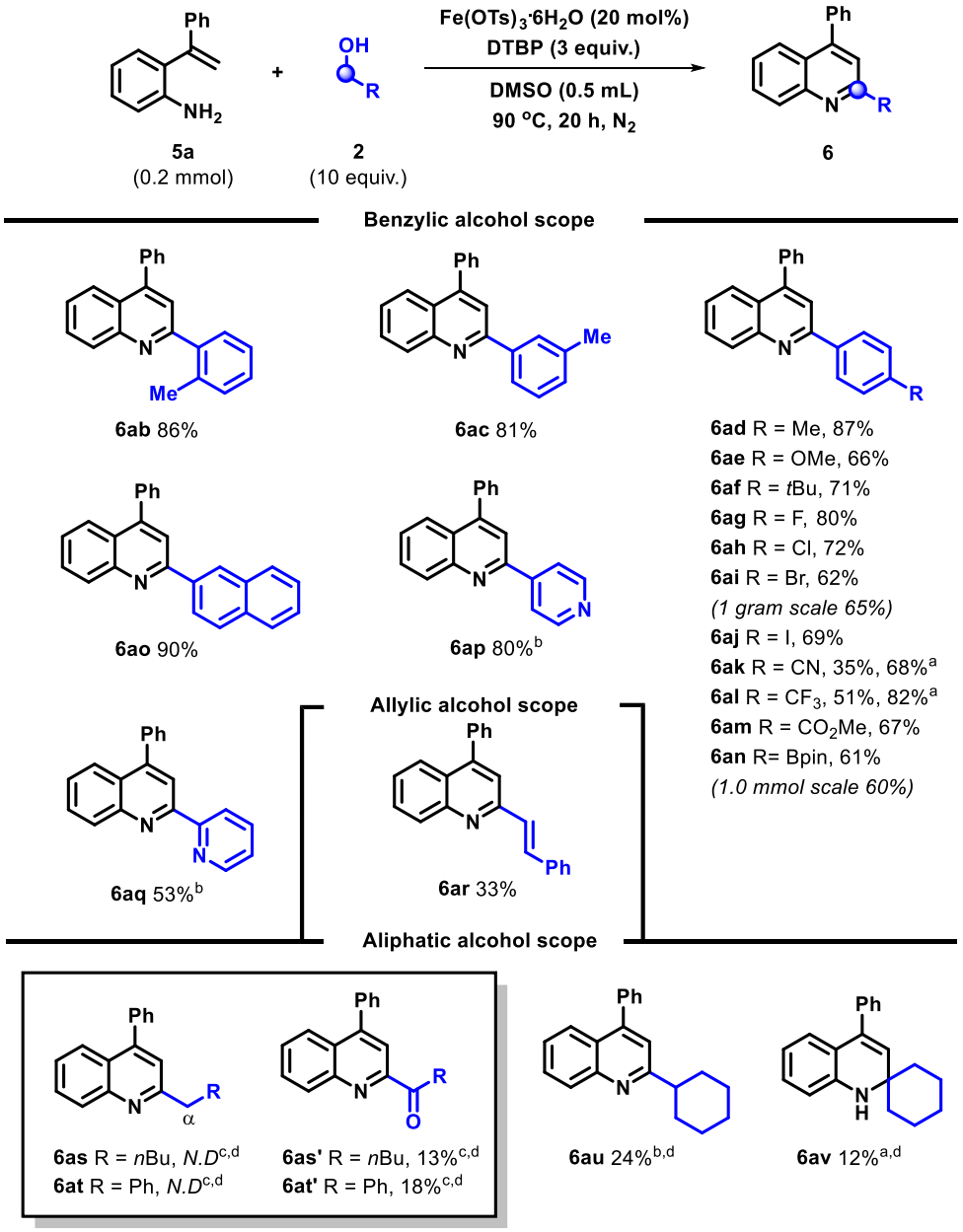
Entry	Catalyst	Oxidant (equiv.)	*T* (°C)	Yield[b] (%)
1	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	100	64
2 [c]	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	100	52
3	$Fe(OTs)_3{\cdot}6H_2O$	TBHP (3.0)	100	Trace
4	$Fe(OTs)_3{\cdot}6H_2O$	H_2O_2 (3.0)	100	N.D
5	$Fe(OTs)_3{\cdot}6H_2O$	BPO (3.0)	100	8
6	$Fe(OTs)_3{\cdot}6H_2O$	Oxone (3.0)	100	19
7	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	90	65
8	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	80	6
9	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (2.0)	90	19
10	$CuCl_2$	DTBP (3.0)	90	Trace
11	$Fe(OTf)_3$	DTBP (3.0)	90	12
12	$FeCl_3{\cdot}6H_2O$	DTBP (3.0)	90	5
13	$Fe(OAc)_2$	DTBP (3.0)	90	Trace
14 [d]	$Fe(OTs)_3{\cdot}6H_2O$	DTBP (3.0)	90	71
15 [e]	**$Fe(OTs)_3{\cdot}6H_2O$**	**DTBP** (3.0)	**90**	**84**
16 [c, e]	$Fe(OTs)_3{\cdot}6H_2O$	None	90	Trace
17 [e]	None	DTBP (3.0)	90	Trace

[a] Reaction conditions: **5a** (0.2 mmol), **2a** (1.0 mmol), catalyst (20mol %), and oxidant (0.6 mmol) in DMSO (0.5 mL) for 20 h under N_2. [b] Isolated yield. [c] Air condition. [d] 1.5mmol **2a** was used. [e] 2.0 mmol **2a** was used.

2.2. Scope of alcohol substrates

After optimization of the reaction conditions, we applied various types of alcohols **2** with **5a** to synthesize 2-substituted quinolines (Scheme 19). Benzylic alcohols with diverse substituents were smoothly reacted with **5a** to afford a good yield of the corresponding quinoline products (**6ab**–**6ao**), except for the nitrile and trifluoromethyl groups (**6ak** and **6al**). Because the strong electron-withdrawing groups destabilized the radical intermediate in the reaction, the nitrile and trifluoromethyl groups did not show complete conversion of the starting material at 90°C. Therefore, a higher reaction temperature was required for a satisfactory yield for **6ak** and **6al**. Various substituents, such as t-butyl, halogen, ester, Bpin, and naphthyl groups, were tolerated under the reaction conditions. In particular, quinoline products containing halogen (**6ah**–**6aj**) and Bpin (**6an**) can be subjected to cross-coupling reactions with the umpolung strategy. The reactions with alcohols containing pyridine groups were not completed at 90°C, but sufficient yields of quinoline products **6ap** and **6aq** were obtained at 110°C. We supposed that the Lewis basic pyridine group captured the Lewis acidic iron catalyst and disturbed the iron-mediated oxidation process. Cinnamyl alcohol could be applied in the reaction, but led to low yields of product **6ar**. Aliphatic alcohols were also applied to the reaction system, and different results were observed depending on the aliphatic group. If the α-position of the quinoline was methylene, additional oxidation occurred (**6as′** and **6at′**). In addition to this side reaction, aliphatic alcohols tend to be less reactive due to their lower oxidative potential properties compared to benzyl alcohols. In the cyclohexyl group, a low yield of the desired product **6au** was obtained even with excess alcohol and high temperature. For the secondary alcohol, the expected spiro-dihydroquinoline product **6av** was formed at a poor yield. To show synthetic utility, large-scale reactions were

conducted for **6ai** (65%), **6an** (60%).

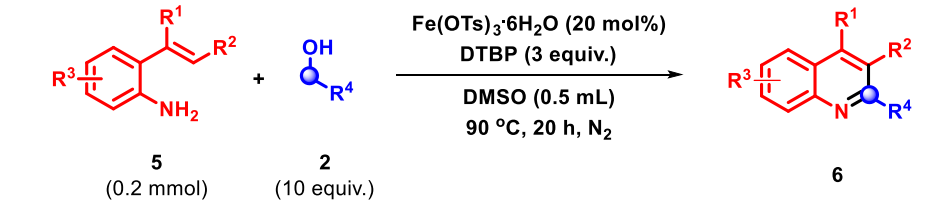


[a] 100 °C [b] 110 °C [c] 120 °C [d] 4.0 mmol of alcohol.

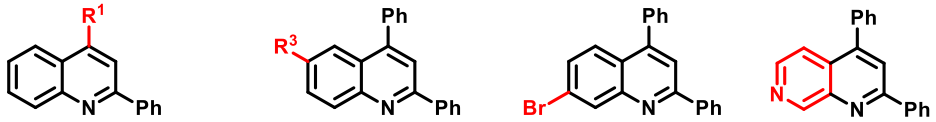
Scheme 19. Synthesis of quinoline using alcohol derivatives

2.3. Scope of 2-amino styrene substrates

Next, we employed various 2-amino styrenes **5** for further extension of the substrate scope (Scheme 21). The reaction of R^1-substituted styrene substrates proceeded well (**6ba**–**6ja**). The diverse phenyl and aliphatic groups, and heteroaromatic groups resulted in moderate to good yields. Regardless of the electron relationship, the R^3-substituted styrene substrates showed good conversion to the desired product (**6ka**–**6oa**). Generally, the substrates containing bromine showed higher conversion when the reaction temperature was increased to 100°C (**6ha**, **6na**, and **6oa**). The use of a pyridine substrate instead of a phenyl group led to a very poor yield of product **6pa**. R^1 and R^2 disubstituted styrene substrates were also explored in the reaction system at a reaction temperature of 110°C, in which the methyl–methyl disubstituted product **6qa** was synthesized at a lower yield with an overoxidized side product (similar to **6as′**, **6at′** in Scheme 20). Phenyl-methyl (**5r**) and phenyl-ester (**5s**) disubstituted substrates afforded good yields of the corresponding products **6ra** and **6sa**, whereas the phenyl-nitrile disubstituted substrate was unsuitable for use in the reaction system (**6ta**). The substrate with a rigid cyclohexyl group showed a moderate yield under standard conditions (**6ua**). In the case of (*E*)-2-styrylaniline **5v**, the cyclization step was forbidden, and imine **6va″** was observed instead of **6va** under standard conditions. Even though the temperature was increased to 110°C, **6va** remained at a very low yield. Bioactive quinoline derivatives, such as antifungal (**6wa**), DPPH radical scavenger (**6nd**), and anticancer (**6nh**) compounds, were synthesized to show synthetic utility.. A large-scale reaction was also conducted for **6na** (65%).



Aliphatic, Aryl, Hetero aryl, Halide styrene scope



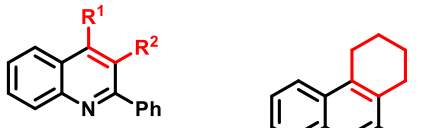
6ba R^1 = Me,70%
6ca R^1 = Cyclohexyl, 69%
6da R^1 = 4-Me-Ph, 82%
6ea R^1 = 4-OMe-Ph, 79%
6fa R^1 = 4-F-Ph, 79%
6ga R^1 = 4-CF_3-Ph, 43%[a]
6ha R^1 = 4-Br-Ph, 68%[a]
6ia R^1 = 2-Thienyl, 87%
6ja R^1 = 2-Furyl, 48%

6ka R^3 = Me, 53%
6la R^3 = OMe, 72%
6ma R^3 = F, 68%
6na R^3 = Br, 71%[a]
(1.0 mmol scale 65%)

6oa 68%[a]

6pa 10%[b]

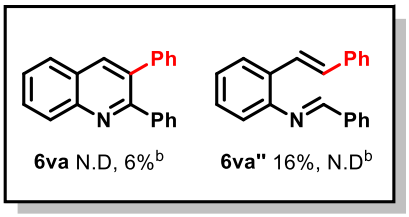
Muti-substituted styrene scope



6qa R^1 = Me, R^2 = Me, 25%[b]
6ra R^1 = Ph, R^2 = Me, 74%[b]
6sa R^1 = Ph, R^2 = CO_2Et, 79%[b]
6ta R^1 = Ph, R^2 = CN, 12%[b]

6ua 45%

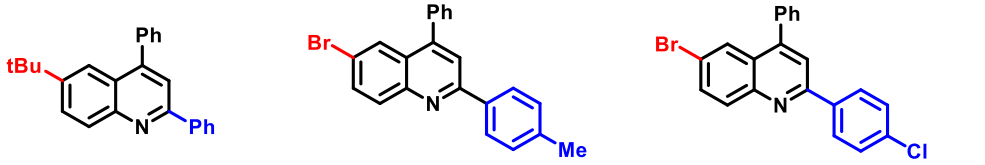
Stibene scope



6va N.D, 6%[b]

6va" 16%, N.D[b]

Bioactive derivatives



6wa 74%
Antifungal

6nd 86%[a]
DPPH radical scavenger

6nh 60%[a]
Anticancer

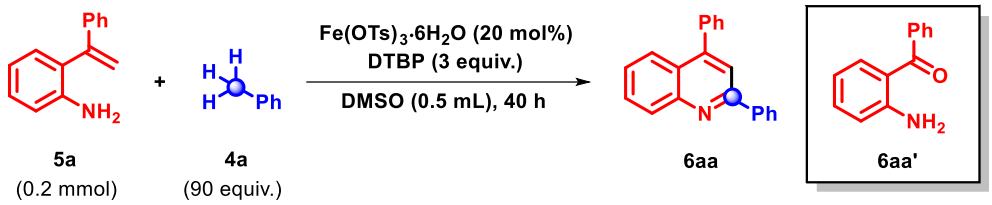
[a] 100 °C [b] 110 °C

Scheme 20. Synthesis of quinolines using 2-amino styrene derivatives

2.4. Optimization of reaction condition using methyl arene substrates

Following successful synthesis of quinolines using alcohol substrates, we attempted to apply methyl arenes as a coupling partner. Based on the reaction conditions of 4-quinolones, the preliminary study proceeded using toluene **4a** as a cosolvent, as shown in Table 4. However, the oxidation of methyl arenes did not occur smoothly at 90°C, and only a low yield of the desired product **6aa** was obtained (entry 1). As the oxidation process of methyl arenes was accelerated by O_2 in the previous study, the reaction mixture was exposed to air; however, the side product **6aa′** was observed to be similar to that in the alcohol system (entry 2). This result indicates that the oxidative cleavage of styrenes is more favorable than the oxidation of the methyl arenes in the presence of O_2. Thus, we adjusted the reaction conditions under N_2 gas and the reaction temperature gradually increased to improve the formation of **6aa** (entries 3–5). The highest yield was observed at 110°C, and the optimized condition was selected as entry 4 (55%). Lastly, we conducted the control experiment under air based on the optimized condition to establish the effect of O_2. As a result a decreased yield of **6aa** was observed with a significant amount of side product **6aa′** (entry 6).

Table 4. Optimization for the reaction between 2-(1-phenylvinyl)aniline (**5a**) and toluene (**4a**) [a]



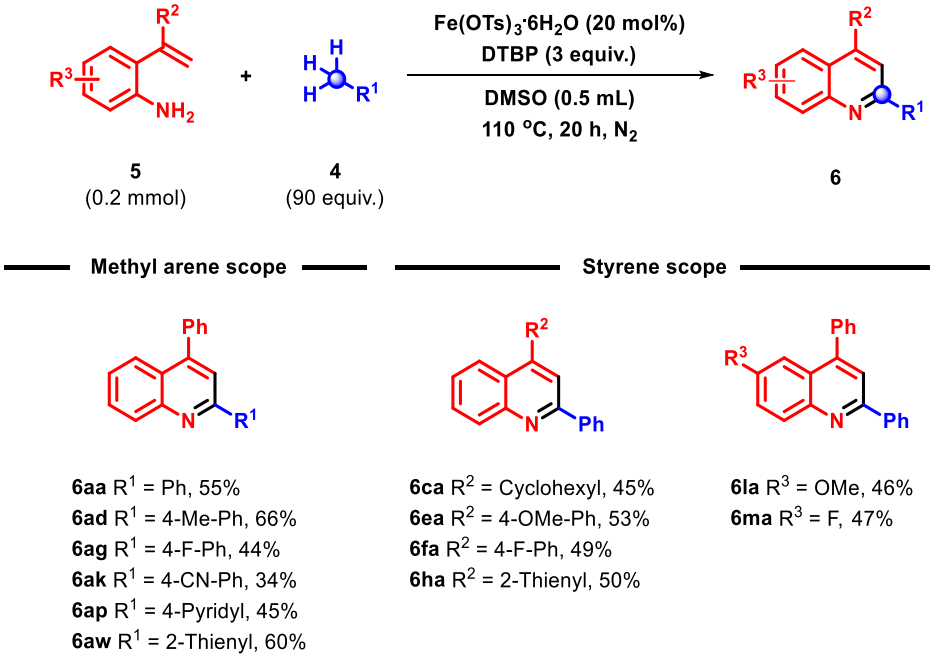
Entry	*T* (°C)	Atmosphere	Yield [b] (%)	
			6aa	**6aa'**
1	90	N_2	6	N.D
2	90	Air	2	9
3	100	N_2	36	N.D
4	**110**	**N_2**	**55**	**N.D**
5	120	N_2	18	N.D
6	110	Air	44	10

[a] Reaction conditions: **5a** (0.2 mmol), **4a** (90 equiv., 1.9 mL), $Fe(OTs)_3·6H_2O$ (20 mol%), and DTBP (0.6 mmol) in DMSO at 110 °C for 40 h. [b] Isolated yield.

2.5. Substrate scope in the reaction between 2-amino styrene substrates and methyl arene substrates

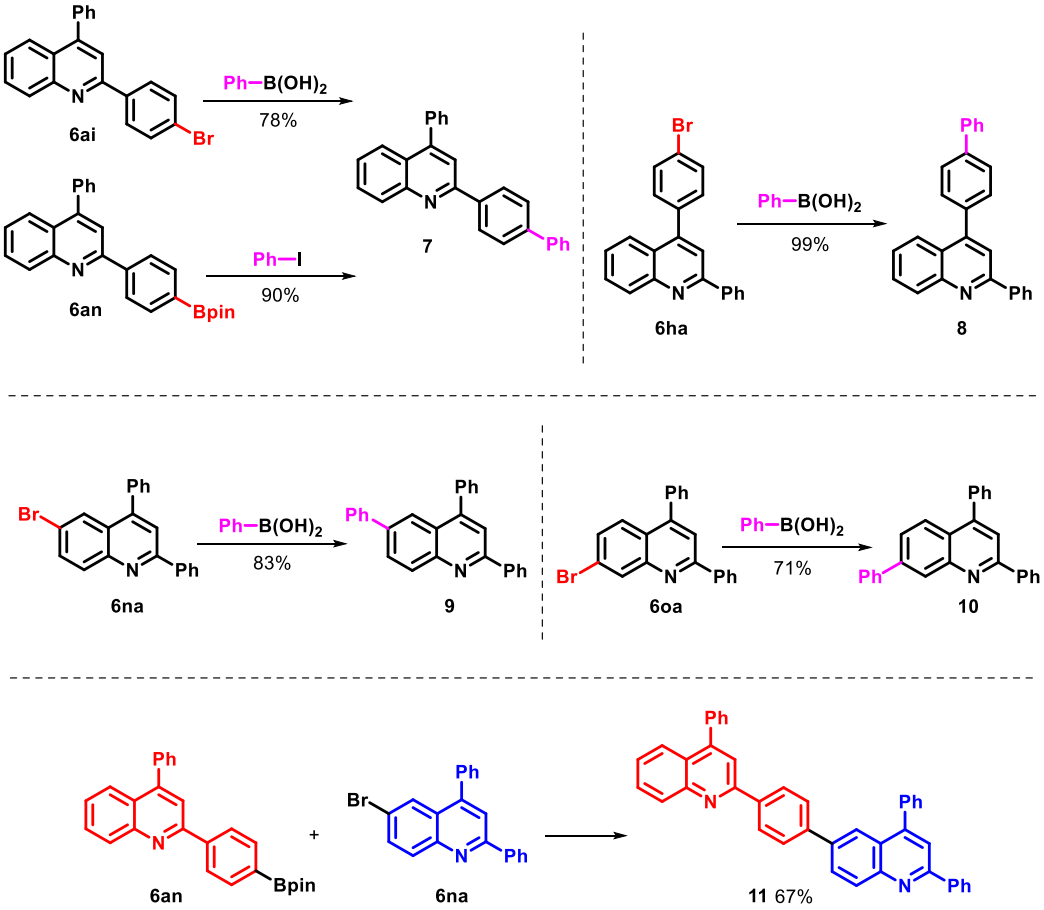
We next explored the reaction scope using methyl arenes (Scheme 21). Under optimal conditions, various methyl arenes **4** were successfully employed in the reaction. Generally, electron-deficient methyl arenes (**6ag** and **6ak**) were less reactive than electron-rich methyl arenes (**6ad**). Additionally, heteroaromatic groups, such as pyridine and thiophene, could be introduced into the 2-position of the quinoline products (**6ap** and **6aw**). We also

attempted to extend the various substituted 2-amino styrene substrate scope and methyl arenes. The reaction system revealed tolerance in styrene substrates **5** including R^2 and R^3 substituents, such as alkyl (**6ca**), electron-donating (**6ea** and **6ka**), electron-withdrawing (**6fa** and **6la**), and heterocycle (**6ha**) substituents.



Scheme 21. Synthesis of quinolines using methyl arene substrates and 2-amino styrene derivatives

2.6. Synthetic applications



All reactions were carried out under the following conditions: aryl halide (1.0 equiv), aryl boron (1.5 equiv), $Pd(OAc)_2$ (5 mol %), PPh_3 (15 mol %), and K_2CO_3 (4.0 equiv) in H_2O/EtOH/toluene = 2:1:4 at 100 ℃ for 24 h.

Scheme 22. Applications of quinoline derivatives through Suzuki coupling

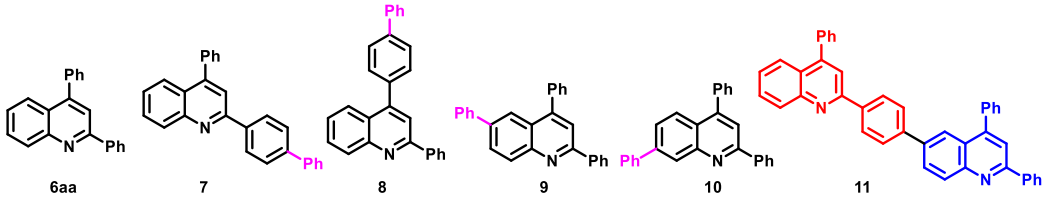
To demonstrate the synthetic utility, we applied quinoline products containing Br and Bpin to Suzuki coupling (Scheme 22). Each aryl boron and aryl halide were coupled

under a given condition to synthesize highly conjugated quinolines **7−10**, in which a phenyl group was introduced at a specific position of the quinoline products. Moreover, the coupling between Bpin-quinoline **6an** and Br-quinoline **6na** afforded dimerized quinoline **11**.

2.7. Fluorescence activities[41]

We next explored the fluorescence activity using the synthesized quinoline derivatives (Table 5 and Figure 11). The wavelength of the maximum emission and the intensity of the emission spectrum varied depending on the position of the phenyl group. Introducing a π-conjugated phenyl group induced a redshift in all compounds **7**−**11**. Quinolines **7**, **8**, **9,** and **10** showed a 92-, 12-, 268-, and 195-fold increase in fluorescence intensity, respectively, compared to that observed for **6aa**. In terms of the tendency of the phenyl-substituted position, the 6-position (**9**) had the greatest effect on the fluorescence intensity and red-shift. Moreover, the dimerized quinoline **11** showed the highest fluorescence and red-shift because it contains two fluorophores.

Table 5. Spectroscopic properties of quinolines **6aa**, **7**−**11** (5.0 μM) in EtOH.



Comp.	λ_{ex} *(nm)*	λ_{em} *(nm)*
6aa	*260*	*367*
7	*272*	*386*
8	*260*	*392*
9	*284*	*397*
10	*270*	*378*
11	*282*	*410*

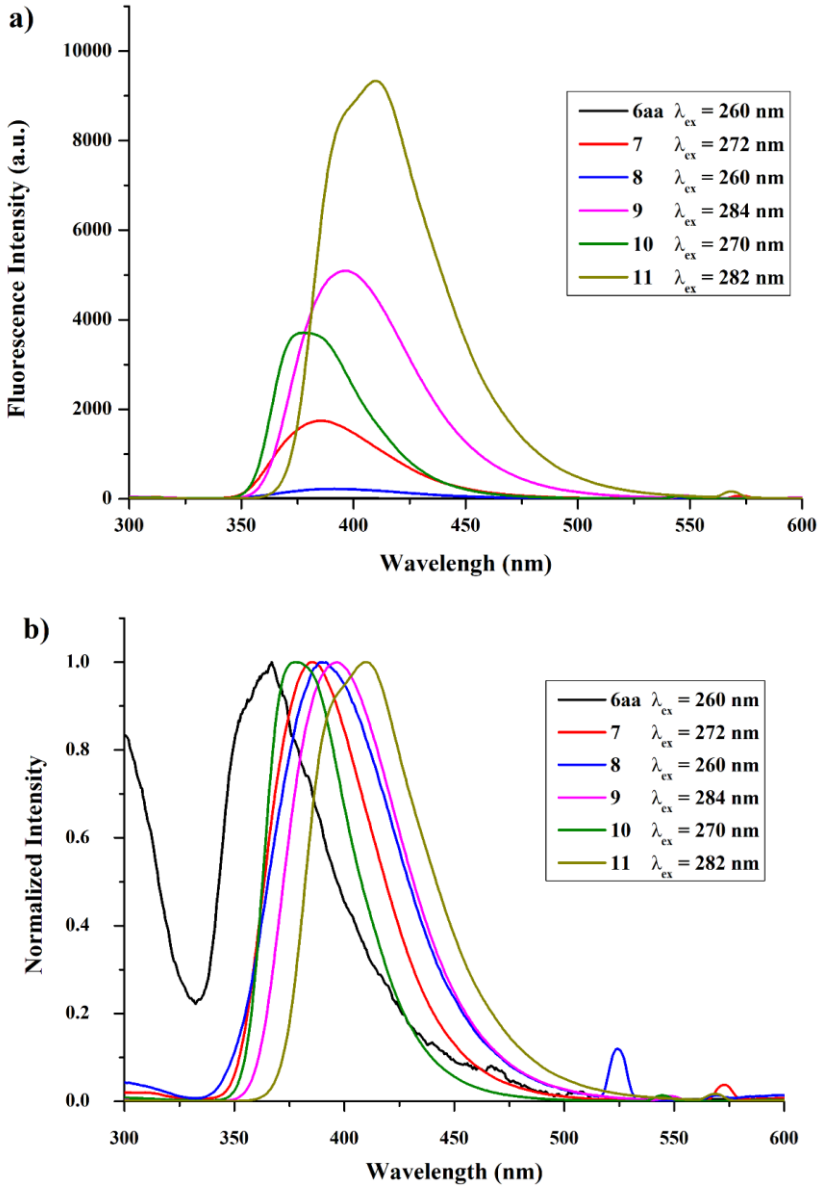


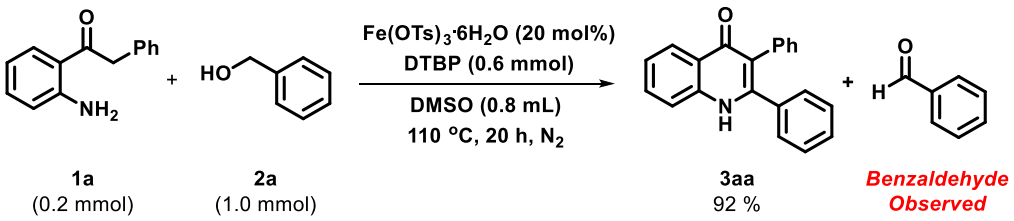
Figure 11. a) Fluorescence emission spectra of **6aa**, **7**−**11**. b) Normalized emission spectra of **6aa**, **7**−**11** to compare the change in the wavelength. Each quinoline compounds (10.0 µL, 1.0 mM solution in DMSO, final concentration: 5.0 µM) were dissolved into EtOH (1990.0 µL). Excitation spectra of **6aa**, **7-11** were recorded from 200 - 400 nm and then, the emission spectra were measured by entering maximum excitation.

3. Mechanism studies

3.1. Mechanism studies on the 4-quinolone synthesis

3.1.1. Observation of aldehyde intermediate

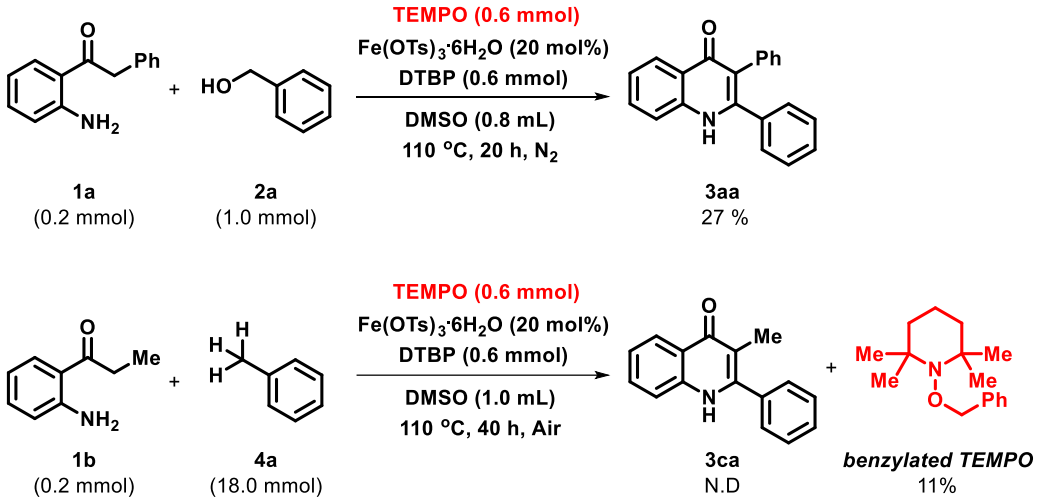
In all reactions for the synthesis of 4-quinolones, the corresponding aldehyde with alcohols (**2**) and methyl arenes (**4**) was detected in TLC. Thus, we assumed that the reaction begins with oxidation to an aldehyde. Even though we could not calculate the exact amount of aldehyde because of its volatility and instability, it was confirmed by the ^{1}H-NMR spectrum of the crude mixture (Scheme 23). According to the ^{1}H-NMR spectrum and TLC of the crude mixture, no over-oxidation products such as benzoic acid were observed.



Scheme 23. Observation of aldehyde in reaction for 4-quinolones

3.1.2. Radical trap reactions with TEMPO

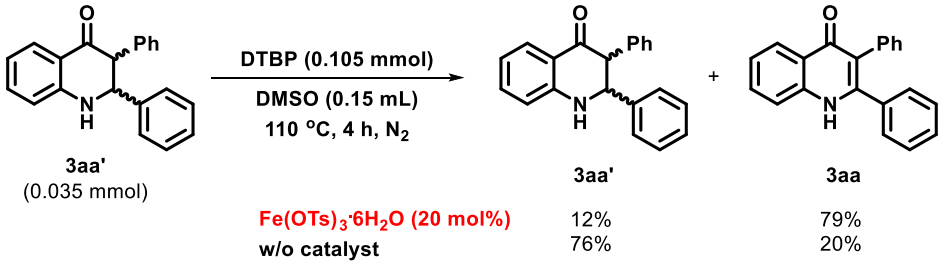
The reactions with TEMPO as radical scavenger were performed in both reaction system with alcohols and methyl arenes (Scheme 24). The formation of 4-quinolone **3aa** was significantly decreased compared to the standard reaction with alcohols **2a** (92% yield of **3aa**). Moreover, none of the desired product **3ca** was observed in the reaction with methyl arenes **4a**, although the benzylated-TEMPO was obtained. Based on these results, we assume that the reaction proceeds through a radical pathway, where a benzyl radical is generated as an intermediate in the oxidation process of methyl arene **4a**.



Scheme 24. Checking the radical pathway using TEMPO in synthesis of 4-quinolones

3.1.3. Important role of iron in the oxidation process

We next captured the dihydroquinolone intermediate in the reaction with methyl arenes during the exploration of the substrate scope. We believed that the pyridine group would prevent the final oxidation process by deactivating the iron catalyst. These results indicate that final oxidation is not proceeded well by DTBP itself, and that iron is also involved in the oxidation process. To confirm this assumption, we conducted control experiments using dihydroquinolone **3aa′** (Scheme 25). In the presence of iron catalysts, most of the **3aa′** was converted to **3aa**, while the oxidation process was significantly reduced without iron catalysts.

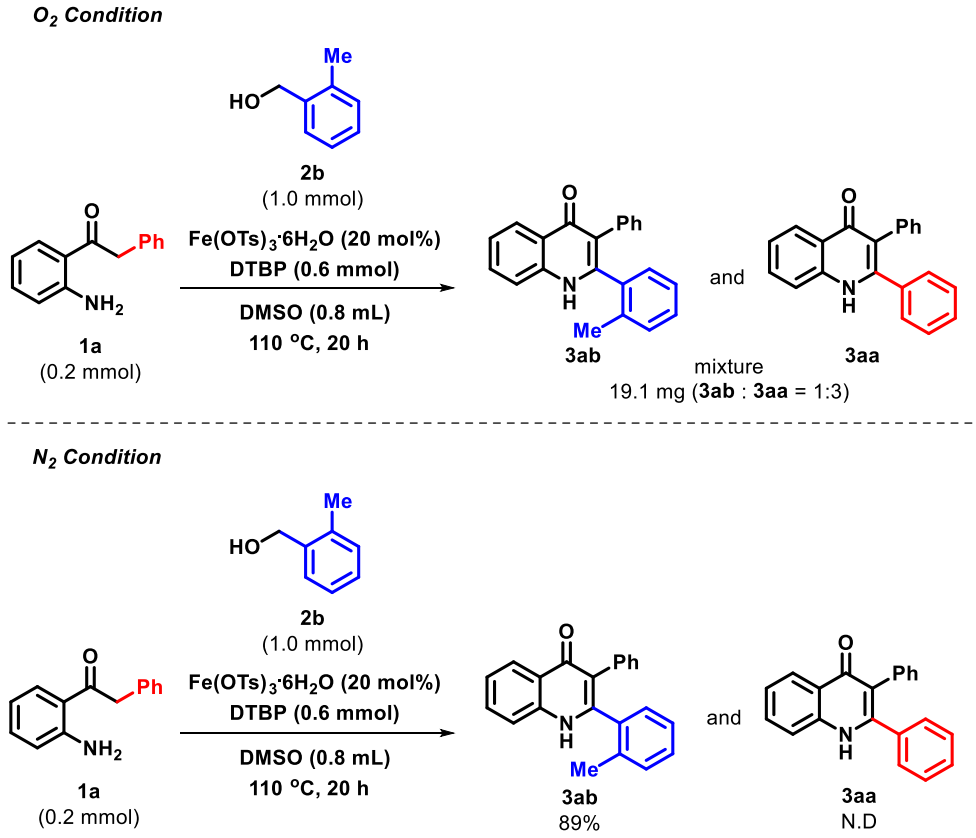


Scheme 25. Important role of iron in the oxidation process

3.1.4. Observation of side products originated from oxidative cleavage

As shown in Scheme 26, we observed inseparable side products in the reaction between **1a** and **2b** under O_2 gas. This side product was identified as **3aa** by ^{1}H NMR analysis. We speculated that this side product originated from the oxidative cleavage of **1a**. However, this side product was not observed in standard conditions under N_2 gas. The α-position of ketone **1a**, which is also the benzylic position, can be easily oxidized in the presence of O_2, and benzaldehyde is formed through oxidative cleavage. The generated benzaldehyde could competitively react with another **1a** with coupling partner **2b**, leading

to the production of a mixture (**3ab** and **3aa)** was produced.



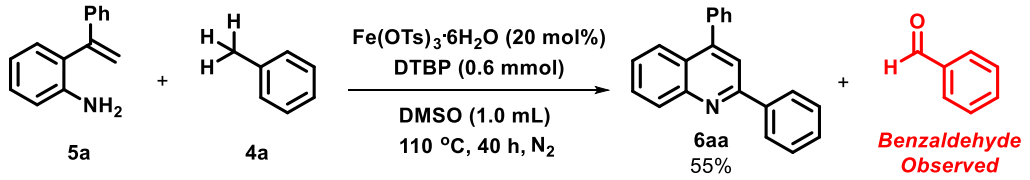
Scheme 26. Observation of side products by oxidative cleavage

3.2. Mechanism studies on the quinoline synthesis

3.2.1. Observation of aldehyde intermediate

Similar to that observed during the synthesis of 4-quinolone, the corresponding aldehydes with alcohols (**2**) and methyl arenes (**4**) were detected in all reactions for the synthesis of quinolines (Scheme 27). The authentic benzaldehyde peaks were observed in

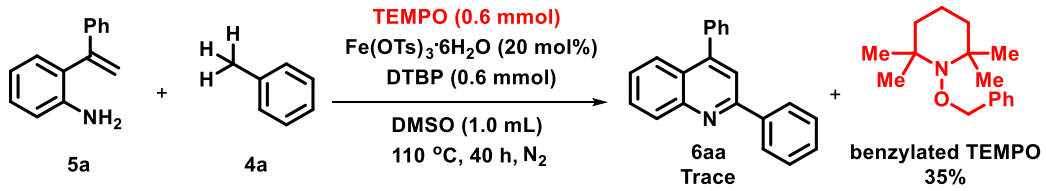
^{1}H NMR spectrum of the mixture fraction; thus, we could assume that the reaction for quinolines also begins with oxidation to the aldehydes.



Scheme 27. Observation of aldehyde in reaction for quinolines

3.2.2. Radical trap reactions with TEMPO

We applied the radical scavenger TEMPO to the reaction system using methyl arenes (Scheme 28). The benzylated-TEMPO was obtained at a yield of 35%, while only trace amounts of the desired product **6aa** was formed. Based on these results, we confirmed that a benzyl radical was generated as an intermediate in the oxidation process of the reaction using methyl arene **4a**.



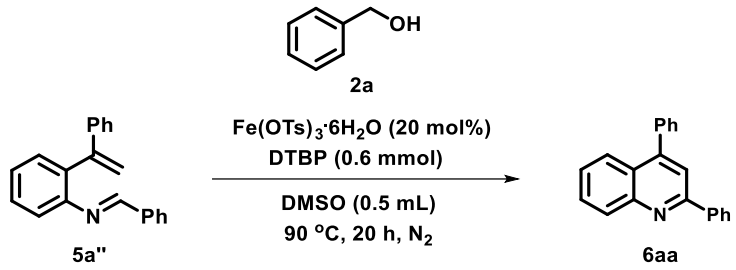
Scheme 28. Checking the radical pathway using TEMPO in synthesis of quinolines

3.2.3. Control experiments to investigate cyclization

To investigate the cyclization mechanism in quinoline synthesis, several control experiments were performed (Table 6). As an imine intermediate **5a″** was observed during the reaction, control experiments were designed using **5a″** as a model substrate. We next examined the effect of each reagent on the cyclization process. Because the imine moiety was already installed in **5a″,** the absence of the benzyl alcohol **2a** did not

affect the formation of the desired product **6aa** (entry 1). However, the formation of **6aa** was significantly suppressed without DTBP or iron catalysts, while 5a″ remained in the reaction mixture (entries 2–3). We assumed that both iron catalysts and oxidants play important roles in the cyclization process. As expected, the reactions without both iron catalysts and DTBP were shut down, and no desired product **6aa** was detected on TLC (entry 4). To further investigate the cyclization mechanism, the reaction with the radical scavenger TEMPO was performed under standard conditions using **5a″** as the starting material. The yield of **6aa** was significantly decreased in reactions using TEMPO (entry 1 in parenthesis). The results of these control experiments highlight that the iron catalyst-DTBP oxidation system plays a crucial role in the cyclization step to form a quinoline structure, and this process proceeds through a radical pathway.

Table 6. Variation from standard condition to investigate cyclization.



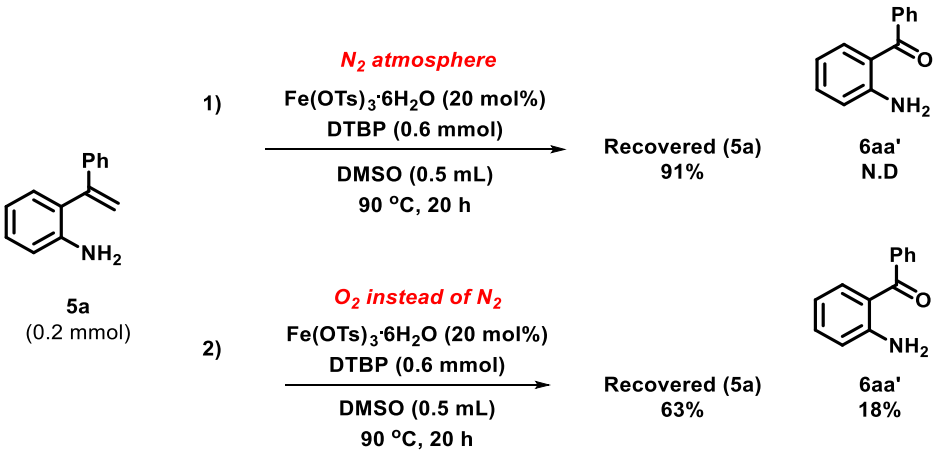
Entry	variation from above condition	**6aa** yield (%) [a]
1	without **2a**	82, (7)[b]
2	without **2a** & DTBP	56
3	without **2a** & Catalyst	18
4	without **2a** & DTBP & Catalyst	N.D

[a] Isolated yield. [b] With TEMPO (3.0 equiv.).

3.2.4. Observation of side products by oxidative cleavage

Based on the observation of ketone **6aa′** during the optimization process, we hypothesized that an olefin of a styrene substrate could be converted to ketone in the

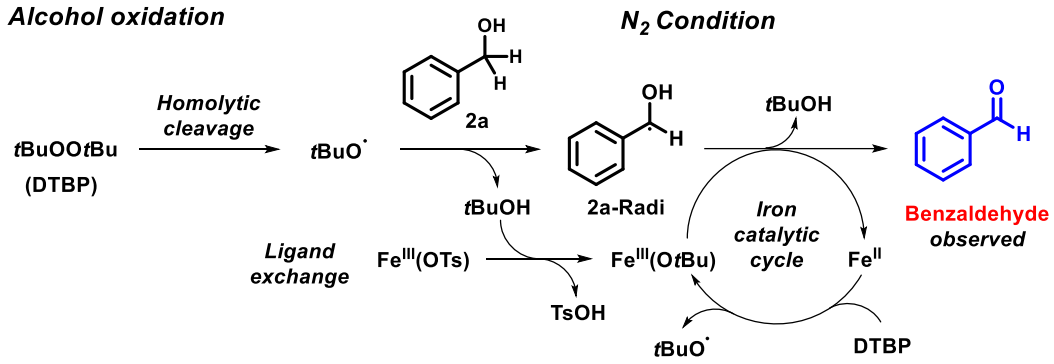
presence of O_2. We employed **5a** as the sole starting material and applied it to standard reaction conditions under N_2 or O_2 atmosphere (Scheme 29). As a result, no ketone product **6aa′** was observed under N_2 conditions, and most of the **5a** remained in the reaction mixture. The ketone product **6aa′** was significantly formed under O_2 conditions. These results show that O_2 facilitated the oxidative cleavage of olefin in the reaction condition, and the developed reaction is suitable under N_2 condition.



Scheme 29. Observation of ketone products by oxidative cleavage

3.3. Plausible Mechanism

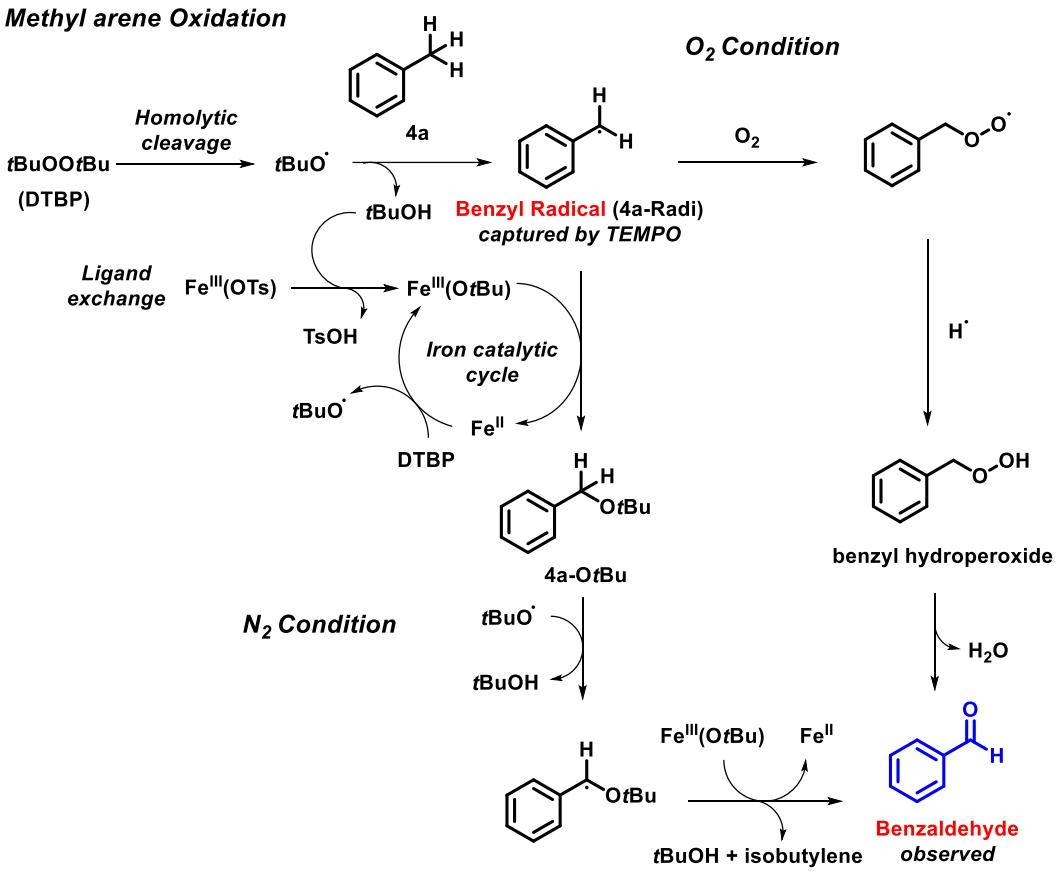
3.3.1 Mechanism of alcohol oxidation



Scheme 30. Mechanism of alcohol oxidation

Based on the results of previous studies[40, 41] and the mechanism studies, the following oxidation mechanism of alcohol was proposed (Scheme 30). At first, *t*BuO• radicals can be generated from DTBP by homolytic cleavage at high temperatures. Then, the *t*BuO• radical abstracts hydrogen radicals from the carbon adjacent to the hydroxyl group of benzyl alcohol (**2a**) to form a benzylic radical intermediate **2a-Radi**, with *t*BuOH produced as a byproduct. This *t*BuOH can undergo ligand exchange with Fe^{III}(OTs) to form Fe^{III}(O*t*Bu). Subsequently, Fe^{III}(O*t*Bu) oxidizes the benzylic radical intermediate **2a-Radi** to a benzaldehyde, and is reduced to Fe^{II} species. Fe^{II} is re-oxidized to Fe^{III}(O*t*Bu) by DTBP and the iron catalytic cycle generates *t*BuO•, which can participate in the oxidation process with another alcohol **2a**.

3.3.2 Mechanism of methyl arene oxidation



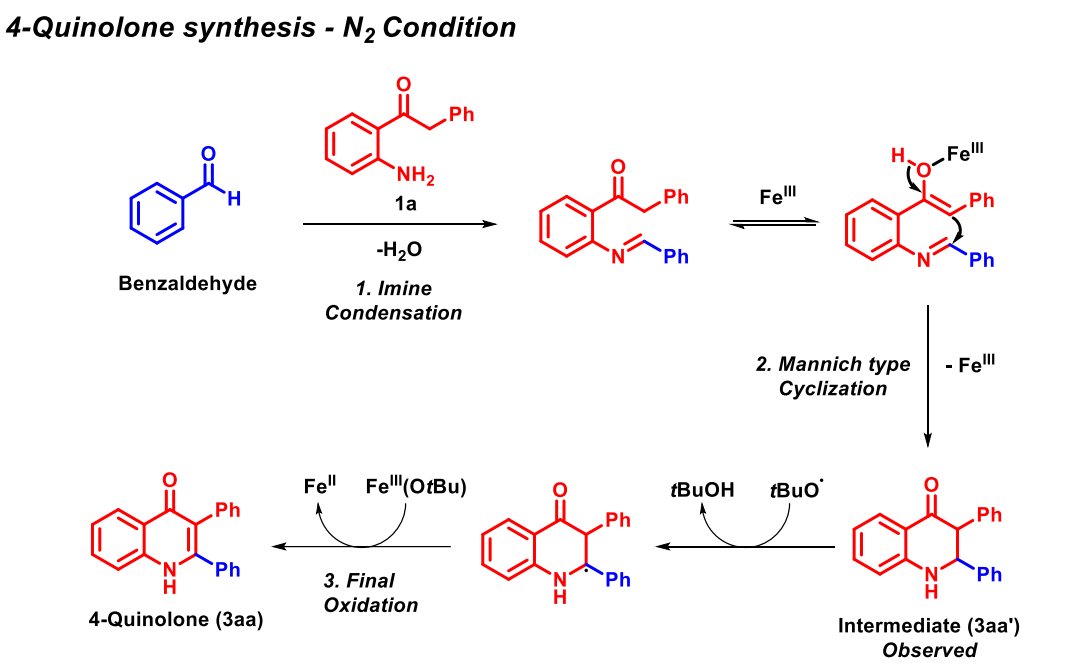
Scheme 31. Mechanism of methyl arene oxidation

In the case of methyl arene (Scheme 31), the hydrogen radical on the benzylic position of **4a** is abstracted by the *t*BuO• radical, and the benzylic radical intermediate **4a-Radi** is produced, similar to that in the oxidation of alcohol. Fe^{III}(O*t*Bu) reacts with the benzylic radical **4a-Radi**, and then **4a-O*t*Bu** and Fe^{II} species are generated. Fe^{II} can participate in the iron catalytic cycle and regenerate Fe^{III}(O*t*Bu) along with the *t*BuO• radical. From **4a-**

O*t*Bu, a similar oxidation process occurs and benzaldehyde is produced. Through these 2-step oxidation processes, 2 equiv. of DTBP is required for methyl arene to oxidize to the benzaldehyde oxidation level. Under the O_2 condition, the benzyl radical intermediate **4a-Radi** captures the O_2 molecule and is oxidized to benzaldehyde through benzyl hydroperoxide. Through this mechanism, O_2 can accelerate the oxidation process of methyl arene.

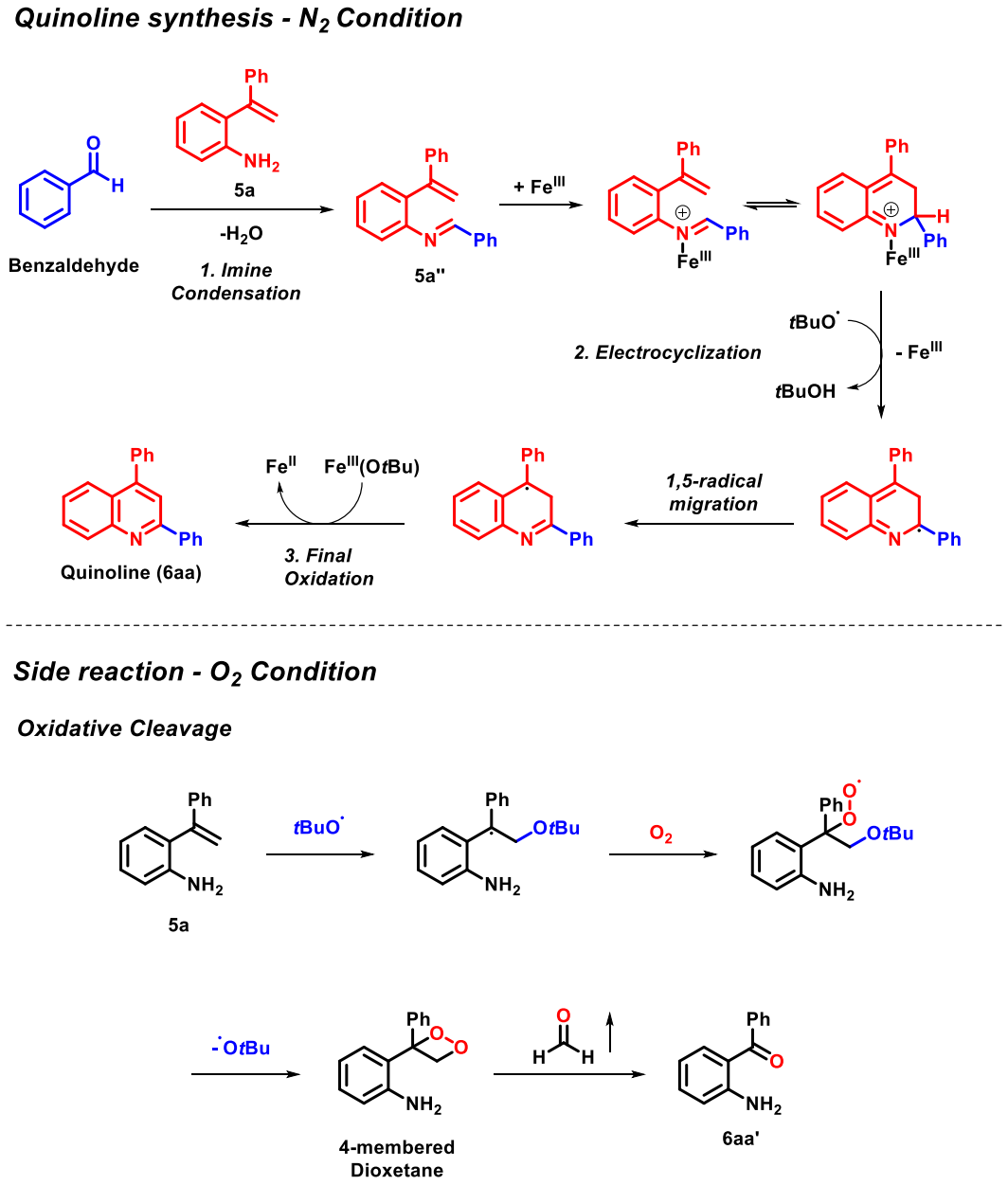
3.3.3 Mechanism of synthesis of 4-quinolones

As shown in Scheme 32, benzaldehyde, which is generated from alcohol and methyl arene, undergoes imine condensation with the amine-based nucleophilic substrate (**1a**). After forming an imine intermediate, iron-mediated intramolecular Mannich-type cyclization afforded the dihydroquinoline intermediate **3aa′**. The desired 4-quinolone **3aa** was produced through the final oxidation of **3aa′** by an iron catalyst and DTBP. In the presence of O_2, the side reaction of **1a** can occur through oxidative cleavage.[47] After a *t*BuO• radical abstracts benzylic hydrogen (H•), which is located at α-position to the carbonyl group of **1a**, it couples with an O_2 molecule to form the hydrogen peroxide intermediate. Then, this intermediate suffers nucleophilic attack by an H_2O molecule, and C−C bond cleavage occurs to form benzaldehyde and anthranilic acid. The generated benzaldehyde can competitively react with **1a** and another coupling partner (**2b**), resulting in the production of a **3aa-side** byproduct.



Scheme 32. Mechanism of synthesis of 4-quinolones

3.3.4 Mechanism of synthesis of quinolines



Scheme 33. Mechanism of synthesis of quinolines

In the case of quinoline synthesis (Scheme 33), the amine-based nucleophilic substrate **5a** reacts with the generated benzaldehyde to form an imine intermediate. Subsequently, a cyclic structure is constructed through an iron-mediated electrocyclization, similar to the aza-Cope rearrangement, and a 1,5-radical shift occurs to form a stable radical intermediate. Finally, the quinoline product **6aa** can be obtained through a final oxidation process using an iron catalyst and DTBP. In the presence of O_2, the olefin of **5a** is attacked by a *t*BuO• radical with the assistance of iron, and the formed carbon radical sequentially reacts with O_2 molecule. The oxidative cleavage occurred through the 4-membered dioxetane and generated a ketone side-product **6aa′**.

CONCLUSIONS

Here, we developed an iron-catalyzed oxidative coupling system using low-oxidation level substrates, such as alcohol and methyl arene, and applied it to the synthesis of *N*-heterocyclic compounds. In the reaction, low oxidation-level substrates are readily activated by iron catalysts and DTBP, leading to the formation of an oxidized electrophilic aldehyde intermediate. The aldehyde intermediate reacted with aniline-type nucleophilic substrates and afforded *N*-heterocyclic compounds through imine condensation, cyclization, and final oxidation. Depending on the nucleophilic substrates, 4-quinolone products were synthesized from the 2-aminophenyl ketone, and quinoline products were obtained from the 2-amino styrene. The developed method not only showed a broad reaction scope with various substrates, but also synthetic utility on large-scale reactions and diverse chemical transformation of *N*-heterocyclic products. A rational mechanism was also proposed through systematic mechanism studies. The iron catalyst is the most abundant and low-toxic transition metal, and all of the reagents used in the reaction were readily available. Moreover, as peroxide generates low-toxic byproducts after the reaction, the developed reaction system is considered to be both economic and eco-friendly. Various alcohol and methylarene structures are widely commercially available. As these low-oxidation level substrates were applied in the developed reaction as pro-electrophiles, the scope of the reaction system could be more generalized and extended than previous *N*-heterocycle synthesis methods using an aldehyde substrate. Based on the developed iron-catalyzed oxidative cyclization method, synthetic methods for other *N*-heterocyclic compounds have been continuously developed using various nucleophiles.

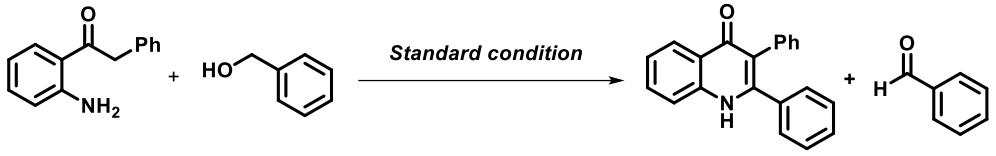
EXPERIMENTAL SECTIONS

1. General information

All commercially available reagents and solvents (purchased from Sigma-Aldrich, TCI, Alfa-Aesar, Acros, Combi-block) were used without further purification unless otherwise noted. All reactions were carried out in oven-dried round bottom flask & seal tube. Reactions were monitored by thin layer chromatography on silica gel 60 F254 plate (Merck, Darmstadt, Germany) using UV illumination at 254 nm (VL-4.LC, Vilber Lourmat, Eberhardzell, Germany). Column chromatography was performed on silica gel (230~400 mesh; Zeochem, Lake Zurich, Switzerland), using mixture of hexane and EtOAc as eluents. Nuclear magnetic resonance (^{1}H-NMR and ^{13}C-NMR) spectra were measured on JEOL JNM-ECZ400s [400 MHz (1H), 100 MHz (13C)] spectrometer. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.26 ppm, DMSO-d_6 = 2.50 ppm; for ^{13}C NMR: $CDCl_3$ = 77.16 ppm, DMSO-d_6 = 39.52 ppm. Coupling constants (J) are expressed in hertz (Hz). IR spectra were recorded on a JASCO, FT/IR-4200 Infrared spectro-photometer and are reported as cm^{-1}. All high-resolution mass spectra (HR-MS) were acquired using fast atom bombardments (FAB) ionization method on a double-focusing magnetic sector mass spectrometer, JMS-700 MStation mass spectrometer (JEOL, Tokyo, Japan). Melting points were measured on a Büchi B-540 melting point apparatus. Absorption spectra were recorded on a UV-Vis spectrometer (Thermo, Orion AquaMate 8100). Fluorescence emission spectra were recorded on a spectrofluorometer (JASCO, FP-8350).

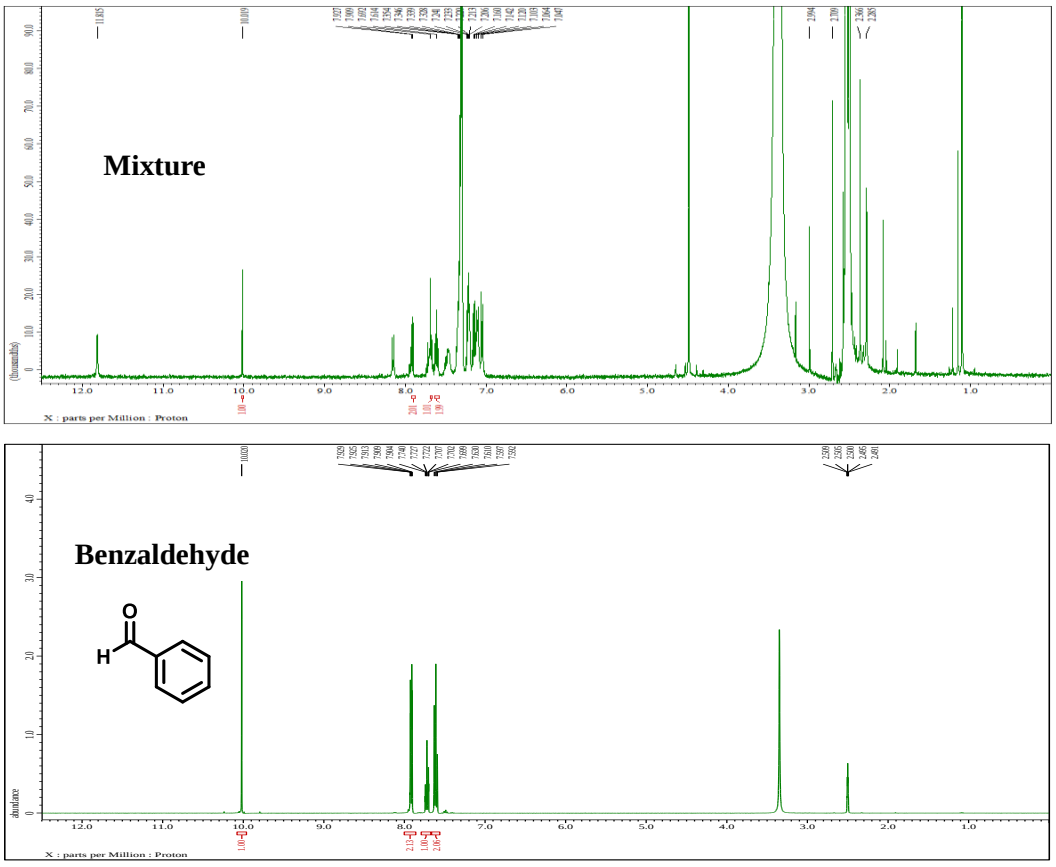
2. Experiment of mechanism studies

2.1. Observation of aldehyde intermediate (Scheme 23)

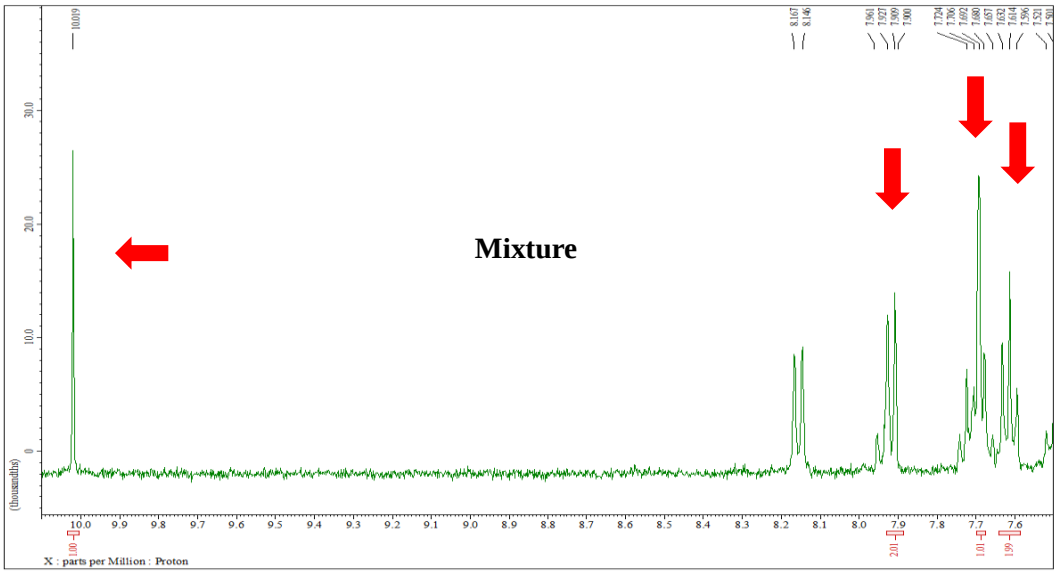


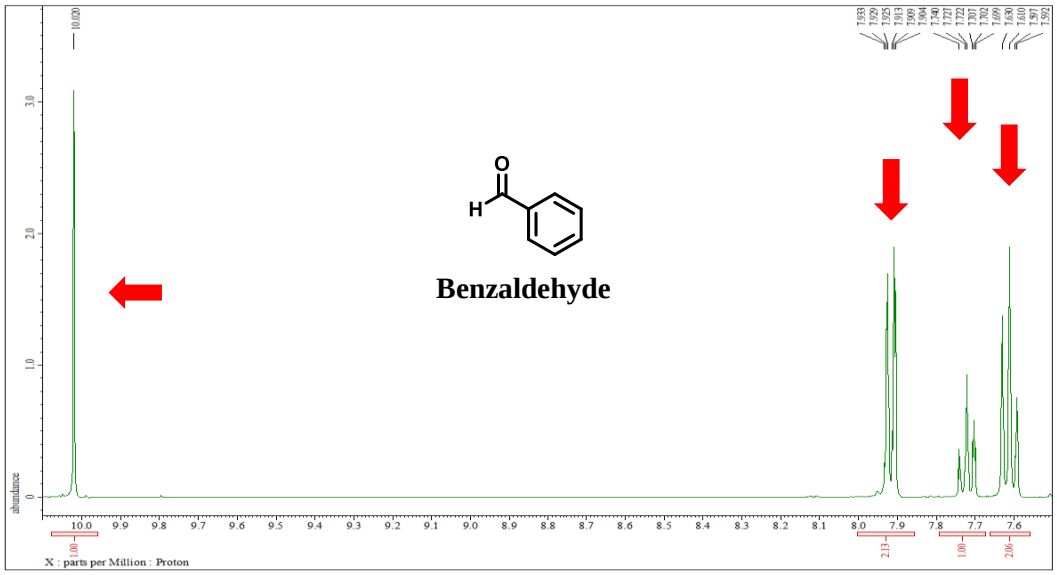
1a (0.2 mmol) **2a** (1.0 mmol) **3aa** 92% ***Benzaldehyde Observed***

^{1}H-NMR spectrum (400 MHz, DMSO) of the mixture (up) and authentic benzaldehyde (down)

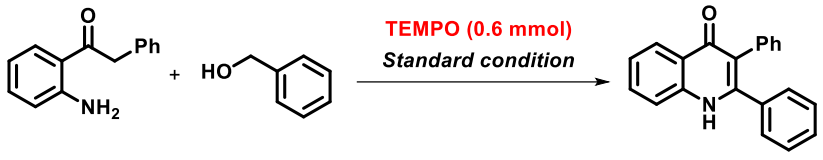


Enlarged ^{1}H-NMR spectrum (400 MHz, DMSO)

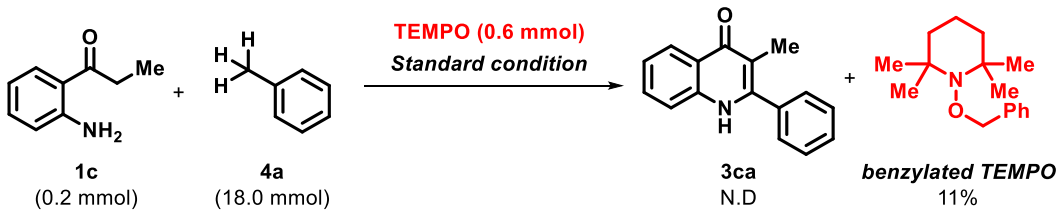




2.2. Radical trap reactions with TEMPO (Scheme 24)



Substrate **1a** (42.3 mg, 0.2 mmol, 1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) and TEMPO (95.7 mg, 0.6 mmol, 3 equiv.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.8 mL), benzyl alcohol **2a** (105.0 μL, 1.0 mmol, 5.0 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 110 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3aa** was obtained as white solid (16.0 mg, 27% yield).



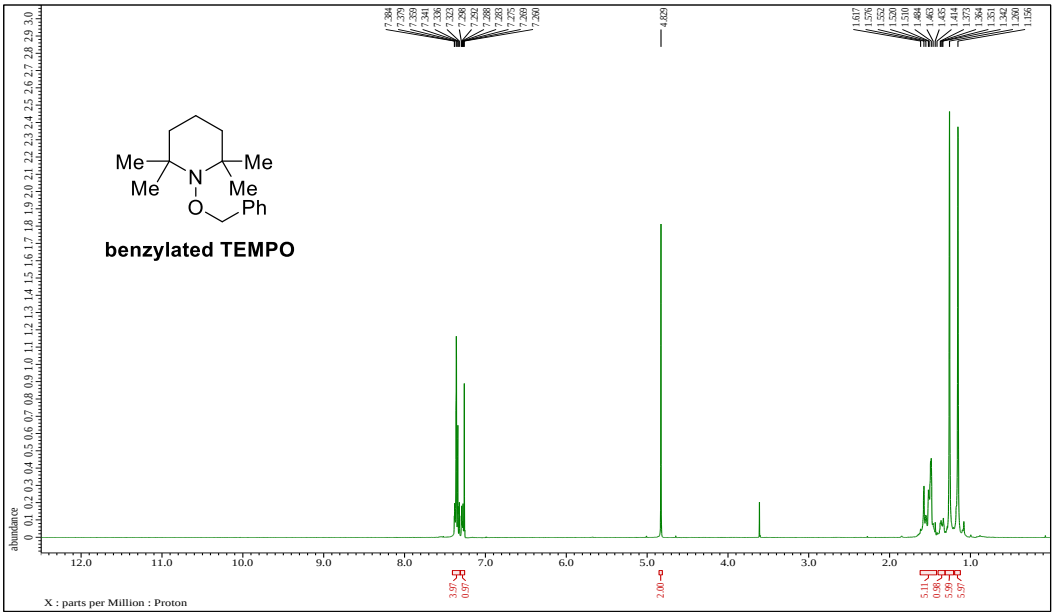
Substrate **1c** (29.8 mg, 0.2 mmol, 1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.), TEMPO (95.7 mg, 0.6 mmol, 3.0 equiv.), DMSO (1.0 mL), methyl arene **4a** (1.9 mL, 18 mmol, 90 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added Borosilicate

Glass Tube. The reaction tube was capped with rubber septum and needle (18/24 gauge) was injected on top of the septum to make the air-opened condition. The reaction mixture was stirred for 40 h at 110 ℃ using oil bath, and then cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc = 40:1), benzylated-TEMPO was obtained as colorless oil (16.9 mg, 11% yield). The spectrum data of benzylated-TEMPO is in agreement with the literature.[48]

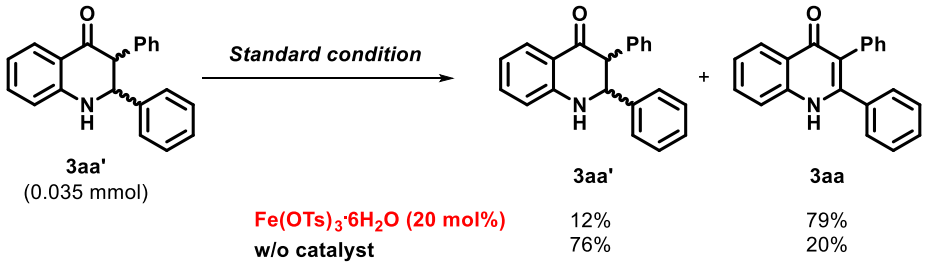
1-(benzyloxy)-2,2,6,6-tetramethylpiperidine (benzlyated-TEMPO)

: ^{1}H -NMR (400 MHz, $CDCl_3$) δ 7.32-7.38 (m, 4H), 7.26-7.30 (m, 1H), 4.83 (s, 2H), 1.44-1.62 (m, 5H), 1.36 (m, 1H), 1.26 (s, 6H), 1.16 (s, 6H).

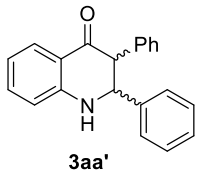
Benzylated TEMPO ^{1}H-NMR (400 MHz, $CDCl_3$)



2.3. Important role of iron in the oxidation process (Scheme 25)



Substrate **3aa′** (10.5 mg, 0.035 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (4.7 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.15 mL) and DTBP (20.0 μL, 0.105 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 110 ℃ using oil bath. After stirring for 4 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc = 12:1 to hexane : EtOAc : DCM = 2:1:1), **3aa′** was obtained as yellow solid (1.3 mg, 12% yield) and **3aa** was obtained as white solid (8.2 mg, 79% yield). Without iron catalyst, **3aa′** was obtained as yellow solid (8.0 mg, 76% yield) and **3aa** was obtained as white solid (2.1 mg, 20% yield).

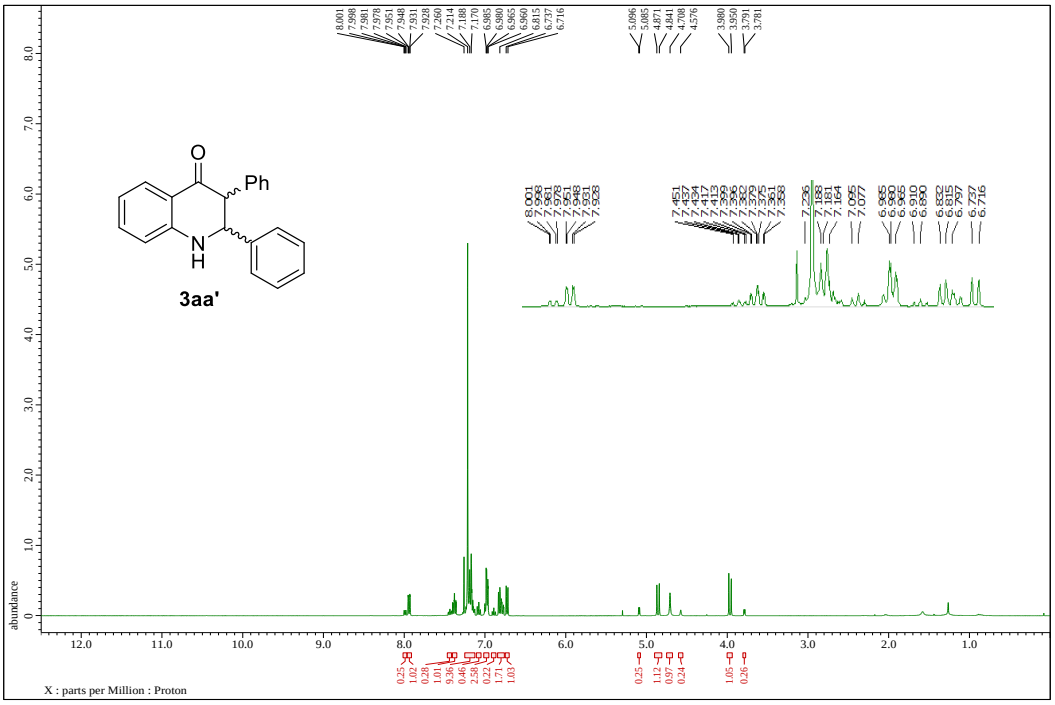


3aa'

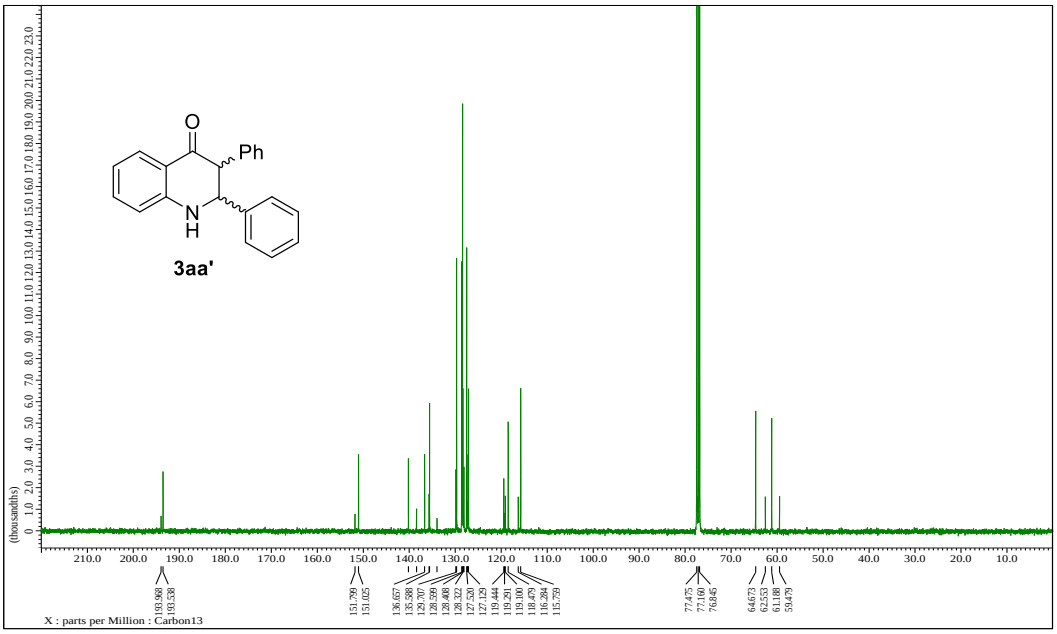
2,3-diphenyl-2,3-dihydroquinolin-4(1H)-one (3aa')

: mp = 110-112 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) major product = δ 7.94 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.36-7.40 (m, 1H), 7.15-7.21 (m, 8H), 6.96-7.00 (m, 2H), 6.81 (t, *J* = 7.1 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 4.86 (d, *J* = 12.3 Hz, 1H), 4.71 (s, 1H), 3.96 (d, *J* = 12.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 193.5, 151.0, 140.2, 136.7, 135.6, 129.7, 128.6, 128.4, 128.3, 127.5, 127.1, 119.4, 118.5, 115.8, 64.7, 61.2; minor product = ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H), (td, *J* = 7.7, 1.6 Hz, 1H), 7.13-7.24 (m, 8H), 7.06-7.09 (m, 2H), 6.89 (t, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 6.8 Hz, 1H), 5.09 (d, *J* = 4.3 Hz, 1H), 4.58 (s, 1H), 3.79 (d, *J* = 3.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 194.0, 151.8, 138.4, 135.7, 134.0, 129.9, 128.2, 128.1, 127.4, 127.2, 119.3, 119.1, 116.3, 62.6, 59.5; IR (neat) υ 3331, 1654, 1607, 1504, 1481, 1453, 1193, 1024, 759 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for C21H18NO 300.1388; Found 300.1388.

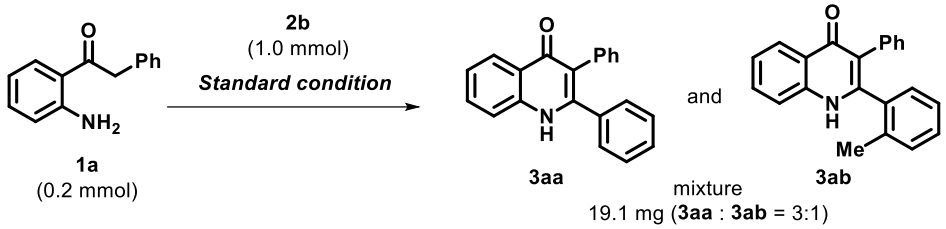
3aa′ ^{1}H-NMR (400 MHz, $CDCl_3$)



3aa′ ^{13}C-NMR (100 MHz, $CDCl_3$)

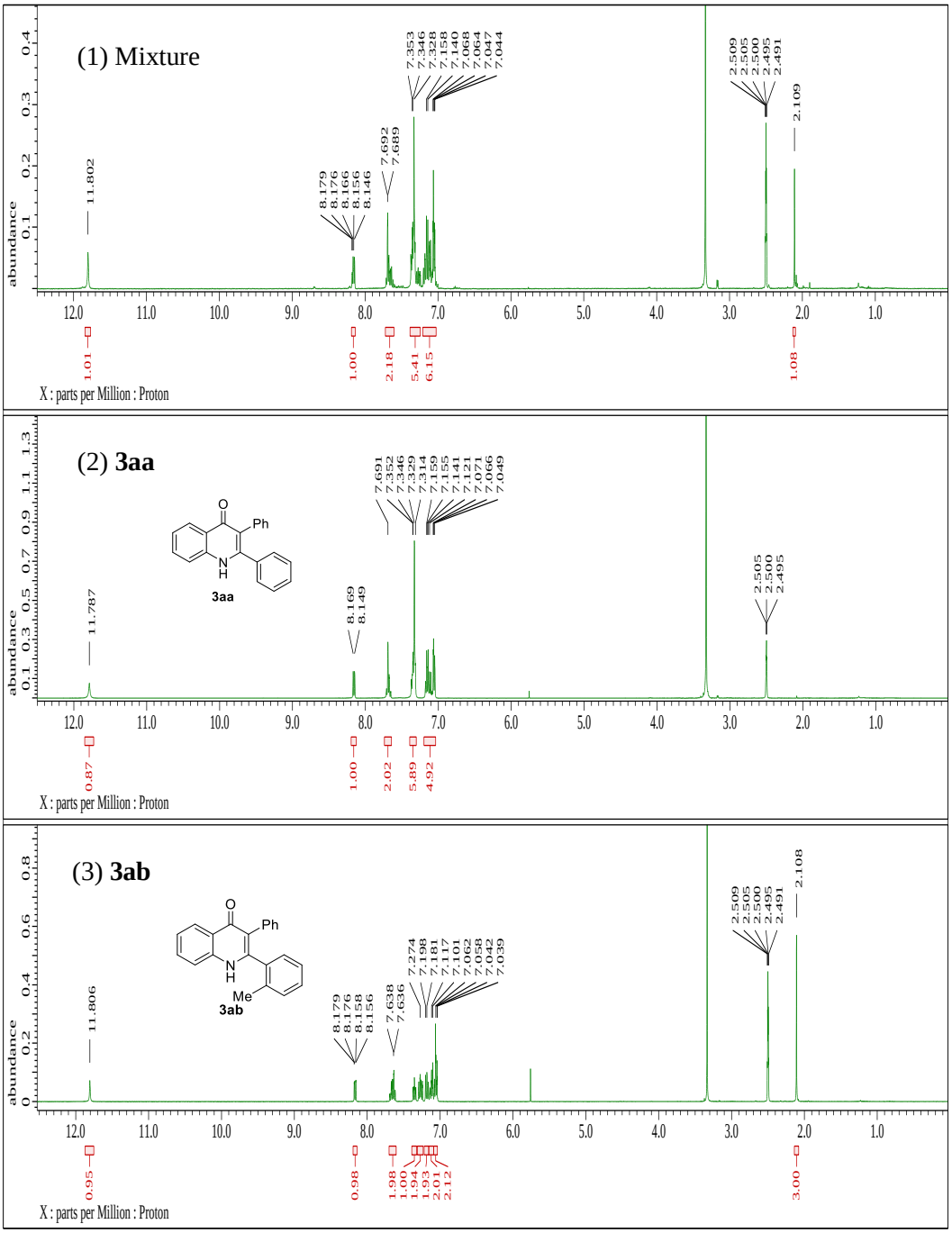


2.4. Observation of side product originated from oxidative cleavage (Scheme 26)

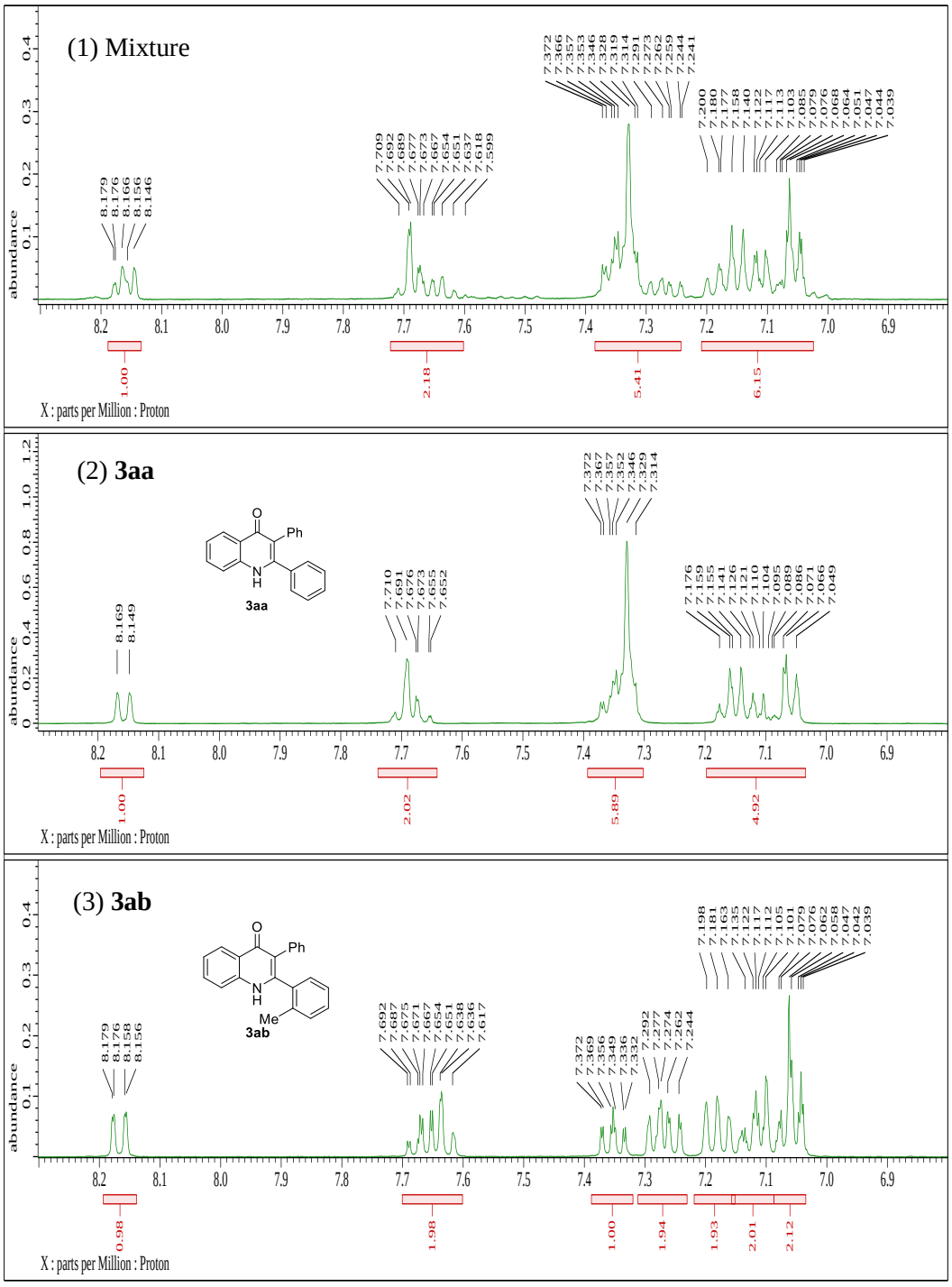


Substrate **1a** (42.3 mg, 0.2 mmol, 1.0 equiv.) was added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with O_2 balloon. DMSO (0.8 mL), 2-Methylbenzyl alcohol **2b** (123.4 mg, 1.0 mmol, 5.0 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 110 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), mixture of product was obtained as brown solid (19.1 mg, **3aa** : **3ab** = 3:1).

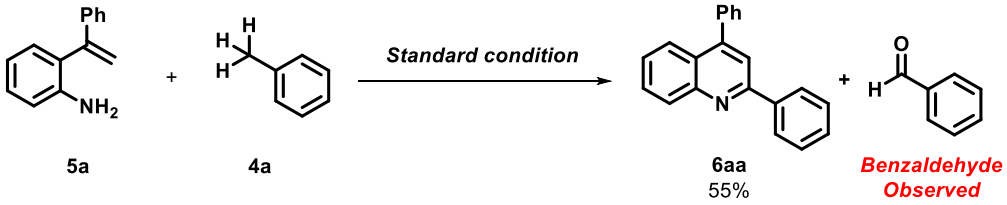
^{1}H-NMR spectrum (400 MHz, DMSO) of the mixture (1), **3aa** (2) and **3ab** (3)



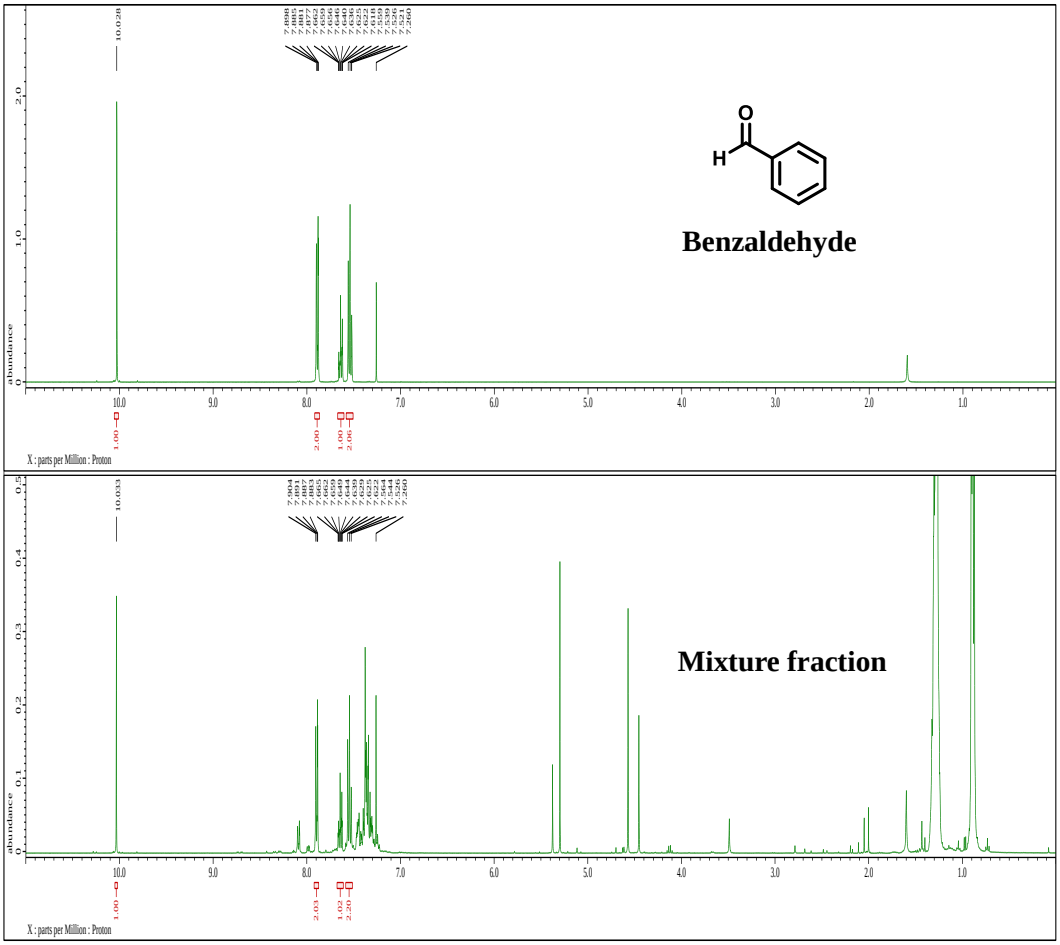
Enlarged ^{1}H-NMR spectrum (400 MHz, DMSO)



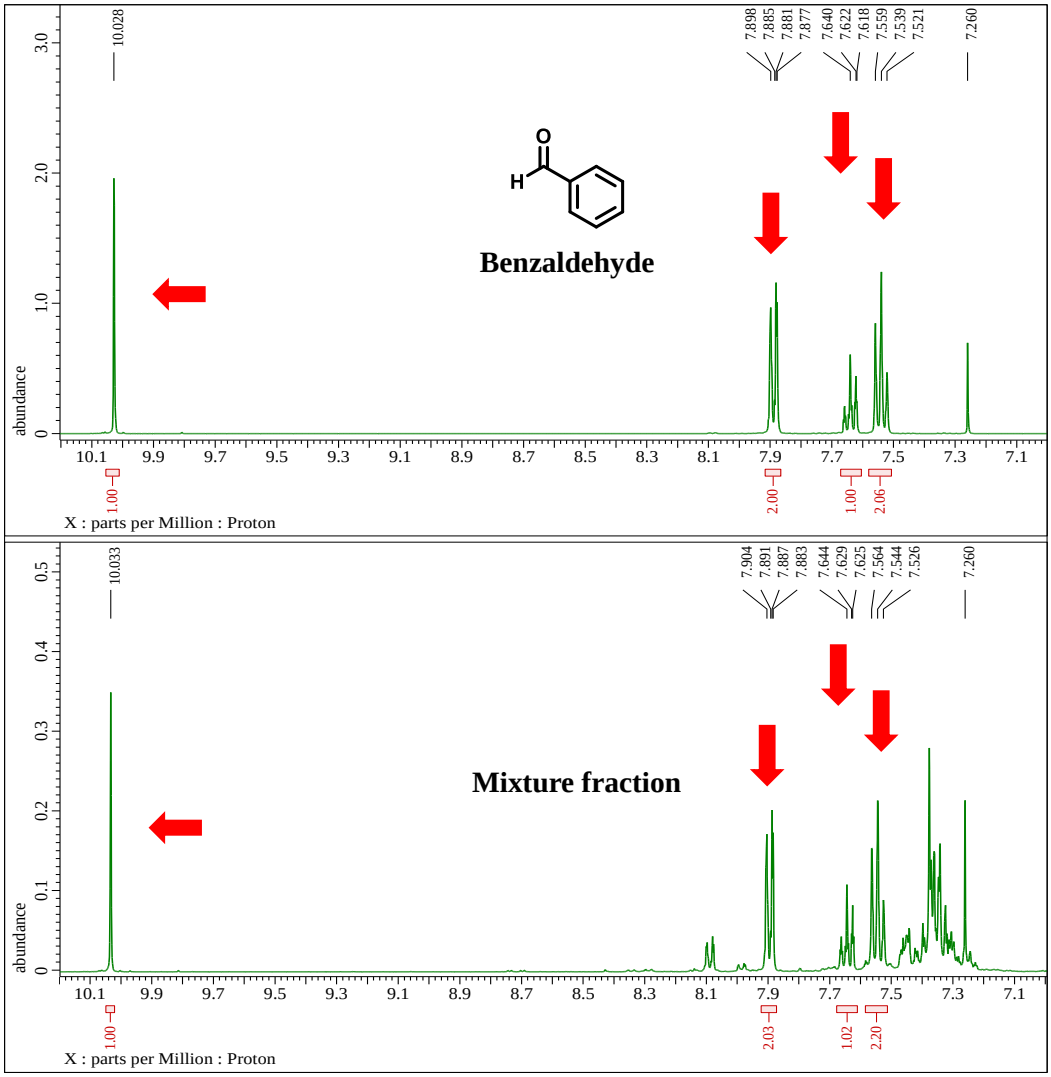
2.5. Observation of aldehyde intermediate (Scheme 27)



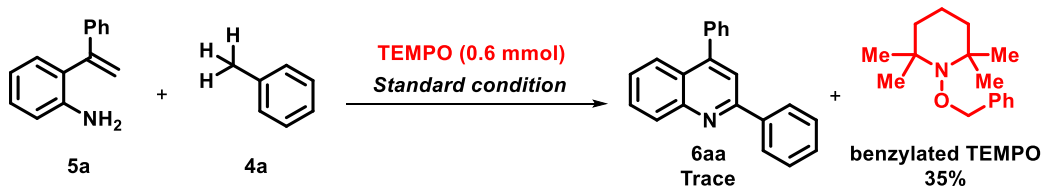
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of the and authentic benzaldehyde (up) and mixture fraction (down)



Enlarged ^{1}H NMR spectrum (400 MHz, $CDCl_3$)



2.6. Radical trap reactions with TEMPO (Scheme 28)

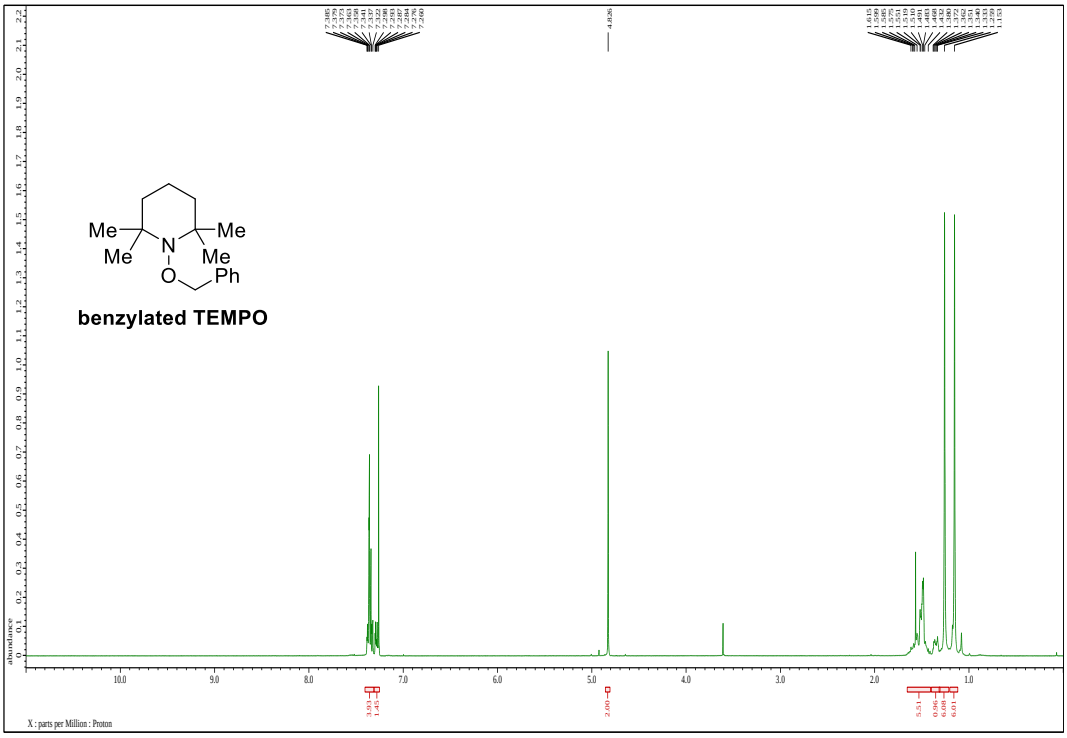


Substrate **5a** (39.1 mg, 2.0 mmol, 1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) and TEMPO (95.7 mg, 0.6 mmol, 95.7 mg, 3 equiv.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.5 mL), methyl arene **4a** (1.9 mL, 18.0 mmol, 90 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added Borosilicate Glass Tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred for 40 h 110 ℃ using oil bath. Reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc = 200 : 1 to 100 : 1), benzylated-TEMPO was obtained as colorless oil (46.9 mg, 35% yield). The spectrum data of benzylated-TEMPO is in agreement with the literature. [48]

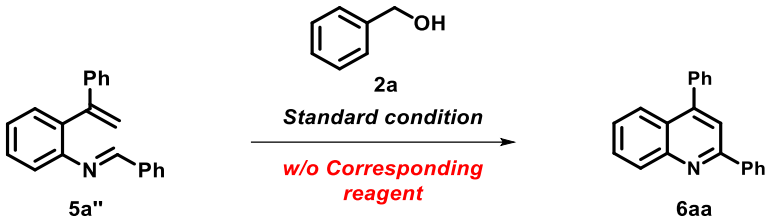
1-(benzyloxy)-2,2,6,6-tetramethylpiperidine (benzylated-TEMPO)

: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.32 (m, 4H), 7.30-7.26 (m, 1H), 4.83 (s, 2H), 1.65-1.41 (m, 6H), 1.36 (dt, *J* = 12.0, 3.5 Hz, 1H), 1.26 (s, 6H), 1.15 (s, 6H).

benzylated TEMPO ^{1}H NMR (400 MHz, $CDCl_3$)



2.7. Control experiment (Table 6)



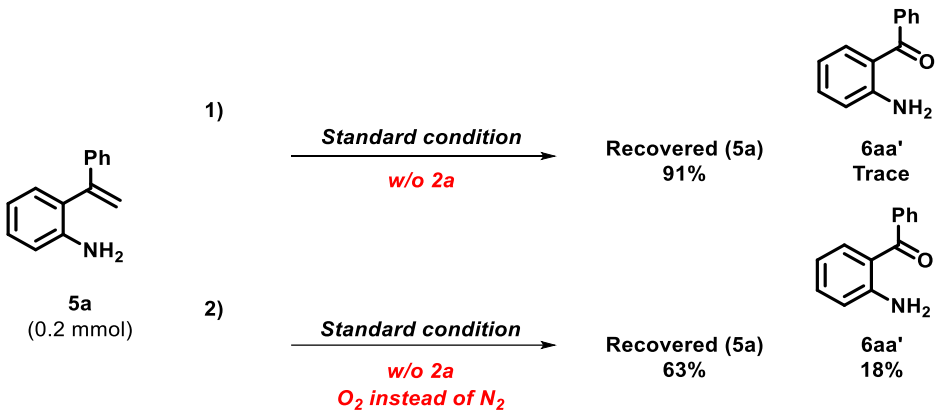
Substrate **5a''** (56.7 mg, 0.2 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.5 mL), and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 90 ℃ using oil bath (excluding the reagent according to each equation). After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (10 mL), dried over anhydrous $MgSO_4$, After purification by column chromatography (hexane : EtOAc = 100 : 1), **6aa** was obtained as white solid depending on the reaction conditions. (Entry 1 : 46.3 mg, 82% yield; Entry 2 : 31.4 mg, 56% yield; Entry 3 : 10.3 mg, 18% yield; Entry 4 : N.D).

Experimental procedure of Entry 1 with TEMPO

Substrate **5a''** (56.7 mg, 0.2 mmol,1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.), and TEMPO (95.7 mg, 0.6 mmol, 3 equiv.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.5

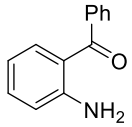
mL), and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 90 ℃ using oil bath (excluding the reagent according to each equation). After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (10 mL), dried over anhydrous $MgSO_4$, After purification by column chromatography (hexane : EtOAc = 100 : 1), **6aa** was obtained as white solid (4.0 mg, 7% yield).

2.8. Observation of side product by oxidative cleavage (Scheme 29)



Substrate **5a** (39.1 mg, 0.2 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon or O_2 balloon. DMSO (0.5 mL), and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon or O_2 balloon, and then the mixture was stirred at 90 ℃ using

oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (10 mL), dried over anhydrous $MgSO_4$, After purification by column chromatography (hexane : EtOAc = 100 : 1 to 20 : 1), **6aa′** was obtained as yellow solid (trace amount, under N_2 condition; 7.2 mg, 18% yield, under O_2 condition).

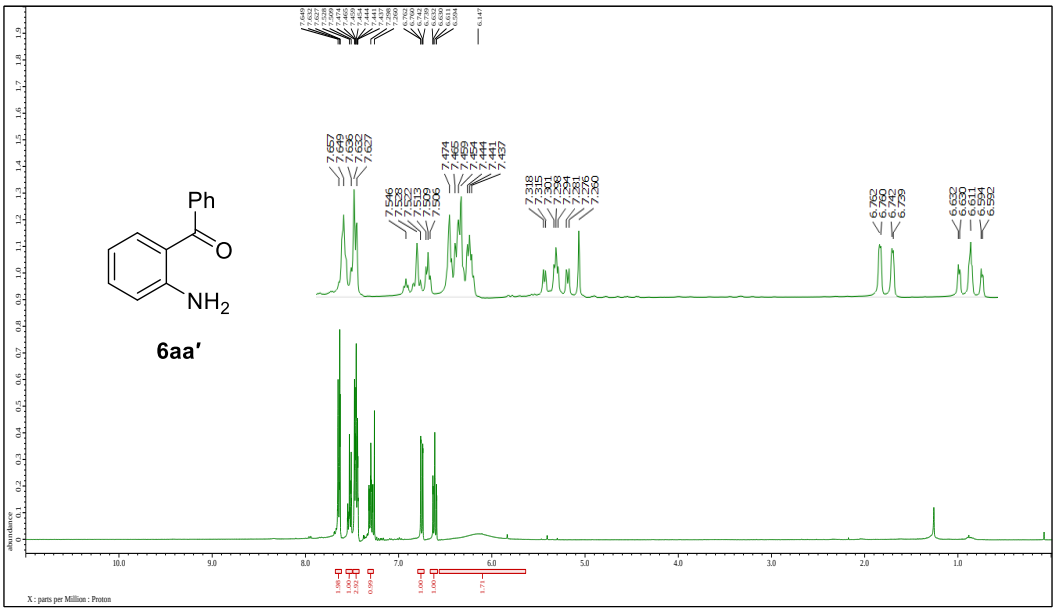


6aa′

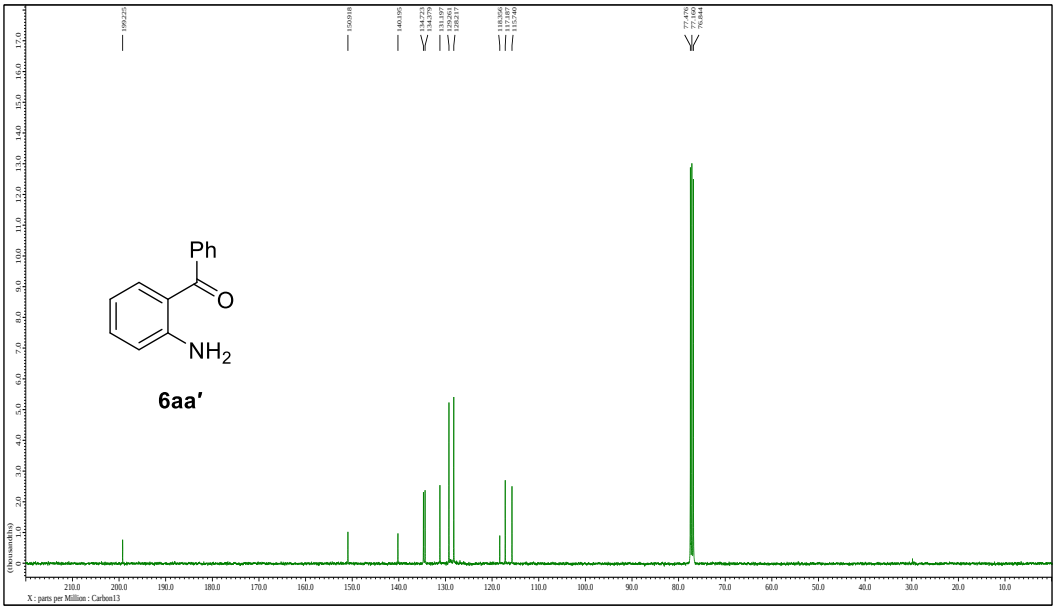
(2-Aminophenyl)(phenyl)methanone (6aa′).

mp = 105-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.63 (m, 2H), 7.55-7.51 (m, 1H), 7.47-7.43 (m, 3H), 7.32-7.28 (m, 1H), 6.75 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.63-6.59 (m, 1H), 6.15 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 199.2, 150.9, 140.2, 134.7, 134.4, 131.2, 129.3, 128.2, 118.4, 117.2, 115.7; IR (neat) υ 3057, 1616, 1579, 1548, 1448, 1269, 752, 644 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{13}H_{12}NO$ 198.0919; Found 198.0915.

6aa′ ^{1}H NMR (400 MHz, $CDCl_3$)

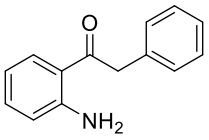


6aa′ ^{13}C NMR (100 MHz, $CDCl_3$)

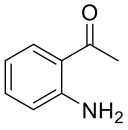


3. Synthesis of 4-quinolones

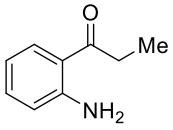
List of substrates



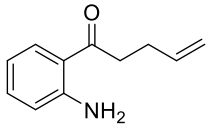
1a



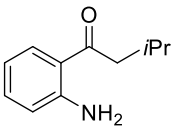
1b



1c



1d



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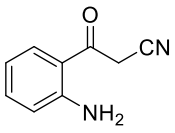
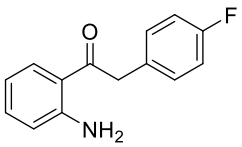
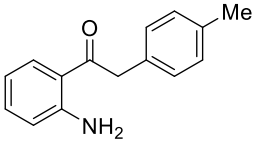


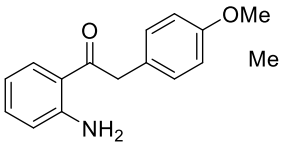
1f



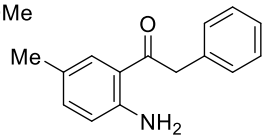
1g



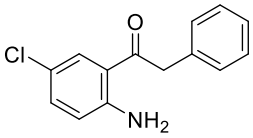
1h



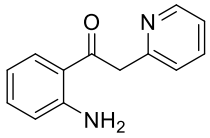
1i



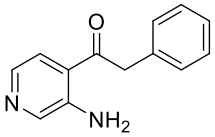
1j



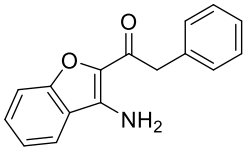
1k



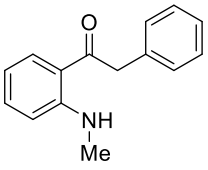
1l



1m



1n



1o

1b is commercially available. Other substrates were synthesized following the known method or modified method in literature.

3.1 Synthetic procedures for amino ketones

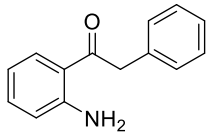
3.1.1. Synthesis of substrates: 1a, 1h-1i, 1k-1m[49]

Preparation of Grignard reagent

Magnesium turnings (4.75 equiv.), iodine crystalline (1 piece, catalytic amount) and dry THF (1.0 M) were added to an oven-dried 2-necked round bottom flask under argon gas. Benzyl halide (4.75 equiv.) was added to a stirred mixture and then, reaction mixture was heated to 60 ℃ using oil bath and stirred for 1.5 h. After the reaction mixture was cooled to room temperature, a freshly prepared grignard was directly used in next reaction.

Synthetic procedure

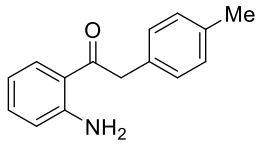
Grignard reagent (4.75 equiv.) was added dropwise to a solution of benzonitrile (1.0 equiv.) in dry THF (0.5 M) for 1 h using syringe pump. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl was added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel. Additional recrystallization was performed according to need.



1a

1-(2-aminophenyl)-2-phenylethan-1-one (1a)

: Following the above procedure, 2-aminobenzonitrile (1.6 g, 14.0 mmol, 1.0 equiv.), 1.4 M benzylmagnesium chloride in THF (47.0 mL, 66.5 mmol, 4.75 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 8:1:1), the compound was recrystallized from DCM and cooled hexane. **1a** was obtained as crystalline white solid (2.4 g, 78% yield); mp = 99-101 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.91 (dd, J = 8.2, 1.4 Hz, 1H), 7.19-7.32 (m, 8H), 6.74-6.76 (m, 1H), 6.53 (td, J = 7.5, 1.4 Hz, 1H), 4.26 (s, 2H); ^{13}C-NMR (100 MHz, DMSO- d_6) δ 199.6, 151.6, 136.1, 134.2, 131.9, 129.5, 128.3, 126.3, 117.0, 116.0, 114.4, 45.4; IR (neat) υ 3021, 1658, 1614, 1577, 1485, 1453, 1148, 745, 726 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}NO$ 212.1075; Found 212.1075.

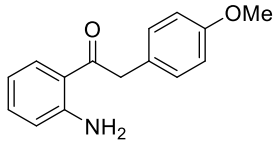


1h

1-(2-aminophenyl)-2-(p-tolyl)ethan-1-one (1h)

: Grignard reagent was prepared from magnesium turnings (469.8 mg, 20.0 mmol, 4.75 equiv.), 4-methylbenzyl chloride (2.8 g, 20.0 mmol, 4.75 equiv.). Following the above procedure, 2-aminobenzonitrile (501.2 mg, 4.2 mmol, 1.0 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 12:1:1), the compound was recrystallized from DCM and cooled hexane. **1h** was obtained as crystalline white solid (722.4 mg, 76% yield); mp = 81-83 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.89-7.81 (1H), 7.16-7.20 (m, 3H), 7.08 (q, J = 7.9 Hz, 4H), 6.69-6.71 (m, 1H), 6.46-6.50 (m, 1H), 4.15 (s, 2H), 2.21 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 161.8, 154.4, 148.7, 136.1, 134.5, 134.2, 130.5, 129.9, 129.1, 127.4, 126.6, 125.8, 125.7,

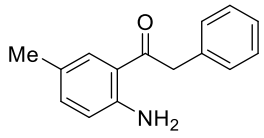
121.0, 19.6; IR (neat) υ 3048, 1661, 1616, 1486, 1452, 1158, 982, 775, 774 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO$ 226.1232; Found 226.1233.



1i

1-(2-aminophenyl)-2-(4-methoxyphenyl)ethan-1-one (1i)

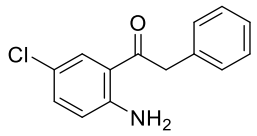
: Grignard reagent was prepared from magnesium turnings (469.8 mg, 20.0 mmol, 4.75 equiv.), 4-methoxybenzyl chloride (2.7 mL, 20.0 mmol, 4.75 equiv.). Following the above procedure, 2-aminobenzonitrile (501.2 mg, 4.2 mmol, 1.0 equiv) was used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 7:1:1), **1i** was obtained as beige solid (311.0 mg, 31% yield); mp = 98–100 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.89 (dd, J = 8.6, 1.2 Hz, 1H), 7.15-7.24 (m, 5H), 6.86 (td, J = 5.8, 3.5 Hz, 2H), 6.74 (d, J = 8.6 Hz, 1H), 6.50-6.55 (m, 1H), 4.17 (s, 2H), 3.71 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 199.9, 157.8, 151.6, 134.1, 131.9, 130.4, 127.9, 117.0, 116.0, 114.3, 113.7, 55.0, 44.5; IR (neat) υ 3048, 1662, 1578, 1548, 1332, 1244, 1034, 786, 754 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_2$ 242.1181; Found 242.1178.



1k

1-(2-amino-5-methylphenyl)-2-phenylethan-1-one (1k)

: Following the above procedure, 2-amino-5-methylbenzonitrile (512.8 mg, 4.0 mmol, 1.0 equiv.) and 1.4 M benzylmagnesium chloride in THF (13.6 mL, 19.0 mmol, 4.75 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 12:1:1), the compound was recrystallized from DCM and cooled hexane. **1k** was obtained as crystalline white solid (854.3 mg, 95% yield); crystalline white solid; mp = 103-105 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.72 (s, 1H), 7.19-7.32 (m, 5H), 7.08 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.03 (s, 2H), 6.72-6.65 (m, 1H), 4.26 (s, 2H), 2.18 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 199.4, 149.5, 136.2, 135.5, 131.1, 129.5, 128.2, 126.2, 122.7, 117.2, 116.0, 45.2, 20.0; IR (neat) υ 3017, 1661, 1624, 1578, 1490, 1159, 818, 721, 617 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO$ 226.1232; Found 226.1234.

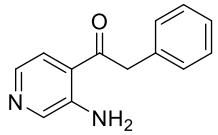


1l

1-(2-amino-5-chlorophenyl)-2-phenylethan-1-one (1l)

: Following the above procedure, 2-amino-5-chlorobenzonitrile (740.0 mg, 5.0 mmol, 1.0 equiv.) and 1.4 M benzylmagnesium chloride in THF (16.8 mL, 23.8 mmol, 4.75 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 12:1:1), the compound was recrystallized from DCM and cooled hexane. **1l** was obtained as crystalline yellow solid (994.6 mg, 81% yield); mp = 118-120 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.17 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.81-7.86 (m, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.50-7.56 (m, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.33 (dd, *J* = 12.7, 6.9 Hz, 2H), 2.39 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 161.8, 154.4, 148.7, 136.1, 134.5, 134.2, 130.5, 129.9, 129.1, 127.4, 126.6, 125.8, 125.7, 121.0, 19.6; IR

(neat) υ 3030, 1646, 1610, 1577, 1517, 1475, 1032, 1009, 814 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}ClNO$ 246.0686; Found 246.0688.



1m

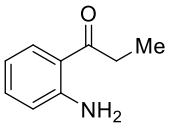
1-(3-aminopyridin-4-yl)-2-phenylethan-1-one (1m)

: Following the above procedure, 3-amino-4-cyanopyridine (288.9 mg, 2.5 mmol, 1.0 equiv.) and 1.4 M benzylmagnesium chloride in THF (8.4 mL, 11.8 mmol, 4.75 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 8:1:1), the compound was recrystallized from DCM and cooled hexane. **1m** was obtained as crystalline yellow solid (149.4 mg, 28% yield); mp = 83-85 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.25 (s, 1H), 7.75 (dd, *J* = 15.3, 5.5 Hz, 2H), 7.29-7.33 (m, 2H), 7.21-7.26 (m, 3H), 7.16 (s, 2H), 4.33 (s, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 200.4, 145.0, 141.8, 135.2, 134.8, 129.7, 128.3, 126.5, 122.9, 118.9, 45.2; IR (neat) υ 3063, 1655, 1602, 1533, 1424, 1187, 1086, 1053, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2O$ 213.1028; Found 213.1028.

3.1.2. Synthesis of substrates: 1c, 1d[50]

Grignard reagent (4.75 equiv.) was added dropwise to a solution of 2-aminobenzonitrile (1.0 equiv.) in dry THF (0.2 M) at 0 ℃ for 0.5 h using syringe pump. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl added (adjusted with pH

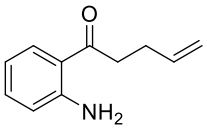
1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel.



1c

1-(2-aminophenyl)propan-1-one (1c)

: Following the above procedure, 2-aminobenzonitrile (935.7 mg, 8.0 mmol, 1.0 equiv.) and 0.9 M ethylmagnesium bromide in THF (26.7 mL, 38.0 mmol, 4.75 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 15:1), **1c** was obtained as pale yellow solid (1.01 g, 85% yield); mp = 37-39 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.76 (d, J = 8.0 Hz, 1H), 7.20-7.24 (m, 1H), 7.17 (s, 2H), 6.74 (d, J = 7.3 Hz, 1H), 6.51-6.55 (m, 1H), 2.94 (q, J = 7.1 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 202.5, 151.0, 133.9, 131.2, 116.9, 116.4, 114.4, 31.6, 8.8; IR (neat) υ 3064, 1658, 1630, 1581, 1552, 1443, 1208, 955, 755 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_9H_{12}NO$ 150.0919; Found 150.0923.



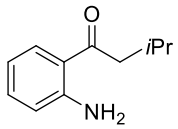
1d

1-(2-aminophenyl)pent-4-en-1-one (1d)

: Grignard reagent was prepared from magnesium turnings (313.2 mg, 13.3 mmol, 4.75 equiv.) and 4-bromo-1-butene (1.8 mL, 13.3 mmol, 4.75 equiv.). Following the above

procedure, 2-aminobenzonitrile (334.1 mg, 2.8 mmol, 1.0 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc = 15:1), **1d** was obtained as yellow oil (429.0 mg, 87% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.74-7.76 (m, 1H), 7.24-7.28 (m, 1H), 6.64-6.68 (m, 2H), 5.86-5.96 (m, 1H), 5.07-5.12 (m, 1H), 5.00-5.03 (m, 1H), 3.05 (t, *J* = 7.7 Hz, 2H), 2.45-2.50 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 202.0, 150.3, 137.7, 134.4, 131.2, 118.2, 117.6, 116.1, 115.3, 38.5, 28.8; IR (neat) υ 3054, 1646, 1560, 1530, 1345, 1253, 1154, 760, 692 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}NO$ 176.1075; Found 176.1075.

3.1.3. Synthesis of 1-(2-aminophenyl)-3-methylbutan-1-one (1e)

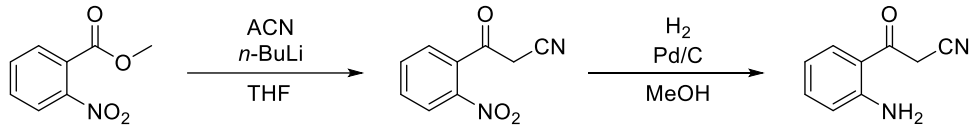


1e

The magnesium turnings (203.5 mg, 8.6 mmol, 1.2 equiv.), iodine crystalline (1 piece, catalytic amount) and dry THF (8.6 mL) were added to an oven-dried 2-necked round bottom flask under argon gas. Bromo-2-methylpropane (1.36 mL, 8.6 mmol, 1.2 equiv.) was added to a stirred mixture and then, reaction mixture was heated to 60 ℃ using oil bath and stirred for 1.5 h. After the reaction mixture was warmed to room temperature, freshly prepared Grignard reagent was added dropwise to a solution of methyl anthranilate (1.1 g, 7.2 mmol, 1.0 equiv.) in dry THF (14.4 mL) at 0 ℃ for 0.5 h by syringe pump. The reaction was allowed to stir for 8 h at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl was added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted

with EtOAc (2 x 40 mL). The organic layer was washed with brine (30 mL), dried over anhydrous Mg_2SO_4 and concentrated. The residues were purified by flash column chromatography on silica gel, using hexane and EtOAc (15:1). **1e** was obtained as pale yellow oil (327.7 mg, 27% yield); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.74 (dd, J = 7.9, 1.2 Hz, 1H), 7.19-7.24 (m, 3H), 6.73-6.75 (m, 1H), 6.50-6.54 (m, 1H), 2.77 (d, J = 6.7 Hz, 2H), 2.07-2.17 (m, 1H), 0.92 (d, J = 6.7 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 202.0, 151.1, 133.9, 131.4, 117.0, 116.8, 114.3, 47.4, 25.2, 22.6; IR (neat) υ 3049, 1644, 1548, 1506, 1484, 1465, 1210, 946, 748 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{11}H_{16}NO$ 178.1232; Found 178.1232.

3.1.4. Synthesis of 3-(2-aminophenyl)-3-oxopropanenitrile (1f)[51]



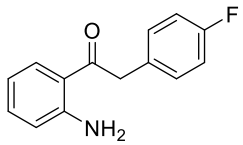
1f

Acetonitrile (0.9 mL, 16.6 mmol, 2.0 equiv.) and dry THF (10.0 mL) were added to an oven-dried round bottom flask under argon gas. The mixture was cooled to -78 ℃ and then, 2.5 M *n*-BuLi in hexane (16.6 mL, 16.6 mmol, 2.0 equiv.) was added to a stirred mixture. After 1 h, methyl-2-nitrobenzoate (1.2 mL, 8.3 mmol, 1.0 equiv.) in THF (5.0 mL) was added dropwise for 15 min by syringe pump. The reaction mixture was stirred for 1 h, and then stirred for further 2 h at -45 ℃. Upon the completion of reaction, mixture was quenched 1 M HCl (25 mL). The mixture was extracted with EtOAc (4 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel using hexane and EtOAc (5:1 to 3:1). 3-(2-nitrophenyl)-3-oxopropanenitrile was obtained as

red solid (1.1 g, 69% yield); mp = 90-92 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26-8.28 (m, 1H), 7.82-7.86 (m, 1H), 7.72-7.76 (m, 1H), 7.47 (dd, *J* = 7.4, 1.2 Hz, 1H), 3.90 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.2, 145.3, 135.4, 134.8, 132.1, 127.7, 124.9, 113.3, 32.6; IR (neat) υ 2975, 2907, 1718, 1526, 1388, 1342, 1325, 744, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_9H_7N_2O_3$ 191.0457, Found 191.0467.

3-(2-nitrophenyl)-3-oxopropanenitrile (800.0 mg, 4.2 mmol, 1.0 equiv.), 10% Pd/C (156.8 mg, 1.5 mmol, 0.35 equiv.) and MeOH (18.0 mL) were added to an oven-dried round bottom flask under argon gas. A reaction vessel was charged with H_2 balloon and stirred for 3 h at room temperature. Upon the completion of reaction, mixture was filtered on celite using DCM. A mixture was concentrated and then, purified by flash column chromatography on silica gel using hexane and EtOAc (3:1). **1f** was obtained as pale yellow solid (560.2 mg, 84% yield); mp = 92-94 °C; ^{1}H-NMR (400 MHz, DMSO-*d*$_6$) δ 7.56 (d, *J* = 7.9 Hz, 1H), 7.27-7.31 (m, 3H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.54 (t, *J* = 7.6 Hz, 1H), 4.63 (s, 2H); ^{13}C-NMR (100 MHz, DMSO-*d*$_6$) δ 190.2, 151.6, 135.2, 131.5, 117.1, 116.4, 114.6, 114.5, 30.4; IR (neat) υ 3076, 1649, 1617, 1586, 1548, 1451, 1209, 1159, 845, 931, 744 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_9H_9N_2O$ 161.0715; Found 161.0715.

3.1.5. Synthesis of 1-(2-aminophenyl)-2-(4-fluorophenyl)ethan-1-one (1g)

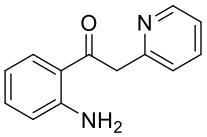


1g

The magnesium turnings (188.4 mg, 8.0 mmol, 4.75 equiv.), iodine crystalline (1 piece,

catalytic amount) and dry Et_2O (8.0 mL) were added to an oven-dried 2-necked round bottom flask under argon gas. 4-fluorobenzyl bromide (1.0 mL, 8.0 mmol, 4.75 equiv.) was added to a stirred mixture and then, reaction mixture was heated to 35 ℃ using oil bath and stirred for 1.5 h. After the reaction mixture was cooled to room temperature, freshly prepared Grignard reagent was added dropwise to a solution of 2-aminobenzonitrile (200.5 mg, 1.68 mmol, 1.0 equiv.) in dry Et_2O (8.4 mL) at -78 ℃ for 1 h using syringe pump. The reaction was allowed to stir for 18 h at 55 ℃ using oil bath. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl was added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4 and concentrated. The residues were purified by flash column chromatography on silica gel using hexane, EtOAc and DCM (10:1:1) to afford desired product. **1g** was obtained as beige solid (121.2 mg, 31% yield); mp = 97-99 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.90 (dd, J = 8.3, 1.5 Hz, 1H), 7.22-7.30 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 7.12 (tt, J = 9.2, 2.6 Hz, 2H), 6.75 (d, J = 8.6 Hz, 1H), 6.52-6.57 (m, 1H), 4.28 (s, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 199.5, 161.0 (d, J_{CF} = 239.6 Hz), 151.5, 134.3, 132.2 (d, J_{CF} = 3.8 Hz), 131.8, 131.5 (d, J_{CF} = 7.6 Hz), 117.0, 116.0, 114.9 (d, J_{CF} = 20.1 Hz), 114.4, 44.3; ^{19}F-NMR (376 MHz, DMSO-d_6) δ -116.81; IR (neat) υ 3029, 1656, 1647, 1578, 1452, 1159, 1032, 791, 749 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}FNO$ 230.0981; Found 230.0982.

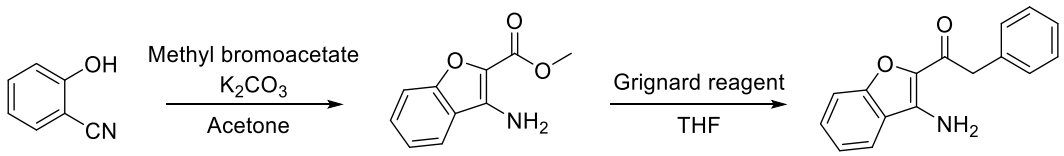
3.1.6. Synthesis of 1-(2-aminophenyl)-2-(pyridin-2-yl)ethan-1-one (1j)



1j

2-picoline (2.2 mL, 22.5 mmol, 4.5 equiv.) and dry THF (15.0 mL) were added to an oven-dried round bottom flask under argon gas. The mixture was cooled to -78 ℃, and then 2.5 M *n*-BuLi in hexane (9.0 mL, 22.5 mmol, 4.5 equiv.) was added to a stirred mixture. The reaction mixture was warmed to room temperature, and stirred for 10 h. The mixture was diluted with dry THF (15 mL), and then 2-aminobenzonitrile (596.7 mg, 5.0 mmol, 1.0 equiv.) in THF (15.0 mL) was added slowly at -78 ℃ for 1 h using syringe pump. The mixture was stirred for 9 h at room temperature. Upon the completion of reaction, the mixture was poured into a crushed ice and 1 M HCl added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 40 mL). The organic layer was washed with brine (40 mL), dried over anhydrous Mg_2SO_4, and concentrated. The residues were purified by flash column chromatography on silica gel using hexane and EtOAc (4:1). **1j** was obtained as yellow oil (1.06 g, 90% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.91 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.65 (td, *J* = 7.7, 1.7 Hz, 1H), 7.28-7.31 (m, 1H), 7.26 (td, *J* = 7.7, 2.0 Hz, 1H), 7.16-7.19 (m, 1H), 6.63-6.67 (m, 2H), 6.29 (s, 2H), 4.48 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 199.2, 156.1, 151.0, 149.7, 136.7, 134.7, 132.1, 124.3, 121.9, 117.7, 117.4, 116.0, 49.3, 19.6; IR (neat) υ 3011, 1646, 1534, 1524, 1339, 1253, 1054, 921, 692 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2O$ 213.1028; Found 213.1034.

3.1.7 Synthesis of 1-(3-aminobenzofuran-2-yl)-2-phenylethan-1-one (1n)



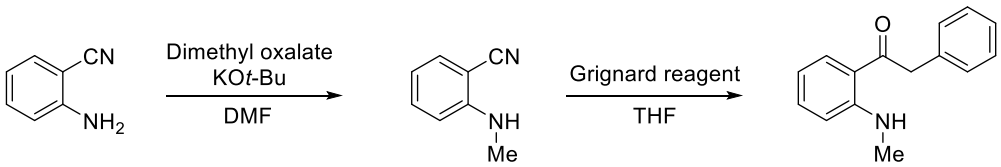
1n

2-cyanophenol (2.0 g, 16.5 mmol, 1.0 equiv.), K_2CO_3 (2.8 g, 19.8 mmol, 1.2 equiv.) and dry acetone (80 mL) were added to an oven-dried round bottom flask under argon gas. The reaction mixture was cooled to 0 ℃, and then methyl bromoacetate (1.7 mL, 18.2 mmol, 1.1 equiv.) was added dropwise to a reaction mixture. The reaction mixture was stirred for 4 h at 50 ℃ using oil bath. The mixture was cooled to room temperature and filtered using DCM. The mixture was concentrated, and then residues were recrystallized from DCM and cooled hexane. 3-aminobenzofuran-2-carboxylate was obtained as white solid (3.1 g, 98% yield); mp = 59-61 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.52 (td, *J* = 7.9, 1.8 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 4.79 (s, 2H), 3.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.4, 159.6, 134.4, 134.2, 122.1, 116.2, 112.4, 102.9, 65.8, 52.6; IR (neat) υ 2960, 2227, 1738, 1493, 1456, 1217, 1169, 763, 713 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{10}H_{10}NO_3$ 192.0661; Found 192.0663.

1.4 M Benyzlymagnesium chloride in THF (3.4 mL, 4.8 mmol, 1.2 equiv.) was added dropwise to a solution of 3-aminobenzofuran-2-carboxylate (741.8 mg, 4.0 mmol, 1.0 equiv.) in dry THF (12.0 mL) at -78 ℃ for 1 h using syringe pump. The reaction was allowed to stir for 2 h at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 40 mL). The organic layer

was washed with brine (30 mL), dried over anhydrous Mg_2SO_4 and concentrated. The residues were purified by flash column chromatography on silica gel using hexane and EtOAc (4:1). Recrystallization from DCM and cooled hexane to afford desired product. **1n** was obtained as whited solid (162.5 mg, 16% yield); mp = 59-61 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.74 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.57-7.62 (m, 1H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.25 (t, *J* = 8.3 Hz, 3H), 7.08 (q, *J* = 8.2 Hz, 2H), 5.18 (s, 2H), 3.92 (s, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 202.6, 159.5, 134.8, 133.7, 129.8, 128.3, 126.7, 121.4, 116.3, 113.0, 100.5, 72.0, 44.6; IR (neat) υ 3032, 1724, 1640, 1598, 1541, 1455, 1303, 753, 695 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}NO_2$ 252.1025; Found 252.1028.

3.1.8. Synthesis of 2-(methylamino)benzonitrile (1o)



1o

2-aminbenzonitrile (1.2 g, 10.0 mmol, 1.0 equiv.), dimethyl oxalate (1.6 mL, 15.0 mmol, 1.5 equiv.), KO*t*-Bu (1.5 g, 12.5 mmol, 1.25 equiv.) and dry DMF (7.5 mL) were added to an oven-dried round bottom flask under argon gas, and then reaction mixture was heated to 150 ℃ using oil bath. After stirring for 10 h, a mixture was diluted with EtOAc (2 x 40 mL) and washed with H_2O (2 x 40 mL). The organic layer was dried over anhydrous Mg_2SO_4 and concentrated. After purification by column chromatography (hexane : EtOAc = 15:1), 2-(methylamino)benzonitrile was obtained as white solid (812.2 mg, 61% yield); mp = 59-61 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.43 (m, 2H), 6.67

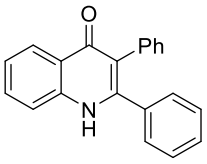
(dd, *J* = 13.4, 7.9 Hz, 2H), 4.65 (s, 1H), 2.93 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.3, 134.4, 132.8, 118.1, 116.5, 110.2, 95.6, 30.1; IR (neat) υ 3080, 1615, 1574, 1524, 1298, 1032, 1013, 932, 737 cm^{1}; HRMS (FAB) m/z: $[M]^+$ Calcd for $C_8H_8N_2$ 132.0687; Found 132.0690.

1.4 M Benyzlymagnesium chloride in THF (13.5 mL, 19.0 mmol, 4.75 equiv.) was added dropwise to a solution of 2-(methylamino)benzonitrile (512.8 mg, 4.0 mmol, 1.0 equiv.) in dry THF (12.0 mL) at -78 ℃ for 1 h using syringe pump. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 40 mL). The organic layer was washed with brine (30 mL), dried over anhydrous Mg_2SO_4 and concentrated. After purification by column chromatography (hexane : EtOAc = 15:1), **1o** was obtained as bright green solid (448.0 mg, 50% yield); mp = 67-69 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.68 (d, *J* = 4.3 Hz, 1H), 8.00 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.45-7.36 (1H), 7.19-7.32 (m, 5H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.59 (t, *J* = 7.0 Hz, 1H), 4.29 (s, 2H), 2.82 (d, *J* = 5.5 Hz, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 199.9, 151.8, 136.1, 135.1, 132.6, 129.4, 128.3, 126.3, 116.3, 113.8, 111.3, 45.3, 29.0; IR (neat) υ 3057, 1628, 1477, 1423, 1257, 1116, 1053, 1013, 744 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO$ 226.1232; Found 226.1233.

3.2. General procedure of 4-quinolones

3.2.1. General procedure A using alcohols

Substrate **1** (0.2 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.8 mL), alcohol **2** (1.0 mmol, 5.0 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 110 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residues were purified by flash column chromatography on silica gel. If the residues are not well soluble in an organic solvent, the purification process was carried out by filtration instead of a column chromatography.

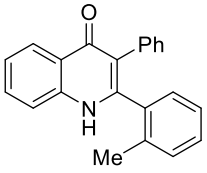


3aa

2,3-diphenylquinolin-4(1H)-one (3aa)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3aa** was obtained as white solid (54.9

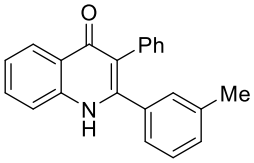
mg, 92% yield); mp = 338-340 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.79 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.65-7.71 (m, 2H), 7.31-7.37 (m, 6H), 7.05-7.18 (m, 5H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 148.5, 139.7, 135.7, 135.2, 131.7, 131.7, 129.5, 128.9, 128.1, 127.2, 126.0, 125.3, 124.7, 123.2, 120.5, 118.4; IR (neat) υ 3019, 1623, 1553, 1514, 1377, 1348, 1308, 758, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}NO$ 298.1232; Found 298.1231.



3ab

3-phenyl-2-(o-tolyl)quinolin-4(1H)-one (3ab)

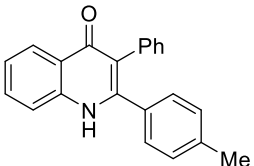
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 2-methylbenzyl alcohol **2b** (124.6 mg, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 3:1:1), **3ab** was obtained as white solid (55.4 mg, 89% yield); mp = 338-340 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.17 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.62-7.69 (m, 2H), 7.33-7.37 (m, 1H), 7.24-7.29 (m, 2H), 7.18 (t, *J* = 7.1 Hz, 2H), 7.10-7.14 (m, 2H), 7.04-7.08 (m, 2H), 2.11 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 148.2, 139.6, 135.5, 134.8, 131.7, 131.1, 130.0, 129.9, 129.0, 127.0, 126.0, 125.4, 125.4, 124.7, 123.1, 121.1, 118.3, 19.2; IR (neat) υ 3024, 1658, 1580, 1509, 1351, 1310, 1289, 761, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1387.



3ac

3-phenyl-2-(m-tolyl)quinolin-4(1H)-one (3ac)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 3-methylbenzyl alcohol **2c** (120.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 3:1:1), **3ac** was obtained as white solid (49.2 mg, 79% yield); mp = 333-335 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.77 (s, 1H), 8.15 (d, *J* = 7.4 Hz, 1H), 7.68 (dd, *J* = 15.6, 6.9 Hz, 2H), 7.33-7.37 (m, 1H), 7.22 (s, 1H), 7.09-7.19 (m, 5H), 7.01-7.07 (m, 3H), 2.25 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 148.6, 139.7, 137.3, 135.8, 135.2, 131.7, 129.9, 129.6, 127.9, 127.3, 126.9, 126.0, 125.4, 124.6, 123.2, 120.4, 118.4, 20.9; IR (neat) υ 3019, 1621, 1603, 1549, 1307, 1287, 1199, 784, 716 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1394.

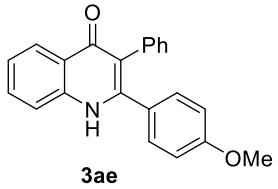


3ad

3-phenyl-2-(p-tolyl)quinolin-4(1H)-one (3ad)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-Methylbenzyl alcohol **2d** (118.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 3:1:1), **3ad** was obtained as white solid (54.2 mg, 87% yield); mp = 327-329 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.72 (s, 1H), 8.14

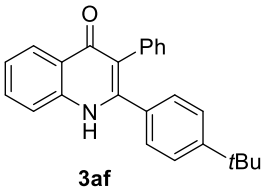
(d, *J* = 7.8 Hz, 1H), 7.64-7.70 (m, 2H), 7.32-7.36 (m, 1H), 7.10-7.21 (m, 7H), 7.05-7.07 (m, 2H), 2.28 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 148.5, 139.7, 138.5, 135.9, 132.4, 131.7, 129.5, 128.6, 127.3, 126.0, 125.3, 124.6, 123.1, 120.4, 118.4, 20.8; IR (neat) υ 3060, 1611, 1552, 1510, 1379, 1284, 1180, 876, 761 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1391.



3ae

2-(4-methoxyphenyl)-3-phenylquinolin-4(1H)-one (3ae)

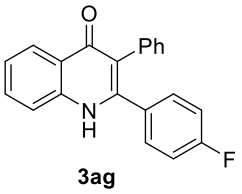
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-Methoxybenzyl alcohol **2e** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3ae** was obtained as white solid (12.6 mg, 19% yield); mp = 348-350 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 8.14 (d, *J* = 7.3 Hz, 1H), 7.64-7.74 (m, 2H), 7.32 (d, *J* = 1.2 Hz, 1H), 7.24 (d, *J* = 9.2 Hz, 2H), 7.16-7.20 (m, 2H), 7.10-7.14 (m, 1H), 7.06-7.08 (m, 2H), 6.88 (d, *J* = 9.2 Hz, 2H), 3.74 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 159.6, 148.3, 139.7, 136.0, 131.7, 131.6, 131.0, 127.4, 127.3, 125.9, 125.3, 124.6, 123.1, 120.3, 118.4, 113.5, 55.2; IR (neat) υ 3056, 1622, 1541, 1534, 1351, 1288, 1151, 946, 760 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO_2$ 328.1338; Found 328.1336.



3af

2-(4-(tert-butyl)phenyl)-3-phenylquinolin-4(1H)-one (3af)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-*tert*-butylbenzyl alcohol **2f** (179.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 3:1:1), **3af** was obtained as white solid (54.9 mg, 79% yield); mp = 344-346 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.72 (s, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.64-7.70 (m, 2H), 7.32-7.37 (m, 3H), 7.25 (dd, *J* = 6.4, 1.8 Hz, 2H), 7.10-7.19 (m, 3H), 7.06-7.08 (m, 2H), 1.24 (s, 9H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 151.5, 148.4, 139.7, 135.8, 132.4, 131.7, 131.7, 129.3, 127.1, 126.0, 125.3, 124.9, 124.6, 123.1, 120.3, 118.4, 34.4, 31.0; IR (neat) υ 3030, 1658, 1558, 1532, 1325, 1232, 1108, 943, 718 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

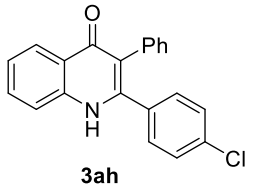


3ag

2-(4-fluorophenyl)-3-phenylquinolin-4(1H)-one (3ag)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-fluorobenzyl alcohol **2g** (112.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ag** was obtained as white solid (58.8 mg, 93% yield); mp = 353-355 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ

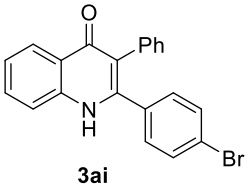
11.82 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 3.2 Hz, 2H), 7.33-7.39 (m, 3H), 7.10-7.20 (m, 5H), 7.06 (dd, *J* = 8.0, 1.1 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 162.2 (d, J_{CF} = 244.4 Hz), 147.6, 139.7, 135.7, 132.0 (d, J_{CF} = 8.6 Hz), 131.8, 131.7, 131.6 (d, J_{CF} = 2.8 Hz), 127.4, 126.1, 125.4, 124.7, 123.3, 120.6, 118.4, 115.1 (d, J_{CF} = 22.0 Hz); ^{19}F-NMR (376 MHz, DMSO-d_6) δ -112.01; IR (neat) υ 3064, 1606, 1551, 1513, 1350, 1291, 1159, 948, 762 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}FNO$ 316.1138; Found 316.1137.



3ah

2-(4-chlorophenyl)-3-phenylquinolin-4(1H)-one (3ah)

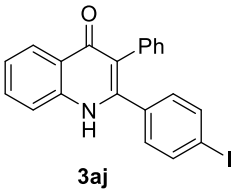
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-chlorobenzyl alcohol **2h** (143.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ah** was obtained as pale yellow solid (58.5 mg, 88% yield); mp = 377-379 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H), 8.09 (t, *J* = 0.9 Hz, 1H), 7.73 (d, *J* = 1.8 Hz, 2H), 7.31-7.36 (m, 5H), 7.09-7.18 (m, 3H), 7.04-7.06 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 147.3, 139.7, 135.5, 134.0, 133.8, 131.9, 131.7, 131.5, 128.2, 127.4, 126.2, 125.4, 124.7, 123.3, 120.6, 118.5; IR (neat) υ 3059, 1621, 1549, 1512, 1379, 1288, 1169, 941, 757 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}ClNO$ 332.0842; Found 332.0846.



3ai

2-(4-bromophenyl)-3-phenylquinolin-4(1H)-one (3ai)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-bromobenzyl alcohol **2i** (187.0 mg, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled DCM and filtered to afford desired product. **3ai** was obtained as pale yellow solid (54.9 mg, 80% yield); mp = 379-381 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.82 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.66-7.71 (m, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.34-7.38 (m, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.12-7.21 (m, 3H), 7.05-7.07 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 147.3, 139.7, 135.5, 134.4, 131.9, 131.7, 131.7, 131.1, 127.4, 126.2, 125.4, 124.7, 123.3, 122.5, 120.6, 118.4; IR (neat) υ 3059, 1621, 1547, 1512, 1348, 1288, 1170, 940, 757 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrNO$ 376.0337; Found 376.0343.

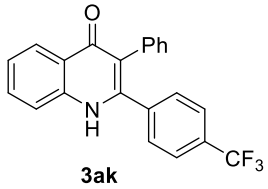


3aj

2-(4-iodophenyl)-3-phenylquinolin-4(1H)-one (3aj)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-iodobenzyl alcohol **2j** (241.3 mg, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled DCM and filtered to afford desired product. **3aj** was obtained as brown solid (59.0 mg, 70% yield); mp = 380-382 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6)

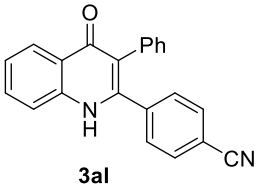
δ 12.52 (brs, 1H), 8.20-8.15 (m, 3H), 7.86-7.82 (m, 1H), 7.75-7.73 (m, 1H), 7.62-7.51 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 147.6, 139.7, 136.9, 135.5, 134.7, 131.9, 131.7, 131.7, 129.6, 127.4, 126.2, 125.4, 124.7, 123.3, 120.5, 118.5; IR (neat) υ 3056, 1601, 1545, 1509, 1347, 1288, 1151, 869, 758 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}INO$ 424.0198; Found: 424.0196.



3ak

3-phenyl-2-(4-(trifluoromethyl)phenyl)quinolin-4(1H)-one (3ak)

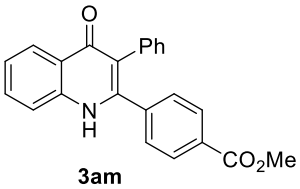
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-(Trifluoromethyl)benzyl alcohol **2k** (181.6 mg, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ak** was obtained as white solid (69.5 mg, 95% yield); mp = 356-358 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.66-7.73 (m, 4H), 7.54-7.60 (m, 2H), 7.35-7.39 (m, 1H), 7.11-7.20 (m, 3H), 7.09 (dd, J = 8.9, 7.0 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 147.0, 139.7, 139.3, 135.2, 132.0, 131.7, 130.6, 129.2 (q, J_{CF} = 31.6 Hz), 127.4, 126.8, 125.4, 125.0 (q, J_{CF} = 3.8 Hz), 124.7, 123.9 (q, J_{CF} = 271.1 Hz), 123.4, 118.5; ^{19}F-NMR (376 MHz, DMSO-d_6) δ -61.09; IR (neat) υ 3062, 1622, 1549, 1514, 1351, 1294, 1155, 945, 756 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}F_3NO$ 366.1106; Found 366.1106.



3al

4-(4-oxo-3-phenyl-1,4-dihydroquinolin-2-yl)benzonitrile (3al)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-cyanobenzyl alcohol **2l** (105.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3al** was obtained as yellow solid (57.2 mg, 88% yield); mp = 361-363 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.93 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.66-7.73 (m, 2H), 7.35-7.39 (m, 1H), 7.12-7.21 (m, 3H), 7.05-7.07 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 146.8, 139.8, 139.7, 135.1, 131.9, 131.7, 130.7, 127.4, 126.3, 125.3, 124.7, 123.4, 120.7, 118.5, 118.5, 118.3, 111.5; IR (neat) υ 3065, 1624, 1553, 1534, 1351, 1289, 1117, 912, 749 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}N_2O$ 323.1184; Found 323.1186.

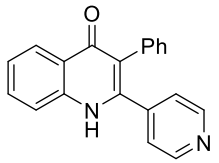


3am

methyl 4-(4-oxo-3-phenyl-1,4-dihydroquinolin-2-yl)benzoate (3am)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), methyl 4-(hydroxymethyl)benzoate **2m** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 1:2:1), **3am** was obtained as white solid (66.1 mg, 92% yield); mp = 312-314 ℃; ^{1}H-NMR (400 MHz,

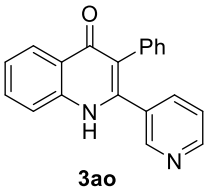
DMSO-d_6) δ 11.90 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.88 (d, J = 8.7 Hz, 2H), 7.67-7.72 (m, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.33-7.41 (m, 1H), 7.10-7.19 (m, 3H), 7.05 (dd, J = 8.0, 1.6 Hz, 2H), 3.84 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 162.3, 152.4, 148.7, 134.6, 132.7, 131.4, 128.6, 127.8, 127.5, 126.6, 125.9, 121.0; IR (neat) υ 3020, 1626, 1534, 1508, 1354, 1277, 1105, 859, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{23}H_{18}NO_3$ 356.1287; Found 356.1287.



3an

3-phenyl-2-(pyridin-4-yl)quinolin-4(1H)-one (3an)

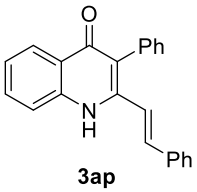
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 4-pyridinemethanol **2n** (110.2 mg, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:8), **3an** was obtained as white solid (38.4 mg, 64% yield); mp = 349-351 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.92 (s, 1H), 8.55 (q, J = 2.0 Hz, 2H), 8.17 (d, J = 7.3 Hz, 1H), 7.67-7.73 (m, 2H), 7.36-7.40 (m, 1H), 7.34 (q, J = 2.0 Hz, 2H), 7.13-7.22 (m, 3H), 7.08 (td, J = 4.1, 1.8 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 149.5, 145.9, 142.6, 139.7, 135.0, 132.0, 131.6, 127.4, 126.4, 125.4, 124.7, 124.2, 123.5, 120.7, 118.5; IR (neat) υ 3062, 1622, 1555, 1517, 1348, 1251, 1114, 988, 784 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2O$ 299.1184; Found 299.1185.



3ao

3-phenyl-2-(pyridin-3-yl)quinolin-4(1H)-one (3ao)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 3-pyridinemethanol **2o** (99.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 1:10:1), **3ao** was obtained as white solid (31.6 mg, 53% yield for 40 h); mp = 325-327 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 8.52 (td, J = 4.3, 1.7 Hz, 2H), 8.17 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.72-7.76 (m, 1H), 7.66-7.70 (m, 2H), 7.36-7.39 (m, 2H), 7.11-7.21 (m, 3H), 7.08 (dd, *J* = 8.0, 1.6 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 149.8, 149.7, 145.6, 139.8, 137.2, 135.3, 132.0, 131.8, 131.2, 127.4, 126.2, 125.4, 124.7, 123.5, 123.0, 121.1, 118.5; IR (neat) υ 3030, 1625, 1565, 1523, 1385, 1288, 1155, 943, 761 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2O$ 299.1184; Found 299.1178.

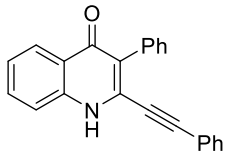


3ap

(E)-3-phenyl-2-styrylquinolin-4(1H)-one (3ap)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), cinnamyl alcohol **2p** (130.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3ap** was obtained as red brown solid (18.2 mg, 28% yield); mp = 305-307 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.45 (s, 1H),

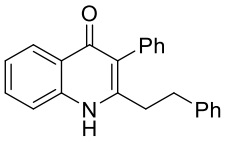
8.11 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.67-7.71 (m, 1H), 7.55 (d, *J* = 16.6 Hz, 1H), 7.28-7.45 (m, 11H), 6.77 (d, J = 16.6 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.4, 143.4, 139.7, 135.5, 135.2, 134.5, 131.9, 131.5, 129.2, 129.1, 127.7, 126.9, 125.3, 124.6, 122.9, 121.7, 121.4, 118.2; IR (neat) υ 3059, 1623, 1608, 1578, 1379, 1288, 1156, 967, 760 cm^{-1}; HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{23}H_{18}NO$ 324.1388; Found 324.1380.



3aq

3-phenyl-2-(phenylethynyl)quinolin-4(1H)-one (3aq)

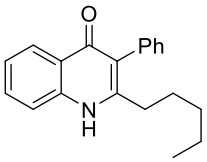
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 3-phenyl-2-propyn-1-ol **2q** (125.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3aq** was obtained as red brown solid (10.1 mg, 16% yield); mp = 168-170 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.20-8.22 (m, 1H), 8.16 (s, 1H), 7.72 (dt, *J* = 8.2, 1.7 Hz, 2H), 7.66 (td, *J* = 7.7, 1.8 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.33-7.41 (m, 2H), 7.28 (td, *J* = 7.4, 1.4 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 174.7, 139.8, 135.1, 132.3, 131.4, 131.1, 130.3, 130.2, 129.1, 127.4, 127.2, 125.5, 125.2, 124.9, 123.5, 120.5, 118.1, 96.7, 83.6; IR (neat) υ 3033, 1658, 1554, 1514, 1397, 1288, 1221, 964, 750 cm^{-1}; HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{23}H_{16}NO$322.1232; Found 322.1234.



3ar

2-phenethyl-3-phenylquinolin-4(1H)-one (3ar)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 3-phenyl-1-propanol **2r** (548.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3ar** was obtained as white solid (51.6 mg, 79% yield for 28 h); mp = 238-241 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.65 (s, 1H), 8.08 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.64-7.68 (m, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.37-7.41 (m, 2H), 7.28-7.35 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.13-7.17 (m, 3H), 6.95 (d, *J* = 8.2 Hz, 2H), 2.80-2.85 (m, 2H), 2.72-2.77 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 149.2, 140.4, 139.6, 136.1, 131.6, 131.0, 128.4, 128.0, 127.9, 126.6, 126.2, 125.3, 124.4, 122.8, 121.3, 117.8, 34.5, 34.0; IR (neat) υ 3059, 1623, 1534, 1534, 1354, 1255, 1156, 967, 760 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}NO$ 326.1545; Found 326.1539.

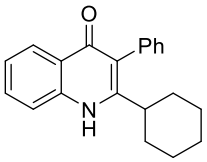


3as

2-pentyl-3-phenylquinolin-4(1H)-one (3as)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), 1-hexanol **2s** (512.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3as** was obtained as white solid (54.9

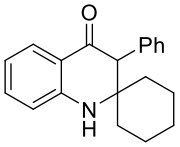
mg, 90% yield for 28 h); mp = 322-324 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.52 (s, 1H), 8.06 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.61-7.66 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.38-7.41 (m, 2H), 7.26-7.33 (m, 2H), 7.19-7.21 (m, 2H), 2.45-2.47 (m, 2H), 1.49-1.56 (m, 2H), 1.06-1.17 (m, 4H), 0.73-0.76 (m, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 150.4, 139.6, 136.3, 131.5, 131.0, 127.9, 126.6, 125.3, 124.3, 122.7, 121.0, 117.7, 31.6, 30.8, 28.2, 21.5, 13.7; IR (neat) υ 3064, 1630, 1607, 1552, 1490, 1351, 1118, 755, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{22}NO$ 292.1701; Found 292.1700.



3at

2-cyclohexyl-3-phenylquinolin-4(1H)-one (3at)

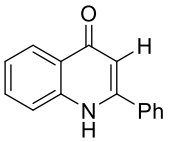
: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), cyclohexaemethanol **2t** (503.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3at** was obtained as white solid (28.8 mg, 47% yield for 28 h); mp = 279-281 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 1H), 8.05 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.61-7.65 (m, 1H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.30-7.34 (m, 1H), 7.26-7.30 (m, 1H), 7.22-7.13 (2H), 2.54 (dd, *J* = 12.3, 3.7 Hz, 1H), 1.60-1.85 (m, 7H), 1.25 (q, *J* = 13.1 Hz, 1H), 1.01 (q, *J* = 12.7 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.5, 153.6, 139.8, 136.6, 131.4, 130.8, 127.9, 126.6, 125.1, 124.2, 122.7, 120.3, 118.0, 40.7, 30.1, 25.9, 25.0; IR (neat) υ 3021, 1646, 1550, 1511, 1347, 1280, 1115, 955, 758 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}NO$ 304.1701; Found 304.1705.



3au

2,3-diphenylquinolin-4(1H)-one (3au)

: Following the general procedure A, **1a** (42.3 mg, 0.2 mmol), cyclohexanol **2u** (430.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc = 10:1), **3au** was obtained as pale yellow solid (26.5 mg, 45% yield for 28 h); mp = 128-130 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.35-7.39 (m, 1H), 7.19-7.25 (m, 4H), 6.71-6.76 (m, 2H), 4.48 (s, 1H), 3.55 (s, 1H), 1.94-1.98 (m, 1H), 1.46-1.59 (m, 5H), 1.31-1.43 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 194.1, 149.0, 135.7, 135.4, 129.7, 128.6, 128.3, 127.4, 117.9, 117.9, 115.9, 62.4, 56.7, 34.7, 33.5, 25.4, 21.8, 21.4; IR (neat) υ 3058, 1606, 1578, 1494, 1346, 1269, 1181, 930, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0868.

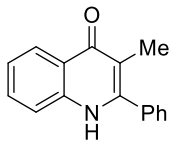


3ba

2-phenylquinolin-4(1H)-one (3ba)

: Following the general procedure A, **1b** (26.5 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:4), **3ba** was obtained as orange solid (20.1 mg, 45% yield); mp = 241-243 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.73 (s, 1H), 8.10 (dd,

J = 7.9, 1.2 Hz, 1H), 7.83 (q, *J* = 3.1 Hz, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.67 (td, *J* = 7.6, 1.2 Hz, 1H), 7.59 (t, *J* = 3.4 Hz, 3H), 7.34 (t, *J* = 7.3 Hz, 1H), 6.34 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 177.0, 150.1, 140.5, 134.3, 131.9, 130.5, 129.0, 127.5, 124.9, 124.8, 123.3, 118.8, 107.4; IR (neat) υ 3011, 1646, 1534, 1524, 1339, 1253, 1054, 921, 692 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}NO$ 222.0919; Found 222.0915.



3ca

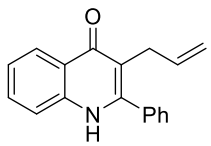
3-methyl-2-phenylquinolin-4(1H)-one (3ca)

: Following the general procedure A, **1c** (29.8 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:2), **3ca** was obtained as beige solid (35.8 mg, 76% yield); mp = 269-271 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.59 (s, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 7.54-7.64 (m, 7H), 7.28-7.33 (m, 1H), 1.89 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.7, 147.6, 139.5, 135.1, 131.2, 129.4, 128.9, 128.6, 124.9, 123.1, 122.6, 118.1, 114.3, 12.1; IR (neat) υ 3064, 1629, 1603, 1524, 1359, 1185, 1113, 760, 728 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}NO$ 236.1075; Found 236.1074.

*For the gram scale synthesis of **3ca***

Substrate **1c** (1.0 g, 6.7 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (898.8 mg, 20 mol%.) were added to an oven-dried 100 ml two-nected round bottom flask. The flask was capped with rubber septum and charged with N_2 balloon. DMSO (27 mL), benzyl alcohol **2a** (3.5 mL, 33.5 mmol, 5.0 equiv) and DTBP (3.7 mL, 20.1 mmol, 3.0 equiv.) were added to the flask.

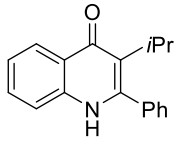
The flask was equipped with reflux condenser and recharged with N_2 Balloon. The reaction mixture was stirred at 110 ℃ using oil bath and monitored by TLC. After stirring for 24 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (30 mL) and H_2O (20 mL). The mixture was extracted with EtOAc (50 mL x 2). Combined organic phase was washed with H_2O (2 x 50 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residues were purified by flash column chromatography on silica gel using hexane, EtOAc and DCM (2:1:1 to 0.5:1:1) as the eluent. The product was further purified by recrystallization using cooled Et_2O. **3ca** was obtained as beige solid (1.23 g, 77% yield).



3da

3-allyl-2-phenylquinolin-4(1H)-one (3da)

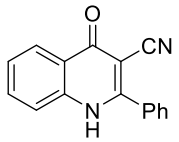
: Following the general procedure A, **1d** (35.1 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 3:1:1), **3da** was obtained as beige solid (39.8 mg, 76% yield); mp = 221-223 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.65 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.52-7.65 (m, 7H), 7.29-7.33 (m, 1H), 5.79-5.89 (m, 1H), 4.85 (dd, *J* = 10.4, 1.8 Hz, 1H), 4.73 (dd, *J* = 17.1, 1.8 Hz, 1H), 3.07 (d, *J* = 6.1 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.0, 148.7, 139.6, 137.2, 134.8, 131.5, 129.5, 128.7, 128.5, 125.0, 123.6, 122.9, 118.2, 116.5, 114.2, 30.0; IR (neat) υ 3061, 1627, 1542, 1501, 1357, 1234, 1184, 956, 759 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO$ 262.1232; Found 262.1235.



3ea

3-isopropyl-2-phenylquinolin-4(1H)-one (3ea)

: Following the general procedure A, **1e** (35.5 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 4:1:1), **3ea** was obtained as beige solid (31.8 mg, 60% yield for 40 h); mp = 253-255 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.43 (s, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.48-7.61 (m, 7H), 7.27 (td, *J* = 7.3, 1.2 Hz, 1H), 2.56-2.67 (m, 1H), 1.25 (d, *J* = 6.7 Hz, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.5, 147.7, 139.1, 135.7, 131.2, 129.2, 128.6, 128.5, 124.9, 124.6, 122.8, 122.5, 117.9, 28.8, 20.2; IR (neat) υ 3031, 1646, 1541, 1535, 1372, 1228, 1135, 968, 760 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO$ 264.1388; Found 264.1387.

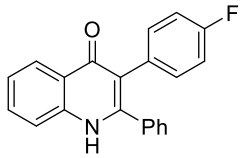


3fa

4-oxo-2-phenyl-1,4-dihydroquinoline-3-carbonitrile (3fa)

: Following the general procedure A, **1f** (32.0 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 1:1:1), **3fa** was obtained as yellow solid (41.6 mg, 84% yield); mp = 348-350 ℃; ^{1}H –NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.16

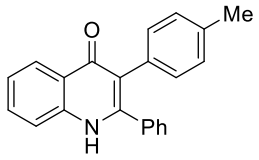
(dd, *J* = 7.9, 1.2 Hz, 1H), 7.81 (dt, *J* = 9.6, 2.9 Hz, 3H), 7.75 (d, *J* = 7.3 Hz, 1H), 7.63-7.72 (m, 3H), 7.49-7.53 (m, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.1, 157.2, 139.2, 133.5, 132.2, 131.5, 128.9, 128.8, 125.6, 124.9, 123.9, 119.5, 116.9, 93.5; IR (neat) υ 3065, 1658, 1565, 1541, 1317, 1268, 1136, 969, 763 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0868.



3ga

3-(4-fluorophenyl)-2-phenylquinolin-4(1H)-one (3ga)

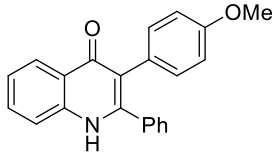
: Following the general procedure A, **1g** (45.9 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ga** was obtained as beige solid (60.4 mg, 96% yield); mp = 367-379 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.66-7.73 (m, 2H), 7.31-7.40 (m, 6H), 7.06-7.10 (m, 2H), 6.96-7.01 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 160.6 (d, J_{CF} = 240.6 Hz), 148.6, 139.6, 135.1, 133.5 (d, J_{CF} = 7.6 Hz) 132.0 (d, J_{CF} = 2.9 Hz), 131.8, 129.5, 129.1, 128.2, 125.3, 124.6, 123.3, 119.4, 118.4, 114.1 (d, J_{CF} = 21.0 Hz); ^{19}F-NMR (376 MHz, DMSO-d_6) δ -116.45; IR (neat) υ 3065, 1658, 1568, 1551, 1376, 1289, 1155, 946, 724 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}FNO$ 316.1138; Found 316.1135.



3ha

2-phenyl-3-(p-tolyl)quinolin-4(1H)-one (3ha)

: Following the general procedure A, **1h** (45.1 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ha** was obtained as pale yellow solid (56.7 mg, 91% yield); mp = 328-331 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.74 (s, 1H), 8.18-8.11 (1H), 7.71-7.62 (2H), 7.31-7.38 (m, 6H), 6.92-6.98 (m, 4H), 2.22 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.5, 148.3, 139.6, 135.3, 134.8, 132.6, 131.7, 131.5, 129.5, 128.9, 128.1, 127.9, 125.3, 124.6, 123.1, 120.3, 118.4, 20.7; IR (neat) υ 3015, 1621, 1551, 1522, 1348, 1287, 1149, 945, 756 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1389.

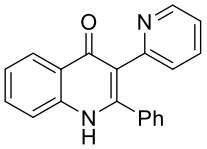


3ia

3-(4-methoxyphenyl)-2-phenylquinolin-4(1H)-one (3ia)

: Following the general procedure A, **1i** (48.3 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. The residues were directly recrystallized using cooled Et_2O and filtered to afford desired product. **3ia** was obtained as beige solid (65.6 mg, 92% yield); mp = 346-348 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.74 (s, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.63-7.69 (m, 2H), 7.31-7.37 (m, 6H), 6.99-6.94 (2H), 6.75-6.70

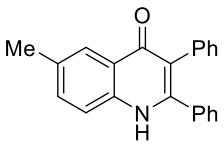
(2H), 3.69 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.6, 157.4, 148.3, 139.6, 135.4, 132.7, 131.6, 129.5, 128.9, 128.1, 127.7, 125.3, 124.6, 123.1, 120.0, 118.4, 112.8, 54.9; IR (neat) υ 3059, 1640, 1570, 1522, 1348, 1293, 1243, 958, 788 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO_2$ 328.1338; Found 328.1342.



3ja

2-phenyl-3-(pyridin-2-yl)quinolin-4(1H)-one (3la)

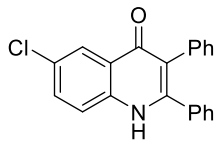
: Following the general procedure A, **1l** (42.5 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:20), **3la** was obtained as white solid (33.8 mg, 57% yield); mp = 338-340 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.28 (d, J = 4.3 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 7.66-7.70 (m, 2H), 7.59-7.64 (m, 1H), 7.08 (dd, J = 6.7, 4.9 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.3, 155.3, 149.4, 148.5, 139.7, 135.2, 135.0, 131.9, 129.2, 128.9, 128.0, 127.1, 125.2, 124.9, 123.4, 121.3, 120.7, 118.6; IR (neat) υ 3064, 1601, 1549, 1508, 1476, 1348, 761, 749, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2O$ 299.1184; Found 299.1183.



3ka

6-methyl-2,3-diphenylquinolin-4(1H)-one (3ka)

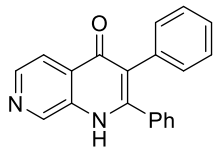
: Following the general procedure A, **1k** (45.1 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3ka** was obtained as pale yellow solid (36.2 mg, 58% yield); mp = 337-339 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.72 (s, 1H), 7.95 (s, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.50 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.29-7.37 (m, 5H), 7.04-7.17 (m, 5H), 2.43 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 175.1, 148.2, 137.8, 135.9, 135.3, 133.1, 132.4, 131.7, 129.5, 128.9, 128.0, 127.2, 125.9, 124.6, 124.5, 120.2, 118.4, 20.9; IR (neat) υ 3031, 1679, 1541, 1535, 1361, 1289, 1151, 720, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1389.



3la

6-chloro-2,3-diphenylquinolin-4(1H)-one (3la)

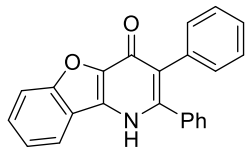
: Following the general procedure A, **1l** (49.1 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3la** was obtained as beige solid (54.7 mg, 82% yield); mp = 381-383 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H), 8.09 (t, *J* = 0.9 Hz, 1H), 7.70-7.75 (m, 2H), 7.31-7.38 (m, 5H), 7.09-7.18 (m, 3H), 7.06 (dt, *J* = 6.1, 1.6 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 174.2, 148.9, 138.3, 135.3, 135.0, 131.9, 131.6, 129.5, 129.1, 128.1, 127.8, 127.3, 126.1, 125.6, 124.2, 121.0, 120.8; IR (neat) υ 3083, 1689, 1542, 1542, 1350, 1279, 1110, 897, 714 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871 Found 223.0868.



3ma

2,3-diphenyl-1,7-naphthyridin-4(1H)-one (3ma)

: Following the general procedure A, **1m** (42.5 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:7), **3ma** was obtained as red brown solid (21.2 mg, 36% yield for 40 h); mp = 331-313 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.23 (s, 1H), 9.12 (s, 1H), 8.48 (d, *J* = 5.5 Hz, 1H), 7.97 (d, *J* = 5.5 Hz, 1H), 7.34-7.40 (m, 5H), 7.11-7.20 (m, 3H), 7.06-7.08 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 174.5, 149.8, 143.1, 142.3, 135.4, 135.1, 134.9, 131.5, 129.6, 129.3, 128.2, 128.2, 127.3, 126.4, 122.2, 117.6 ; IR (neat) υ 3064, 1670, 1556, 1549, 1375, 1230, 1173, 947, 761 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0868.

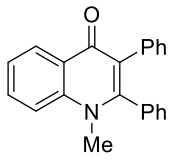


3na

2,3-diphenylbenzofuro[3,2-b]pyridin-4(1H)-one (3na)

: Following the general procedure A, **1n** (50.3 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3na** was obtained as beige solid (trace amount); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.79 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.62-7.66 (m, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.33 (s, 5H), 7.16 (td, *J* =

13.6, 6.7 Hz, 3H), 7.08-7.10 (m, 2H); HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{23}H_{16}NO_2$ 338.1181; Found 338.1177.



3oa

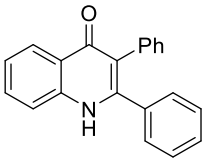
1-methyl-2,3-diphenylquinolin-4(1H)-one (3oa)

: Following the general procedure A, **1o** (45.1 mg, 0.2 mmol), benzyl alcohol **2a** (105.0 μL, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 2:1), **3oa** was obtained as white solid (31.3 mg, 50% yield for 40 h); mp = 236-238 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.70-7.74 (m, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.43 (t, *J* = 7.1 Hz, 1H), 7.25-7.30 (m, 4H), 7.14-7.17 (m, 2H), 7.08-7.12 (m, 2H), 7.03 (td, *J* = 6.7, 1.4 Hz, 2H), 3.54 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.4, 152.2, 141.6, 135.9, 135.2, 132.4, 131.5, 129.7, 128.9, 128.5, 127.6, 127.6, 126.8, 126.3, 124.5, 123.7, 115.9, 77.5, 77.2, 76.8, 37.8; IR (neat) υ 3030, 1747, 1588, 1567, 1374, 1227, 1151, 957, 753 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0868.

3.2.2 General procedure B using methyl arene

Substrate **1** (0.2 mmol, 1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.), DMSO (1.0 mL), methyl arene **4** (18 mmol, 90 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added Borosilicate Glass Tube. The reaction tube was capped with rubber septum and needle (18/24 gauge) was injected on top of the septum to make the air-opened

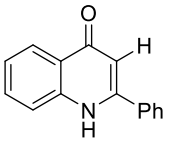
condition. The reaction mixture was stirred for 40 h at 110 ℃ using oil bath, and then cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residues were purified by flash column chromatography on silica gel.



3aa

2,3-diphenylquinolin-4(1H)-one (3aa)

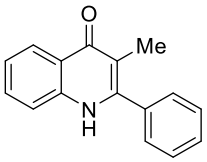
: Following the general procedure B, **1a** (42.3 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3aa** was obtained as pale yellow solid (47.6 mg, 80% yield).



3ba

2-phenylquinolin-4(1H)-one (3ba)

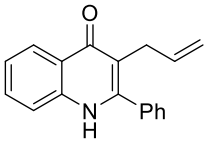
: Following the general procedure B, **1b** (26.5 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:4), **3ba** was obtained as orange solid (19.8 mg, 45% yield).



3ca

3-methyl-2-phenylquinolin-4(1H)-one (3ca)

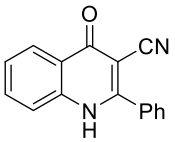
: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:2), **3ca** was obtained as beige solid (34.0 mg, 72% yield).



3da

3-allyl-2-phenylquinolin-4(1H)-one (3da)

: Following the general procedure B, **1d** (35.1 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 3:1:1), **3da** was obtained as beige solid (23.1 mg, 44% yield).

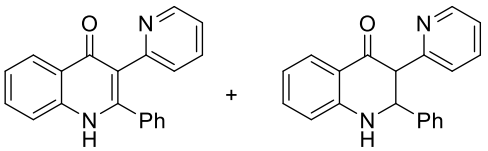


3fa

4-oxo-2-phenyl-1,4-dihydroquinoline-3-carbonitrile (3fa)

: Following the general procedure B, **1f** (32.0 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography

(hexane : EtOAc : DCM = 1:1:1), **3fa** was obtained as yellow solid (28.6 mg, 58% yield).



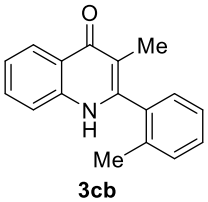
3ja **3ja`**

2-phenyl-3-(pyridin-2-yl)quinolin-4(1H)-one (3ja)

: Following the general procedure B, **1j** (42.5 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1:20), **3ja** was obtained as beige solid (6.3 mg, 11% yield).

2-phenyl-3-(pyridin-2-yl)-2,3-dihydroquinolin-4(1H)-one (3ja´)

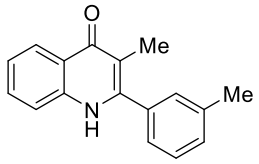
: **3ja´** was also isolated from reaction mixture as yellow solid (19.1 mg, 32% yield); mp = 137-139 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.9 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.72 (td, *J* = 7.7, 1.8 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.41 (td, *J* = 7.7, 1.2 Hz, 1H), 7.18 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H), 7.09-7.13 (m, 3H), 7.00-7.02 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.32 (s, 1H), 3.43 (d, *J* = 13.5 Hz, 1H), 3.23 (d, *J* = 13.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 201.4, 162.0, 156.7, 148.3, 137.4, 137.0, 135.9, 130.5, 127.9, 126.8, 125.0, 123.0, 121.3, 119.6, 113.9, 73.6, 46.0, 29.9; IR (neat) υ 3056, 1622, 1541, 1534, 1351, 1288, 1151, 946, 760 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}N_2O$ 301.1341; Found 301.1336.



3cb

3-methyl-2-(o-tolyl)quinolin-4(1H)-one (3cb)

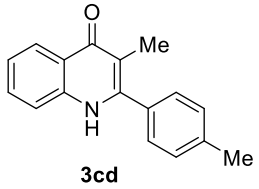
: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), *o*-xylene **4b** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3cb** was obtained as beige solid (42.6 mg, 83% yield); mp = 249-251 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.62 (s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.61 (td, J = 7.5, 1.6 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.42-7.48 (m, 2H), 7.33-7.39 (m, 2H), 7.28-7.32 (m, 1H), 2.16 (s, 3H), 1.71 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.6, 147.4, 139.5, 135.6, 134.8, 131.2, 130.2, 129.3, 128.8, 126.1, 124.9, 123.2, 122.6, 118.0, 114.8, 18.8, 11.6; IR (neat) υ 3064, 1629, 1550, 1534, 1373, 1288, 1185, 886, 760 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1232; Found 250.1232.



3cc

3-methyl-2-(m-tolyl)quinolin-4(1H)-one (3cc)

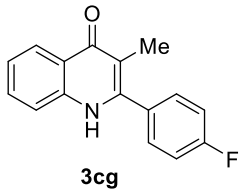
: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), *m*-xylene **2c** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3cc** was obtained as beige solid (40.2 mg, 81% yield); mp = 266-268 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 4.0 Hz, 2H), 7.44-7.48 (m, 1H), 7.33-7.38 (m, 3H), 7.28 (td, J = 8.3, 4.3 Hz, 1H), 2.42 (s, 3H), 1.88 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.7, 147.8, 139.5, 138.0, 135.1, 131.2, 130.0, 129.3, 128.5, 126.1, 125.0, 123.1, 122.6, 118.2, 114.3, 21.0, 12.2; IR (neat) υ 3032, 1629, 1542, 1539, 1315, 1254, 1161, 874, 758 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1232; Found 250.1232.



3cd

3-methyl-2-(p-tolyl)quinolin-4(1H)-one (3cd)

: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), *p*-xylene **4d** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3cd** was obtained as beige solid (39.0 mg, 78% yield); mp = 253-255 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.54 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 3.4 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.25-7.32 (m, 1H), 2.41 (s, 3H), 1.89 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.7, 147.7, 139.5, 139.0, 132.3, 131.2, 129.1, 128.9, 124.9, 123.0, 122.6, 118.1, 114.3, 21.0, 12.2; IR (neat) υ 3063, 1628, 1550, 1504, 1357, 1251, 1153, 817, 760 cm^{-1}; HRMS (FAB) m/z: [M + H]$^{+}$ Calcd for $C_{17}H_{16}NO$ 250.1232; Found 250.1231.

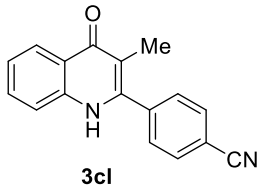


3cg

2-(4-fluorophenyl)-3-methylquinolin-4(1H)-one (3cg)

: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), 4-fluorotoluene **4g** (2.0 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1 to 1:1:1), **3cg** was obtained as beige solid (30.3 mg, 60% yield); mp = 299-301 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.60 (s, 1H), 8.12 (d, J = 7.9

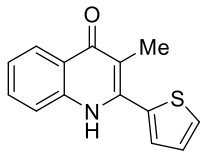
Hz, 1H), 7.58-7.66 (m, 4H), 7.39-7.45 (m, 2H), 7.28-7.32 (m, 1H), 1.88 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.7, 162.6 (d, J_{CF} = 245.4 Hz), 146.7, 139.5, 131.5 (d, J_{CF} = 3.4 Hz), 131.4, 131.3 (d, J_{CF} = 7.6 Hz), 125.0, 123.1, 122.7, 118.2, 115.6 (d, J_{CF} = 21.9 Hz), 114.6, 12.2; ^{19}F-NMR (376 MHz, DMSO-d_6) δ -111.69; IR (neat) υ 3070, 1679, 1541, 1507, 1312, 1298, 1186, 842, 757 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}FNO$ 254.0981; Found 254.0978.



3cl

4-(3-methyl-4-oxo-1,4-dihydroquinolin-2-yl)benzonitrile (3cl)

: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), *p*-tolunitile **4l** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1 to 1:1:1), **3cl** was obtained as beige solid (39.0 mg, 85% yield); mp = 309-311 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.70 (s, 1H), 8.13 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 8.6 Hz, 2H), 7.80 (d, J = 7.9 Hz, 2H), 7.59-7.66 (m, 2H), 7.30-7.34 (m, 1H), 1.86 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.6, 145.0, 139.5, 139.5, 132.6, 131.5, 130.2, 125.0, 123.1, 122.9, 118.5, 118.2, 114.6, 112.2, 12.0; IR (neat) υ 3065, 1630, 1561, 1505, 1358, 1250, 1186, 1010, 761 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}N_2O$ 261.1028; Found 261.1024.

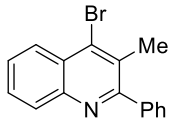


3cv

3-methyl-2-(thiophen-2-yl)quinolin-4(1H)-one (3cv)

: Following the general procedure B, **1c** (29.8 mg, 0.2 mmol), 2-methylthiophene **4v** (1.8 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2:1:1), **3cv** was obtained as red brown solid (34.1 mg, 71% yield); mp = 228-230 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.58 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.89 (d, *J* = 4.9 Hz, 1H), 7.60-7.65 (m, 2H), 7.51 (d, *J* = 3.1 Hz, 1H), 7.30 (td, *J* = 5.3, 3.5 Hz, 2H), 2.04 (s, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 176.6, 140.8, 139.5, 135.0, 131.5, 129.9, 128.9, 128.6, 125.0, 122.9, 122.9, 118.2, 115.6, 12.4; IR (neat) υ 3065, 1688, 1563, 1542, 1373, 1361, 1157, 885, 678 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}N_2O$ 223.0871; Found 223.0868.

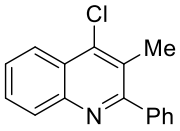
3.3. Diverse chemical conversions of 4-quinolone (3ca)



3ca-1

4-bromo-3-methyl-2-phenylquinoline (3ca-1)

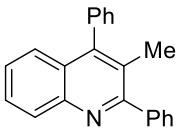
3ca (235.3 mg, 1.0 mmol, 1.0 equiv.) and dry DMF (5 mL) was added to an oven-dried round bottom flask under argon gas. A mixture was cooled to 0 ℃ and then, PBr_3 (0.192 mL, 2.0 mmol, 2.0 equiv.) was added slowly to a stirred mixture. The reaction mixture was warmed to room temperature, and stirred for overnight. The mixture was monitored by TLC and quenched with sat. $NaHCO_3$ to make a mixture neutral. The mixture was extracted with DCM (2 x 15 mL). The organic layer was washed with H_2O (2 x 15 mL) and brine (15 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel, using hexane and EtOAc (30:1). **3ca-1** was obtained as white solid (282.6 mg, 95% yield); m.p = 115-117 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 8.6, 1.2 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.60-7.64 (m, 1H), 7.54-7.57 (m, 2H), 7.43-7.52 (m, 3H), 2.57 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.6, 146.7, 141.0, 136.9, 130.2, 129.8, 129.6, 129.0, 128.6, 128.5, 127.8, 127.4, 126.9, 21.9; IR (neat) υ 3029, 1571, 1547, 1346, 1331, 1317, 1007, 969, 845, 757 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}BrN$ 298.0231; Found 298.0234.



3ca-2

4-chloro-3-methyl-2-phenylquinoline (3ca-2)

3ca (235.3 mg, 1.0 mmol, 1.0 equiv.) and $POCl_3$ (0.753 mL, 8.0 mmol, 8.0 equiv.) were added to an oven-dried round bottom flask. The reaction vessel was equipped with reflux condenser, charged with argon gas and stirred for 3 h at 80 ℃ using oil bath. The mixture was monitored by TLC and quenched with sat. $NaHCO_3$ to make a mixture neutral. The mixture was extracted with DCM (2 x 15 mL). The organic layer was washed with H_2O (2 x 15 mL) and brine (15 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel, using hexane and EtOAc (30:1). **3ca-2** was obtained as white solid (245.3 mg, 97% yield); mp = 97-99 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.62 (dd, *J* = 8.3, 7.1 Hz, 1H), 7.56-7.58 (m, 2H), 7.44-7.53 (m, 3H), 2.53 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.8, 146.7, 142.5, 140.8, 129.8, 129.6, 129.0, 128.6, 128.5, 127.8, 127.5, 125.8, 124.0, 18.5; IR (neat) υ 3057, 1572, 1551, 1479, 1393, 1039, 1009, 922, 757 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}ClN$ 254.0737; Found 254.0741.

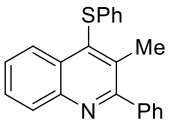


3ca-3

3-methyl-2,4-diphenylquinoline (3ca-3)

3ca-1 (149.1 mg, 0.5 mmol, 1.0 equiv.), phenyl boronic acid (92.4 mg, 8.0 mmol, 8.0 equiv.), anhydrous K_2CO_3 (298.5 mg, 2.0 mmol, 4.0 equiv.), PPh_3 (19.5 mg, 0.075 mmol,

15 mol%.), $Pd(OAc)_2$ (5.7 mg, 0.025 mmol, 5 mol%.), H_2O (1.0 mL), EtOH (0.5 mL) and toluene (2.0 mL) were added to an oven-dried Borosilicate Glass Tube. The reaction vessel was charged with argon and sealed. The mixture was heated to 100 ℃ using oil bath and stirred for 24 h. The mixture was diluted with DCM (5.0 mL) and H_2O (5.0 mL), and extracted with DCM (2 x 15.0 mL). The organic layer was washed with H_2O (10.0 mL) and brine (10.0 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using hexane and EtOAc (30:1). **3ca-3** was obtained as white solid **(**150.3 mg, 98% yield); mp = 141-143 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.6 Hz, 1H), 7.59-7.69 (m, 3H), 7.38-7.58 (m, 8H), 7.30-7.33 (m, 2H), 2.16 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 146.3, 141.5, 137.8, 129.5, 129.5, 129.1, 128.8, 128.7, 128.5, 128.3, 128.0, 127.2, 126.9, 126.4, 126.1, 18.7; IR (neat) υ 3028, 1569, 1553, 1484, 1441, 1396, 1009, 763, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1446.

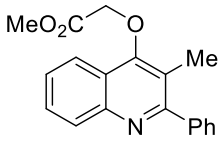


3ca-4

3-methyl-2-phenyl-4-(phenylthio)quinoline (3ca-4)

3ca-2 (126.9 mg, 0.5 mmol, 1.0 equiv.), KOH (29.5 mg, 0.5 mmol, 1.0 equiv.), Thiophenol (52.0 μL, 0.5 mmol, 1.0 equiv.) and DMSO (1.5 mL) were added to an oven-dried round bottom flask. The mixture was stirred at room temperature under air. After 2 h, the mixture was diluted with DCM (5 mL) and H_2O (5 mL), and extracted with DCM (2 x 15 mL). The organic layer was washed with H_2O (2 x 10 mL) and brine (10 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using hexane and EtOAc (30:1) to afford

desired product. **3ca-4** was obtained as white solid (142.2 mg, 87% yield); mp = 122-124 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.6 Hz, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.68-7.72 (m, 1H), 7.53-7.58 (m, 3H), 7.42-7.51 (m, 3H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.12-7.15 (m, 1H), 7.08 (d, *J* = 7.3 Hz, 2H), 2.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.0, 146.6, 141.0, 140.6, 140.0, 136.3, 134.9, 130.0, 129.4, 129.3, 129.1, 128.6, 128.5, 127.6, 127.6, 126.2, 126.0, 20.2; IR (neat) υ 3056, 1580, 1552, 1477, 1438, 1007, 918, 762, 738 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NS$ 328.1160; Found 328.1158.

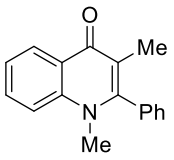


3ca-5

methyl 2-((3-methyl-2-phenylquinolin-4-yl)oxy)acetate (3ca-5)

3ca (164.7 mg, 0.7 mmol, 1.0 equiv.), anhydrous K_2CO_3 (635.2 mg, 4.7 mmol, 6.5 equiv.) and dry DMF (9.5 mL) were added to an oven-dried round bottom flask. Methyl bromoacetate (99.0 μL, 1.1 mmol, 1.5 equiv.) was added to a stirred reaction mixture, and then the mixture was heated to 80 ℃ using oil bath and stirred for 12 h. The mixture was diluted with EtOAc (5 mL) and H_2O (5 mL), and extracted with EtOAc (2 x 15 mL). The organic layer was washed with H_2O (3 x 10 mL) and brine (10 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using hexane and EtOAc (4:1). **3ca-5** was obtained as colorless oil (148.0 mg, 69% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.6 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.67-7.71 (m, 1H), 7.54-7.59 (m, 3H), 7.42-7.51 (m, 3H), 4.74 (s, 2H), 3.88 (s, 3H), 2.40 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.1, 162.5, 160.3, 148.1, 140.7,

129.7, 129.5, 129.1, 128.5, 128.5, 126.7, 122.3, 121.7, 120.7, 70.4, 52.5, 14.2; IR (neat) υ 2968, 1759, 1747, 1590, 1488, 1363, 1215, 1111, 769 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}NO_3$ 308.1287; Found 308.1285.



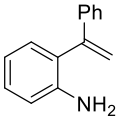
3ca-6

1,3-dimethyl-2-phenylquinolin-4(1H)-one (3ca-6)

3ca (117.7 mg, 0.5 mmol, 1.0 equiv.) and dry THF (10.0 mL) were added to an oven-dried round bottom flask. The mixture was cooled to 0 ℃ and stirred for 10 min, and then NaH (40.0 mg, 1.0 mmol, 2.0 equiv.) was added portionwise for 15 min. Iodomethane (94.0 μL, 1.5 mmol, 3.0 equiv.) was added to the mixture and the mixture was stirred for 3 h at room temperature. The mixture was quenched with H_2O (10 mL) and extracted with EtOAc (2 x 20 mL). The organic layer was washed with brine (10 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using hexane and EtOAc (2:1). **3ca-6** was obtained as beige solid (119.4 mg, 96% yield); mp = 128-130 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.65-7.70 (m, 1H), 7.49-7.57 (m, 4H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.28 (td, *J* = 4.0, 1.6 Hz, 2H), 3.47 (s, 3H), 1.86 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 177.6, 151.3, 141.1, 135.8, 132.0, 129.3, 129.2, 128.6, 127.1, 125.2, 123.2, 118.2, 115.6, 37.4, 13.5; IR (neat) υ 3056, 1615, 1591, 1474, 1456, 1299, 1193, 759, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1232; Found 250.1230.

4. Synthesis of quinoline

List of substrates



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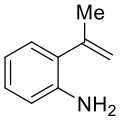

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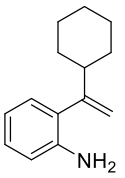

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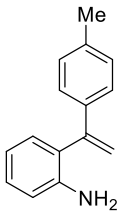

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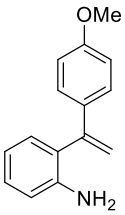

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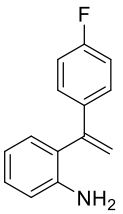

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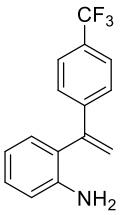

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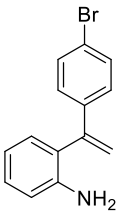

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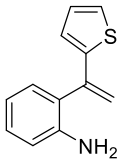

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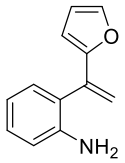

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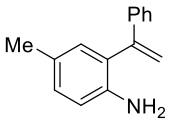

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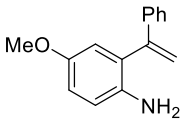

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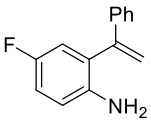

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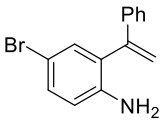

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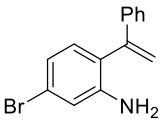

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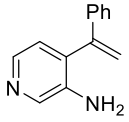

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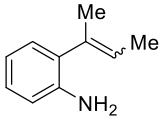

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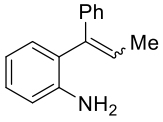

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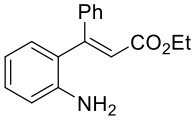

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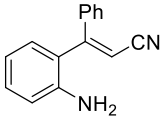

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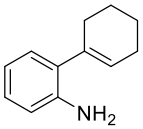

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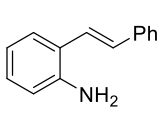

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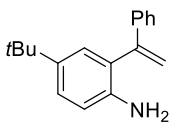

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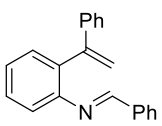
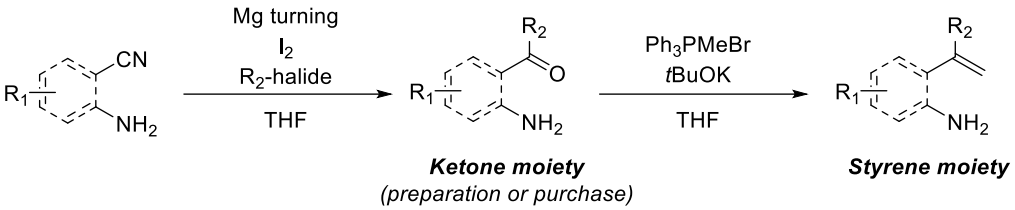


5a″

All substrates were synthesized following the known method

4.1. Synthetic procedures for amino styrene

4.1.1 Synthesis of substrates: 5a-5b, 5e-5h, 5o-5p [52]



preparation of Grignard reagent

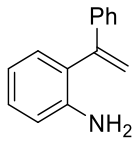
Magnesium turning (4.75 equiv.), I_2 (1piece, catalytic amount), dry THF (1.0 M) was added to a dried 100 mL 2-necked round-bottom flask. After R_2-halide (4.75 equiv.) was added to the flask, the reaction mixture was heated to 70 ℃ for 2 h. The mixture was cooled to room temperature, and the completed mixture was directly used as Grignard reagent.

Synthesis of Ketone moiety

Prepared Grignard reagent (4.75 equiv.) was added dropwise to a solution of benzonitrile (1.0 equiv.) in dry THF (0.5 M) for 1.0 h using syringe pump at -78 ℃. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, mixture was cooled to 0 ℃ and 1 M HCl was added (adjusted with pH 1). After stirring for an additional 0.5 h, the mixture was neutralized by sat. $NaHCO_3$. The mixture was extracted with EtOAc (2 x 50 mL). The organic layer was washed with brine (50 mL), dried over anhydrous $MgSO_4$, concentrated and then, purified by flash column chromatography on silica gel.

Synthesis of Styrene moiety

Ph_3PMeBr (1.5 equiv.), *t*BuOK (1.5 equiv.) and dry THF (0.5 M) was added to an oven dried round bottom flask. After reaction mixture was stirred for 30 min, corresponding ketone (1.0 equiv.) in dry THF (0.5 M) was added dropwise to the activated mixture for 30 min using syringe pump at 0 ℃. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, H_2O (50 mL) was added to the mixture. After stirring for an additional 5 min, the mixture was extracted with EtOAc (2 x 50 mL). The organic layer was washed with brine (50 mL), dried over anhydrous $MgSO_4$, concentrated and then, purified by flash column chromatography on silica gel. Additional recrystallization was performed according to need.

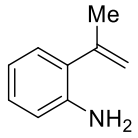


5a

2-(1-phenylvinyl)aniline (5a)

: Following the above procedure, 2-aminobenzophenone (1.97 g, 10.0 mmol, 1.0 equiv.), PPh_3MeBr (5.25 g, 15.0 mmol, 1.5 equiv.), *t*BuOK (2.24 g, 20.0 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), the compound was recrystallized from DCM and cooled hexane. **5a** was obtained as crystalline white solid (1.90 g, 97% yield); mp = 84-86 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41-7.38 (m, 2H), 7.36-7.28 (m, 3H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 7.14 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.81 (td, *J* = 7.4, 1.2 Hz, 1H), 6.71 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.82 (d, *J* = 1.8 Hz, 1H), 5.38 (d, *J* = 1.4 Hz, 1H), 3.54 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.3, 144.0, 139.8, 130.9, 128.9, 128.7, 128.2, 127.4, 126.8, 118.4, 116.3, 115.7; IR (neat) υ 3463, 3380, 3023, 1615, 1494, 1252, 907, 750 cm^{-1}; HRMS (FAB) m/z:

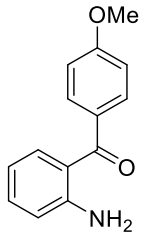
$[M + H]^+$ Calcd for $C_{14}H_{14}N$ 196.1126; Found 196.1128.



5b

2-(prop-1-en-2-yl)aniline (5b)

: Following the above procedure, 2-aminoacetophenone (1.32 g, 10.0 mmol, 1.0 equiv.), PPh_3MeBr (5.25 g, 15.0 mmol, 1.5 equiv.), *t*BuOK (2.24 g, 15.0 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **5b** was obtained as colorless oil (722.4 mg, 76% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.10-7.04 (m, 2H), 6.78-6.74 (m, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.32-5.30 (m, 1H), 5.08 (q, *J* = 1.1 Hz, 1H), 3.80 (s, 2H), 2.09 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 143.6, 142.9, 129.4, 128.3, 128.0, 118.3, 115.7, 115.4, 24.0; IR (neat) υ 3446, 3367, 2969, 1612, 1495, 1292, 905, 749 cm^{-1};

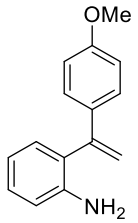


5e′

(2-aminophenyl)(4-methoxyphenyl)methanone (5e′)

: Grignard reagent was prepared from magnesium turnings (855.5 mg, 35.6 mmol, 4.75 equiv.), 4-bromoanisole (2.8 mL, 35.6 mmol, 4.75 equiv.). Following the above procedure,

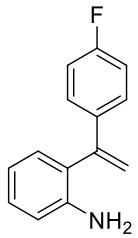
2-aminobenzonitrile (0.90 g, 7.5 mmol, 1.0 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 25 : 1), **5e′** was obtained as pale yellow solid (0.25 g, 15% yield); mp = 85-87 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69 (dt, *J* = 9.5, 2.5 Hz, 2H), 7.46 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.31-7.26 (m, 2H), 6.95 (dt, *J* = 9.3, 2.5 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.64 (t, *J* = 7.6 Hz, 1H), 3.88 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.9, 162.5, 150.4, 134.1, 133.8, 132.4, 131.9, 119.1, 117.1, 115.8, 113.5, 55.6; IR (neat) υ 3481, 3356, 2838, 1604, 1508, 1249, 930, 755 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}NO_2$ 228.1025; Found 228.1037.



5e

2-(1-(4-methoxyphenyl)vinyl)aniline (5e)

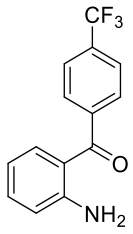
: Following the above procedure, 2-aminoacetophenone (0.23 g, 1.0 mmol, 1.0 equiv.), PPh_3MeBr (0.53 g, 1.5 mmol, 1.5 equiv.), *t*BuOK (0.23 g, 1.5 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **5e** was obtained as colorless oil (0.21 g, 93% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31 (dt, *J* = 9.5, 2.6 Hz, 2H), 7.16 (td, *J* = 7.7, 1.4 Hz, 1H), 7.12 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.85 (dt, *J* = 9.5, 2.6 Hz, 2H), 6.81 (q, *J* = 7.0 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.71 (d, *J* = 1.4 Hz, 1H), 5.25 (d, *J* = 1.4 Hz, 1H), 3.81 (s, 3H), 3.39 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.7, 146.6, 143.9, 132.2, 130.9, 128.8, 128.0, 127.8, 118.5, 115.7, 114.4, 114.0, 55.4; IR (neat) υ 3481, 3383, 2836, 1608, 1508, 1248, 901, 751 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO$ 226.1232; Found 226.1226.



5f

2-(1-(4-fluorophenyl)vinyl)aniline (5f)

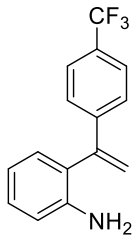
Following the above procedure, 2-Amino-4'-fluorobenzophenone (1.04 g, 5.0 mmol, 1.0 equiv.), PPh_3MeBr (2.63 g, 7.5 mmol, 1.5 equiv.), *t*BuOK (1.12 g, 7.5 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **5f** was obtained as pale yellow solid (0.89 g, 84% yield); mp = 86-88 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.33 (m, 2H), 7.20-7.16 (m, 1H), 7.10 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.04-6.98 (m, 2H), 6.82-6.78 (m, 1H), 6.73-6.71 (m, 1H), 5.75 (s, 1H), 5.34 (s, 1H), 3.51 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 162.0 (d, J_{CF} = 246.1 Hz), 159.5 (d, J_{CF} = 246.1 Hz), 156.4 (d, J_{CF} = 2.9 Hz), 156.4 (d, J_{CF} = 2.9 Hz), 148.9, 148.8, 146.0, 139.4, 138.1, 132.7, 132.6, 129.6, 129.5, 129.0, 128.9, 128.8, 127.6, 126.7 (d, J_{CF} = 9.6 Hz), 126.6 (d, J_{CF} = 9.6 Hz), 120.0, 120.0 (d, J_{CF} = 24.9 Hz), 119.7 (d, J_{CF} = 24.9 Hz), 109.3, 109.1; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -113.97; IR (neat) υ 3481, 3384, 3065, 1614, 1507, 1298, 908, 751 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{12}FN$ 213.0954; Found 213.0956.



5g′

(2-aminophenyl)(4-(trifluoromethyl)phenyl)methanone (5g′)

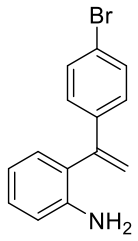
: Grignard reagent was prepared from magnesium turnings (838.4 mg, 35.6 mmol, 4.75 equiv.), 4-bromobenzotrifluoride (5.0 mL, 35.6 mmol, 4.75 equiv.). Following the above procedure, 2-aminobenzonitrile (0.90 g, 7.5 mmol, 1.0 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **5g′** was obtained as yellow solid (0.34 g, 17% yield); mp = 97-99 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.74-7.70 (m, 4H), 7.36 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.34-7.30 (m, 1H), 6.75 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.60 (td, *J* = 7.6, 1.2 Hz, 1H), 6.23 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 197.8, 151.4, 143.5, 135.0, 134.5, 133.1 (q, J_{CF} = 32.6 Hz), 132.7 (q, J_{CF} = 32.6 Hz), 132.4 (q, J_{CF} = 32.6 Hz), 132.1 (q, J_{CF} = 32.6 Hz), 129.3 (q, J_{CF} = 271.0 Hz), 128.0 (q, J_{CF} = 271.0 Hz), 125.4 (q, J_{CF} = 3.8 Hz), 125.3 (q, J_{CF} = 3.8 Hz), 125.3 (q, J_{CF} = 271.0 Hz), 125.3 (q, J_{CF} = 3.8 Hz), 125.2 (q, J_{CF} = 3.8 Hz), 122.6 (q, J_{CF} = 271.0 Hz), 119.9 (q, J_{CF} = 271.0 Hz), 117.4, 117.3, 115.8; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -62.74; IR (neat) υ 3481, 3355, 3065, 1617, 1508, 1250, 932, 754 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}F_3NO$ 266.0793; Found 266.0788.



5g

2-(1-(4-(trifluoromethyl)phenyl)vinyl)aniline (5g)

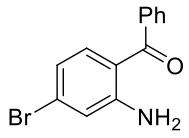
: Following the above procedure, 2-aminoacetophenone (0.32 g, 1.2 mmol, 1.0 equiv.), PPh_3MeBr (0.64 g, 1.8 mmol, 1.5 equiv.), *t*BuOK (0.27 g, 1.8 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 30 : 1), **5g** was obtained as yellow oil (0.22 g, 68% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.19 (td, *J* = 7.7, 1.4 Hz, 1H), 7.09 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.81 (td, *J* = 7.5, 1.1 Hz, 1H), 6.73 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.90 (d, *J* = 0.9 Hz, 1H), 5.49 (d, *J* = 1.4 Hz, 1H), 3.58 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.2, 143.9, 143.4, 130.9, 130.6 (q, J_{CF} = 32.6 Hz), 130.3 (q, J_{CF} = 32.6 Hz), 129.9 (q, J_{CF} = 32.6 Hz), 129.6 (q, J_{CF} = 32.6 Hz), 129.3, 128.3 (q, J_{CF} = 270.0 Hz), 127.1, 126.5, 125.7 (q, J_{CF} = 3.8 Hz), 125.7 (q, J_{CF} = 3.8 Hz), 125.7 (q, J_{CF} = 3.8 Hz), 125.6 (q, J_{CF} = 270.0 Hz), 125.6 (q, J_{CF} = 3.8 Hz), 122.9 (q, J_{CF} = 270.0 Hz), 120.2 (q, J_{CF} = 270.0 Hz), 118.6, 118.3, 115.8; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -62.43; IR (neat) υ 3481, 3384, 3030, 1617, 1495, 1327, 916, 751 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{15}H_{12}F_3N$ 263.0922; Found 263.0919.



5h

2-(1-(4-bromophenyl)vinyl)aniline (5h)

: Following the above procedure, 2-Amino-4'-bromobenzophenone (0.68 g, 2.5 mmol, 1.0 equiv.), PPh_3MeBr (1.31 g, 3.75 mmol, 1.5 equiv.), *t*BuOK (0.56 g, 3.75 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **5h** was obtained as brown solid (0.57 g, 83% yield); mp = 71-73 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (dt, *J* = 9.0, 2.3 Hz, 2H), 7.26-7.22 (m, 2H), 7.20-7.16 (m, 1H), 7.09 (dd, *J* = 7.3, 1.4 Hz, 1H), 6.80 (td, *J* = 7.5, 1.2 Hz, 1H), 6.72 (dd, *J* = 8.3, 0.9 Hz, 1H), 5.80 (d, *J* = 1.4 Hz, 1H), 5.38 (d, *J* = 0.9 Hz, 1H), 3.67 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.2, 143.8, 138.7, 131.8, 130.9, 129.1, 128.4, 126.9, 122.3, 118.7, 116.8, 115.9; IR (neat) υ 3463, 3383, 3024, 1613, 1487, 1299, 910, 750 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}BrN$ 274.0231; Found 274.0222.

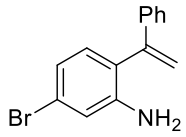


5o′

(2-amino-4-bromophenyl)(phenyl)methanone (5o′)

: Grignard reagent was prepared from magnesium turnings (402.7 mg, 17.1 mmol, 4.75 equiv.), chlorobenzene (1.8 mL, 17.1 mmol, 4.75 equiv.). Following the above procedure, 2-Amino-4-bromobenzonitrile (0.72 g, 3.6 mmol, 1.0 equiv.) was used as a starting

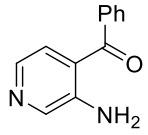
material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **5o′** was obtained as brown solid (0.68 g, 68% yield); mp = 70-72 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61 (dt, *J* = 6.6, 1.6 Hz, 2H), 7.56-7.52 (m, 1H), 7.48-7.44 (m, 2H), 7.30 (d, *J* = 8.7 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 6.72 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.16 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 198.6, 151.8, 139.8, 136.0, 131.5, 129.2, 128.4, 119.5, 119.0, 117.0, 77.5, 77.2, 76.8; IR (neat) υ 3481, 3337, 3057, 1605, 1534, 1241, 924, 748 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{13}H_{10}BrNO$ 274.9946; Found 274.9947.



5o

5-bromo-2-(1-phenylvinyl)aniline (5o)

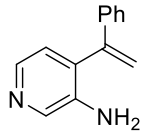
: Following the above procedure, 2-amino-4-bromophenyl)(phenyl)methanone (0.66 g, 2.4 mmol, 1.0 equiv.), PPh_3MeBr (1.26 g, 3.6 mmol, 1.5 equiv.), *t*BuOK (0.54 g, 3.6 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **5o** was obtained as brown solid (0.60 g, 91% yield); mp = 66-68 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.91 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.85 (d, *J* = 1.8 Hz, 1H), 5.81 (d, *J* = 1.4 Hz, 1H), 5.35 (d, *J* = 1.4 Hz, 1H), 3.62 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.3, 145.5, 139.2, 132.2, 128.8, 128.4, 126.7, 126.1, 122.4, 121.2, 118.1, 116.6; IR (neat) υ 3480, 3384, 3025, 1613, 1487, 1299, 909, 746 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{12}BrN$ 273.0153; Found 273.0155.



5p′

(3-aminopyridin-4-yl)(phenyl)methanone (5p′)

: Grignard reagent was prepared from magnesium turnings (0.49 g, 16.6 mmol, 4.75 equiv.), chlorobenzene (1.70 mL, 16.6 mmol, 4.75 equiv.). Following the above procedure, 3-Amino-4-pyridinecarbonitrile (0.42 g, 3.5 mmol, 1.0 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc = 1 : 1), **5p′** was obtained as yellow solid (0.59 g, 84% yield); mp = 137-139 ℃; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.33 (d, J = 0.9 Hz, 1H), 7.75 (d, J = 5.5 Hz, 1H), 7.64 (qt, J = 4.7, 1.7 Hz, 3H), 7.56-7.52 (m, 2H), 7.09 (d, J = 5.0 Hz, 1H), 6.88 (s, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 197.3, 145.1, 141.2, 138.0, 134.7, 132.2, 129.0, 128.5, 124.4, 120.2; IR (neat) υ 3446, 3309, 3025, 1608, 1423, 1225, 943, 761 cm^{-1}; HRMS (FAB) m/z: [M + H]$^{+}$ Calcd for $C_{12}H_{11}N_2O$ 199.0871; Found 199.0867.



5p

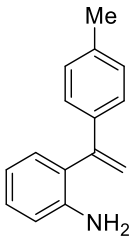
4-(1-phenylvinyl)pyridin-3-amine (5p)

: Following the above procedure, **5p′** (0.52 g, 2.6 mmol, 1.0 equiv.), PPh_3MeBr (1.37 g, 3.9 mmol, 1.5 equiv.), *t*BuOK (0.58 g, 3.9 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 2 : 1 :1), **5p** was obtained as brown oil (0.24 g, 46% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.05 (d, J = 5.0 Hz, 1H), 7.38-7.32 (m, 5H), 7.02 (d, J = 4.6 Hz, 1H), 5.86 (d, J = 0.9 Hz, 1H), 5.41 (d, J = 0.9 Hz, 1H), 3.57 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ

145.3, 140.3, 140.1, 138.2, 133.7, 129.0, 128.7, 126.7, 124.7, 117.3; IR (neat) υ 3446, 3310, 3057, 1621, 1422, 1320, 912, 782 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2$ 197.1079; Found 197.1075.

4.1.2. Synthesis of substrates: 5d, 5k-5n, 5t [53]

Aniline (1 equiv.), phenylacetylene (2 equiv.), montraorillonite KSF (190 mg/1 mmol), and *o*-xylene (0.1 M) was added to a dried round-bottom flask. The flask was equipped with reflux condenser and the reaction mixture was heated to 140 ℃ for overnight. Upon the completion of reaction, mixture was cooled to room temperature. Solvent was removed by evaporator and mixture residues was directly purified by flash column chromatography on silica gel.

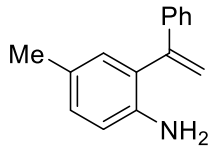


5d

2-(1-(p-tolyl)vinyl)aniline (5d)

: Following the above procedure, aniline (0.46 g, 5.0 mmol, 1.0 equiv.) and *p*-tolylacethylene (1.24 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **5d** was obtained as pale yellow oil (0.48 g, 46% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 7.19-7.11 (m, 4H), 6.80 (td, *J* = 7.3, 1.4 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 5.77 (d, *J* = 0.9 Hz, 1H), 5.31 (d, *J* = 1.4 Hz, 1H), 3.44 (s, 2H), 2.35 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.1, 143.9, 138.1, 136.9, 130.9, 129.4, 128.8, 127.7, 126.7, 118.5, 115.7,

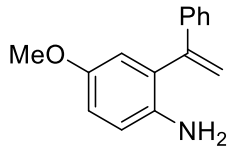
115.4, 21.3; IR (neat) υ 3463, 3380, 3023, 1614, 1493, 1299, 903, 750 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N$ 209.1204; Found 209.1213.



1k

4-methyl-2-(1-phenylvinyl)aniline (1k)

: Following the above procedure, *p*-toluidine (0.53 g, 5.0 mmol, 1.0 equiv.) and phenylacethylene (1.08 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 40 : 1), **1k** was obtained as orange oil (0.80 g, 77% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (dt, *J* = 8.3, 2.2 Hz, 2H), 7.35-7.29 (m, 3H), 7.00-6.97 (m, 1H), 6.94 (d, *J* = 1.8 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 5.79 (d, *J* = 1.4 Hz, 1H), 5.35 (d, *J* = 1.4 Hz, 1H), 3.35 (s, 2H), 2.27 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.4, 141.4, 139.9, 131.4, 129.4, 128.7, 128.2, 127.7, 127.6, 126.8, 116.1, 116.0, 20.6; IR (neat) υ 3462, 3371, 3080, 1621, 1502, 1288, 905, 782 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{15}H_{15}N$ 209.1204; Found 209.1200.

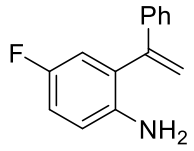


1l

4-methoxy-2-(1-phenylvinyl)aniline (1l)

: Following the above procedure, *p*-anisidine (0.61 g, 5.0 mmol, 1.0 equiv.) and phenylacethylene (1.08 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After

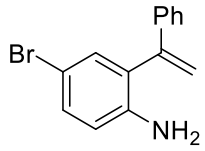
purification by column chromatography (hexane : EtOAc = 20 : 1), **1l** was obtained as yellow oil (0.52 g, 46% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.35-7.28 (m, 3H), 6.78 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.73 (d, *J* = 2.8 Hz, 1H), 6.67 (d, *J* = 8.7 Hz, 1H), 5.81 (d, *J* = 1.4 Hz, 1H), 5.36 (d, *J* = 1.4 Hz, 1H), 3.76 (s, 3H), 3.10 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.7, 147.2, 139.5, 137.6, 128.8, 128.7, 128.3, 126.7, 117.1, 116.3, 116.2, 114.7, 55.9; IR (neat) υ 3446, 3363, 2946, 1604, 1498, 1281, 907, 782 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{15}H_{15}NO$ 225.1154; Found 225.1151.



1m

4-fluoro-2-(1-phenylvinyl)aniline (1m)

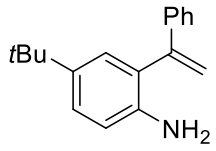
: Following the above procedure, 4-fluoroaniline (0.55 g, 5.0 mmol, 1.0 equiv.) and phenylacethylene (1.08 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 40 : 1), **1m** was obtained as pale yellow oil (0.48 g, 45% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 6.91-6.85 (m, 2H), 6.66-6.60 (m, 1H), 5.82 (d, *J* = 0.9 Hz, 1H), 5.37 (d, J = 0.9 Hz, 1H), 3.41 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.4 (d, J_{CF} = 235.7 Hz), 155.0 (d, J_{CF} = 235.7 Hz), 146.5, 140.2 (d, J_{CF} = 1.9 Hz), 140.2 (d, J_{CF} = 1.9 Hz), 139.1, 128.8, 128.5, 128.5, 126.7, 117.3 (d, J_{CF} = 22.0 Hz), 117.1 (d, J_{CF} = 22.0 Hz), 116.8, 116.6 (d, J_{CF} = 7.7 Hz), 116.5 (d, J_{CF} = 7.7 Hz), 115.5, 115.2; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -127.02; IR (neat) υ 3446, 3376, 3023, 1608, 1497, 1277, 910, 781 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{12}FN$ 213.0954; Found 213.0958.



1n

4-bromo-2-(1-phenylvinyl)aniline (1n)

: Following the above procedure, 4-bromoaniline (0.85 g, 5.0 mmol, 1.0 equiv.) and phenylacethylene (1.08 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **1n** was obtained as pale yellow oil (0.53 g, 39% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (m, 5H), 7.27-7.24 (m, 2H), 6.59 (dd, *J* = 5.3, 3.9 Hz, 1H), 5.81 (d, *J* = 0.9 Hz, 1H), 5.36 (d, *J* = 0.9 Hz, 1H), 3.44 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 146.1, 143.1, 139.0, 133.2, 131.6, 129.3, 128.8, 128.5, 126.7, 117.3, 117.0, 110.1; IR (neat) υ 3481, 3420, 3025, 1609, 1489, 1339, 912, 780 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{12}BrN$ 273.0153; Found 273.0148.



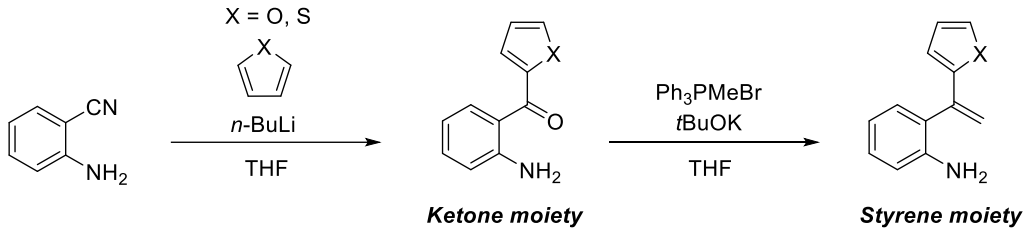
1t

4-(tert-butyl)-2-(1-phenylvinyl)aniline (1t)

: Following the above procedure, *t*-butylaniline (0.74 g, 5.0 mmol, 1.0 equiv.) and phenylacethylene (1.08 mL, 10.0 mmol, 2 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **1t** was obtained as yellow oil (0.40 g, 32% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.39 (m, 2H), 7.36-7.28 (m, 3H), 7.22 (dd, *J* = 8.3, 2.8 Hz, 1H), 7.15 (d, *J* = 2.3 Hz, 1H), 6.67 (d, *J* = 8.3 Hz,

1H), 5.82 (d, *J* = 1.4 Hz, 1H), 5.38 (d, *J* = 1.6 Hz, 1H), 3.35 (s, 2H), 1.32 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 147.8, 141.5, 141.3, 139.8, 128.7, 128.2, 127.8, 127.1, 126.8, 125.7, 116.1, 115.5, 34.1, 31.7; IR (neat) υ 3463, 3377, 2961, 1619, 1502, 1260, 900, 781 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{18}H_{21}N$ 251.1674; Found 251.1672.

4.1.3 Synthesis of substrates: 5i-5j[54]

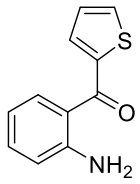


Synthesis of Ketone moiety

n-BuLi (2.5 M in hexane, 45.0 mmol, 18.0 mL, 4.5 equiv.) was dropwise added to a solution of hetero cycle (45.0 mmol, 4.5 equiv.) in dry THF (29.0 mL) at - 78 ℃. The reaction mixture was cooled to room temperature and stirred for overnight. A solution of 2-aminobenzonitrile (1.17 g, 10.0 mmol, 1.0 equiv.) in THF (29.0 mL) was dropwise added to a reaction mixture using syringe pump for 1 h at -78 ℃. The reaction was allowed to stir for 12 h at room temperature. Upon the completion of reaction, mixture was cooled to 0 ℃ and 1 M HCl was added to the mixture (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (60 mL). The organic layer was washed with brine (50 mL), dried over anhydrous Mg_2SO_4 and concentrated. The residues were purified by flash column chromatography on silica gel, using hexane and EtOAc (15 : 1).

Synthesis of Styrene moiety

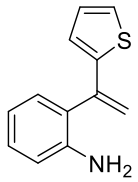
Ph_3PMeBr (2.63 g, 7.5 mmol, 1.5 equiv.), *t*BuOK (1.12 g, 7.5 mmol, 1.5 equiv.) and dry THF (10 mL) was added to a oven dried round bottom flask. After reaction mixture was stirred for 30 min, prepared ketone (5.0 mmol, 1.0 equiv.) in dry THF (10 mL) was added dropwise to the activated mixture for 30 min using syringe pump at 0 ℃. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, H_2O (50 mL) was added to the mixture. After stirring for an additional 5 min, the mixture was extracted with EtOAc (2 x 50 mL). The organic layer was washed with brine (50 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel, using hexane and EtOAc (25 : 1).



5i′

(2-aminophenyl)(thiophen-2-yl)methanone (5i′)

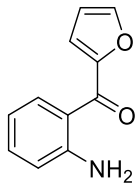
: Following the above procedure, Thiophene (3.6 mL, 10.0 mmol, 4.5 equiv.) was used as a starting material. **5i′** was obtained as pale yellow oil (1.43 g, 56% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.66 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.58 (q, *J* = 1.7 Hz, 1H), 7.33-7.29 (m, 1H), 7.14 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.75 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.70 (td, *J* = 7.6, 0.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 189.6, 150.0, 144.9, 134.0, 133.8, 132.9, 132.9, 127.7, 119.2, 117.1, 116.1; IR (neat) υ 3446, 3364, 2945, 1603, 1498, 1229, 907, 782 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{11}H_{10}NOS$ 204.0483; Found 204.0477.



5i

2-(1-(thiophen-2-yl)vinyl)aniline (5i)

: Following the above procedure, **5i′** (0.99 g, 5.0 mmol, 1.0 equiv.) was used as a starting material. **5i** was obtained as yellow oil (0.85 g, 84% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 5.3, 1.1 Hz, 1H), 7.18 (td, *J* = 7.7, 1.5 Hz, 1H), 7.14 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.94 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.82-6.78 (m, 2H), 6.76-6.74 (m, 1H), 5.80 (d, *J* = 0.9 Hz, 1H), 5.19 (d, *J* = 0.9 Hz, 1H), 3.44 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.3, 143.7, 140.7, 130.4, 129.1, 127.7, 126.9, 126.3, 125.5, 118.5, 115.9, 114.7; IR (neat) υ 3481, 3356, 3133, 1620, 1464, 1258, 952, 753 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{12}H_{11}NS$ 201.0612; Found 201.0614.

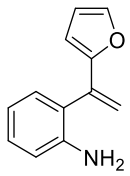


5j′

(2-aminophenyl)(furan-2-yl)methanone (5j')

: Following the above procedure, Furan (4.09 mL, 45.0 mmol, 4.5 equiv.) was used as a starting material. **5j′** was obtained as pale yellow oil (0.83 g, 44% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.67 (d, *J* = 1.8 Hz, 1H), 7.32-7.28 (m, 1H), 7.13 (d, *J* = 3.7 Hz, 1H), 6.73-6.68 (m, 2H), 6.56 (q, *J* = 1.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.0, 152.8, 150.5, 146.5, 134.1, 132.4, 119.6, 118.4, 117.2, 116.1, 112.0; IR (neat) υ 3481, 3356, 3133, 1620, 1464, 1258, 952, 753 cm^{-1}; HRMS (FAB) m/z:

$[M + H]^+$ Calcd for $C_{11}H_{10}NO_2$ 188.0712; Found 188.0716.

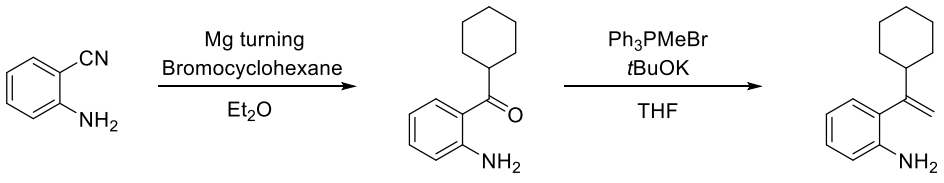


1j

2-(1-(furan-2-yl)vinyl)aniline (5j)

: Following the above procedure, Furan (3.59 mL, 10.0 mmol, 4.5 equiv.) and (2-aminophenyl)(furan-2-yl)methanone (0.94 g, 5.0 mmol, 1.0 equiv.) were used as a starting material. **5j** was obtained as pale yellow oil (0.86 g, 93% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 1.4 Hz, 1H), 7.19-7.11 (m, 2H), 6.80-6.74 (m, 2H), 6.36 (q, *J* = 1.7 Hz, 1H), 6.05 (d, *J* = 3.2 Hz, 1H), 5.94 (d, *J* = 1.1 Hz, 1H), 5.21 (d, *J* = 1.8 Hz, 1H), 3.53 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 153.6, 144.1, 142.8, 136.2, 130.5, 129.1, 125.0, 118.3, 115.7, 113.2, 111.6, 109.4; IR (neat) υ 3446, 3383, 3032, 1616, 1453, 1210, 901, 746 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{12}H_{11}NO$ 185.0841; Found 185.0827.

4.1.4. Synthesis of 2-(1-cyclohexylvinyl)aniline (5c)[55]



5c′ **5c**

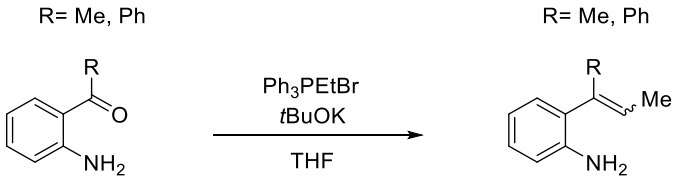
The magnesium turnings (0.35 g, 15.0 mmol, 3.0 equiv.) and dry Et_2O (15.0 mL) were added to an oven-dried 2-necked round bottom flask under argon gas. Bromocyclohexane (1.87 mL, 15.0 mmol, 3.0 equiv.) was added to a stirred mixture and then, further mixture

stirred at room temperature for 1 h. 2-aminobenzonitrile (0.60 g, 5.0 mmol, 1.0 equiv.) in dry Et_2O (15.0 mL) was added to the reaction mixture at for 0.5 h by syringe pump at 0 ℃. The reaction was allowed to stir for 10 h at room temperature. Upon the completion of reaction, mixture was poured into a crushed ice and 1 M HCl was added (adjusted with pH 1). After neutralization using sat. $NaHCO_3$, the mixture was extracted with EtOAc (2 x 30 mL). The organic layer was washed with brine (30 mL), dried over anhydrous Mg_2SO_4 and concentrated. The residues were purified by flash column chromatography on silica gel, using hexane and EtOAc (20 : 1). (2-aminophenyl)(cyclohexyl)methanone **5c′** was obtained as pale yellow solid (0.45 g, 44% yield); mp = 75-77 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.27-7.23 (m, 1H), 6.67-6.63 (m, 2H), 6.27 (s, 2H), 3.27 (tt, *J* = 11.3, 3.1 Hz, 1H), 1.89-1.82 (m, 4H), 1.77-1.70 (m, 1H), 1.56-1.46 (m, 2H), 1.39 (qt, *J* = 12.7, 3.3 Hz, 2H), 1.26 (qt, *J* = 12.3, 3.1 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 206.6, 150.9, 134.2, 131.1, 117.7, 117.1, 115.9, 46.0, 30.0, 26.2, 26.1; IR (neat) υ 3461, 3338, 2930, 1614, 1450, 1244, 971, 747 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}NO$ 204.1388, Found 204.1383.

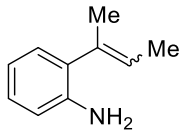
Ph_3PMeBr (1.05 g, 3.0 mmol, 1.5 equiv.), *t*BuOK (0.45 g, 3.0 mmol, 1.5 equiv.) and dry THF (4.0 mL) was added to an oven dried round bottom flask. After reaction mixture was stirred for 30 min, **5c′** (0.39 g, 2.0 mmol, 1.0 equiv.) in dry THF (4.0 mL) was added dropwise to the activated mixture for 30 min using syringe pump at 0 ℃. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, H_2O (20 mL) was added to the mixture. After stirring for an additional 5 min, the mixture was extracted with EtOAc (2 x 20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel, using hexane and EtOAc (100 : 1). **5c** was obtained as

colorless oil (0.32 g, 80% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.07 (td, *J* = 7.7, 1.5 Hz, 1H), 6.96 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.75-6.70 (m, 2H), 5.24 (t, *J* = 1.6 Hz, 1H), 5.01 (d, *J* = 0.9 Hz, 1H), 3.70 (s, 2H), 2.21 (t, *J* = 11.0 Hz, 1H), 1.89-1.67 (m, 5H), 1.33-1.11 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 153.4, 143.5, 129.6, 129.0, 127.8, 118.0, 115.3, 112.5, 44.6, 32.3, 26.8, 26.4; IR (neat) υ 3473, 3382, 2925, 1611, 1493, 1296, 907, 748 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{19}N$ 201.1517; Found 201.1517.

4.1.5. Synthesis of substrate 5q-5r[56]



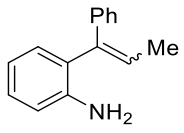
Ph_3PMeBr (1.5 equiv.), *t*BuOK (1.5 equiv.) and dry THF (0.5 M) was added to an oven dried round bottom flask. After reaction mixture was stirred for 30 min, corresponding ketone (1.0 equiv.) in dry THF (0.5 M) was added dropwise to the activated mixture for 30 min using syringe pump at 0 °C. The reaction was allowed to stir for overnight at room temperature. Upon the completion of reaction, H_2O (50 mL) was added to the mixture. After stirring for an additional 5 min, the mixture was extracted with EtOAc (2 x 50 mL). The organic layer was washed with brine (50 mL), dried over anhydrous Mg_2SO_4, concentrated and then, purified by flash column chromatography on silica gel.



5q

2-(but-2-en-2-yl)aniline (5q)

: Following the above procedure, 2-aminoacetophenone (1.35 g, 10.0 mmol, 1.0 equiv.), PPh_3EtBr (5.40 g, 15.0 mmol, 1.5 equiv.), *t*BuOK (2.24 g, 15.0 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 25 : 1), **5q** was obtained as brown oil (0.25 g, 17% yield, *E* : *Z* = 3 : 1); ^{1}H-NMR (400 MHz, $CDCl_3$) *E*-Product : δ 7.07-7.03 (td, *J* = 7.8, 1.6 Hz, 1H), 6.99 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.76-6.69 (m, 2H), 5.57 (qq, J = 6.8, 1.4 Hz, 1H), 3.68 (s, 2H), 1.96 (t, *J* = 1.4 Hz, 3H), 1.79 (dd, J = 6.9, 0.9 Hz, 3H), *Z*-Product : δ 7.11-7.06 (td, *J* = 7.6, 1.2 Hz, 0.33H), 6.95 (dd, J = 7.3, 1.4 Hz, 0.33H), 5.69-5.64 (m, 0.33H), 3.68 (s, 0.66 H), 1.97 (t, *J* = 1.6 Hz, 1H), 1.48 (qd, *J* = 3.2, 1.5 Hz, 1H) ^{13}C-NMR (100 MHz, $CDCl_3$) *E*-Product : δ 143.1, 134.5, 131.8, 128.9, 127.8, 127.5, 124.6, 118.4, 115.5, 17.2, 14.0, *Z*-Product : δ 142.8, 134.5, 128.8, 127.7, 123.6, 115.1, 24.7, 14.7; IR (neat) υ 3446, 3378, 2913, 1611, 1495, 1296, 1026, 747 cm^{-1}.



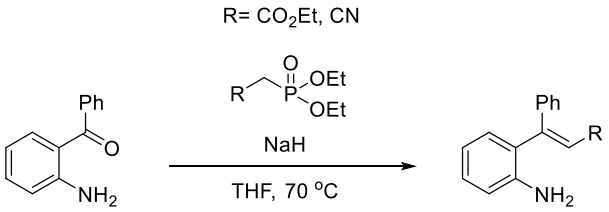
5r

2-(1-phenylprop-1-en-1-yl)aniline (5r)

: Following the above procedure, 2-aminobenzophenone (0.99 g, 5.0 mmol, 1.0 equiv.), PPh_3EtBr (2.70 g, 7.5 mmol, 1.5 equiv.), *t*BuOK (1.12 g, 7.5 mmol, 1.5 equiv.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 25 : 1), **5r** was obtained as brown oil (0.46 g, 44% yield, *E* : *Z* = 1 : 2); ^{1}H-NMR (400

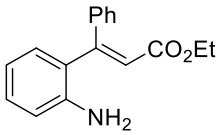
MHz, $CDCl_3$) *E*-Product : δ 7.37-7.20 (m, 8H), 7.11-7.08 (d, *J* = 7.6, 0.5H), 7.09 (dd, *J* = 7.3, 1.4 Hz, 0.5H), 6.76 (t, *J* = 7.6 Hz, 0.5H), 6.63 (d, *J* = 7.8 Hz, 0.5H), 5.96 (q, *J* = 7.0 Hz, 0.5H), 3.48 (s, 1H), 1.93 (d, *J* = 7.3 Hz, 1.5H), *Z*-Product : δ 7.37-7.20 (m, 8H), 7.17 (td, *J* = 7.6, 1.4 Hz, 1H), 7.00 (dd, *J* = 7.3, 1.4 Hz, 1H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.38 (q, *J* = 6.9 Hz, 1H), 3.48 (s, 2H), 1.72 (d, *J* = 6.9 Hz, 3H) ^{13}C-NMR (100 MHz, $CDCl_3$) *E*-Product : δ 144.0, 140.1, 139.4, 131.1, 130.2, 128.4, 128.3, 127.3, 126.0, 125.1, 118.4, 115.8, 15.6, *Z*-Product : δ 144.2, 141.0, 139.0, 131.0, 129.3, 128.5, 128.4, 127.2, 127.2, 126.3, 118.4, 115.5, 15.7; IR (neat) υ 3446, 3378, 2913, 1611, 1495, 1296, 1026, 747 cm^{-1}; IR (neat) υ 3468, 3378, 2910, 1613, 1493, 1298, 1032, 750 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}N$ 210.1283; Found 210.1275.

4.1.6. Synthesis of substrate 5s-5t



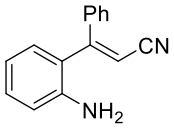
NaH (0.3 g, 7.5 mmol, 1.5 equiv.) was added portionwise to a solution of phosphonate (7.5 mmol, 1.5 equiv.) in THF (20 mL) at 0 ℃. After the mixture was stirred for 30 min at 0 ℃, 2-aminobenzophenone (0.99 g, 5.0 mmol, 1.0 equiv.) in THF (10 mL) was added dropwise to a reaction mixture at 0 ℃. The reaction was allowed to stir for overnight at 70 ℃ under heating block. Upon the completion of reaction, reaction mixture was quenched with H_2O (30 mL). The mixture was extracted with EtOAc (2 x 30 mL). The organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4,

concentrated and then, purified by flash column chromatography on silica gel.



5s

: Following the above procedure, triethyl phosphonoacetate (1.46 mL, 7.5 mmol, 1.5 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc = 25 : 1), **5s** was obtained as pale yellow oil (0.30 g, 22% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 5H), 7.15 (td, *J* = 7.7, 1.4 Hz, 1H), 7.08 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.75 (td, *J* = 7.5, 1.2 Hz, 1H), 6.63 (dd, *J* = 7.8, 0.9 Hz, 1H), 6.21 (s, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.58 (s, 2H), 1.17 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 154.8, 144.5, 138.5, 130.9, 130.0, 129.1, 128.9, 128.2, 127.2, 120.2, 118.3, 116.4, 77.5, 77.2, 76.8, 60.3, 14.1; IR (neat) υ 3446, 3371, 2850, 1658, 1490, 1267, 876, 750 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{17}H_{17}NO_2$ 267.1259; Found 267.1256.

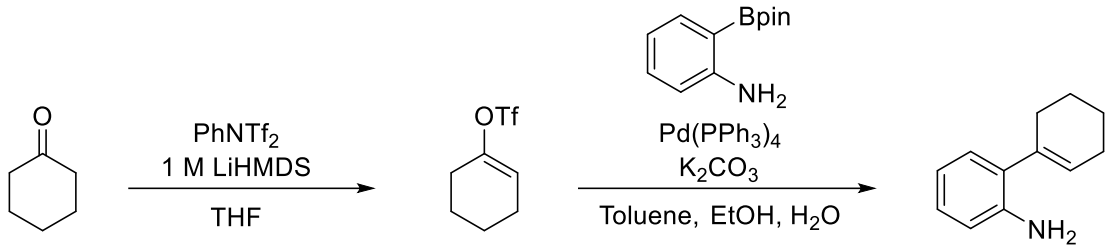


5t

: Following the above procedure, diethyl cyanomethylphosphonate (1.17 mL, 7.5 mmol, 1.5 equiv.) was used as a starting material. After purification by column chromatography (hexane : EtOAc : DCM = 15 : 1 : 1), **5t** as obtained as pale yellow solid (0.25 g, 21% yield); mp = 111-113 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60-7.55 (m, 2H), 7.50-7.42 (m, 3H), 7.22 (td, *J* = 7.7, 1.4 Hz, 1H), 7.09 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.79 (td, *J* = 7.4, 1.1 Hz, 1H), 6.66 (dd, *J* = 8.2, 0.9 Hz, 1H), 5.66 (s, 1H), 3.49 (s, 2H); ^{13}C-NMR (100 MHz,

$CDCl_3$) δ 161.6, 144.4, 136.4, 131.1, 130.9, 130.8, 129.1, 128.8, 124.8, 118.6, 117.9, 116.6, 97.1; IR (neat) υ 3474, 3374, 2211, 1621, 1490, 1309, 1030, 755 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{15}H_{13}N_2$ 221.1079; Found 221.1078.

4.1.7. Synthesis of 2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-amine (5u)[57]



5u

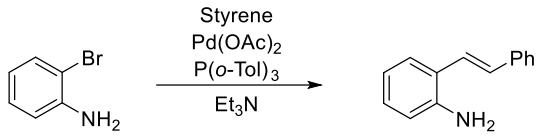
1.0 M LiHMDS in THF (4.8 mL, 4.8 mmol, 1.2 equiv.) was added to a solution of cyclohexanone (0.39 g 4.0 mmol, 1.0 equiv.) in dry THF (18.4 mL) -78 ℃ under Ar. After further stirring, a solution of $PhNTf_2$ (2.02 g, 5.6 mmol, 1.4 equiv.) in dry THF (20 mL) was dropwise added to a reaction mixture using syringe pump for 1 h at -78 ℃. The reaction mixture was allowed to warm to room temperature over a period of 4 h and stirred for additional 12 h. Upon the completion of reaction, sat. NH_4Cl (10 mL) was added to the resulting solution. The mixture was extracted with EtOAc (2 x 20 mL) and the organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4, and concentrated. The residues were purified by flash column chromatography on silica gel using hexane (100%). cyclohex-1-en-1-yl trifluoromethanesulfonate was obtained as colorless oil (0.51 g, 55% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 5.77-5.74 (m, 1H), 2.34-2.29 (m, 2H), 2.18 (qd, *J* = 6.3, 2.8 Hz, 2H), 1.78 (tt, *J* = 9.1, 3.1 Hz, 2H), 1.60 (tt, *J*

= 8.9, 3.1 Hz, 2H).

The spectrum data of cyclohex-1-en-1-yl trifluoromethanesulfonate is in agreement with the literature

Cyclohex-1-en-1-yl trifluoromethanesulfonate (0.46 g, 2.0 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (0.24 g, 0.2 mmol, 0.1 equiv.), K_2CO_3 (1.12 g, 8.0 mmol, 4.0 equiv.), 2-aminobenzeneboronic acid pinacol ester (0.66 g, 3.0 mmol, 1.5 equiv.) and Toluene/EtOH/H_2O (25/10/5 mL) were added to a dried round-bottom flask. The flask was equipped with reflux condenser and recharged with Ar balloon. The reaction mixture was heated to 100 ℃ for 20 h using oil bath. H_2O (15 mL) was added to a resulting solution and the mixture was extracted with EtOAc (2 x 20 mL). the organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4, and concentrated. The residues were purified by flash column chromatography on silica gel using hexane and EtOAc (50 : 1). **5u** was obtained as white solid (0.24 g, 69% yield); mp = 88-90 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.05 (td, *J* = 7.7, 1.5 Hz, 1H), 6.99 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.76-6.72 (m, 1H), 6.70 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.78-5.75 (m, 1H), 3.76 (s, 2H), 2.27-2.23 (m, 2H), 2.21-2.16 (m, 2H), 1.81-1.75 (m, 2H), 1.73-1.67 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 143.2, 136.5, 130.6, 128.7, 127.6, 126.9, 118.4, 115.5, 29.5, 25.5, 23.3, 22.3; IR (neat) υ 3446, 3367, 2927, 1611, 1492, 1290, 918, 748 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{12}H_{15}N$ 173.1204; Found 173.1198.

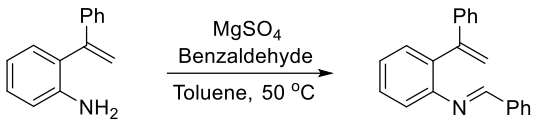
4.1.8. Synthesis of (*E*)-2-styrylaniline (5v)[56]



5v

2-bromoaniline (0.44 g, 2.5 mmol, 1.0 equiv.), styrene (0.34 mL, 3.0 mmol, 1.2 equiv.), $Pd(OAc)_2$ (5.73 mg, 0.025 mmol, 0.01 equiv.), P(*o*-Tol)$_3$ (62.12 mg, 0.2 mmol, 0.08 equiv.) and Et_3N (2.5 mL) were added to a dried borosilicate glass tubes under argon gas. The reaction mixture was heated to 100 ℃ for 20 h using oil bath. The mixture was cooled to room temperature and solvent was removed by *vacuo*. H_2O (15 mL) was added to residues and the mixture was extracted with EtOAc (2 x 20 mL). the organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4, and concentrated. The residues were purified by flash column chromatography on silica gel using hexane and EtOAc (100 : 1) and then residues were recrystallized from DCM and cooled hexane. **5v** was obtained as beige solid (0.45 g, 92% yield); mp = 106-108 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.43 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 16.0 Hz, 1H), 7.13 (td, *J* = 7.8, 1.4 Hz, 1H), 7.02 (d, *J* = 16.5 Hz, 1H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 3.82 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.1, 137.7, 130.4, 128.8, 127.7, 127.4, 126.5, 124.4, 124.0, 119.3, 116.4; IR (neat) υ 3481, 3357, 3031, 1610, 1489, 1339, 968, 755 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{14}H_{13}N$ 192.0661; Found 192.0663.

4.1.9. Synthesis of (*E*)-1-phenyl-*N*-(2-(1-phenylvinyl)phenyl)methanimine (5a′′)[57]



5a **5a″**

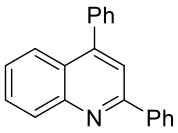
5a (0.20 g, 1.0 mmol, 1.0 equiv.), $MgSO_4$ (50 mg / 1.0 mmol), benzaldehyde (0.13 mL, 2.5 mmol, 1.0 equiv.) and dry toluene (2.0 mL) were added to a dried borosilicate glass tubes under argon gas. The reaction mixture was heated to 50 ℃ for overnight using oil bath. The mixture was cooled to room temperature and solvent was removed by *vacuo*. H_2O (15 mL) was added to residues and the mixture was extracted with EtOAc (2 x 20 mL). the organic layer was washed with brine (20 mL), dried over anhydrous Mg_2SO_4, and concentrated. The residues were purified by flash column chromatography on silica gel using hexane and Et_3N (10 : 1). **5a′′** was obtained as yellow oil (0.22 g, 77% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.54-7.52 (m, 2H), 7.40 (dtd, *J* = 12.8, 3.7, 1.6 Hz, 3H), 7.36-7.32 (m, 2H), 7.31-7.28 (m, 2H), 7.26-7.22 (m, 3H), 7.20-7.16 (m, 1H), 7.01 (dd, *J* = 7.8, 0.9 Hz, 1H), 5.68 (d, *J* = 1.4 Hz, 1H), 5.34 (d, *J* = 1.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.0, 150.6, 148.6, 142.0, 136.4, 135.4, 131.2, 130.8, 128.9, 128.7, 128.5, 128.1, 127.3, 127.1, 125.5, 118.8, 116.6.

The spectrum data of **1a′′** is in agreement with the literature

4.2 General procedure of quinoline

4.2.1 General procedure C using alcohol

Substrate **5** (0.2 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.5 mL), alcohol **2** (2.0 mmol, 10.0 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 90 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residues were purified by flash column chromatography on silica gel.

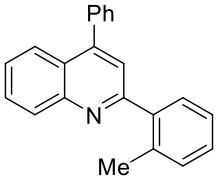


6aa

2,4-diphenylquinoline (6aa)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), benzyl alcohol **2a** (210.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6aa** was obtained as white solid (47.1 mg, 84% yield); mp = 75-77 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.7 Hz, 1H), 8.22-8.19 (m, 2H), 7.92 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.84 (s, 1H), 7.77-7.73 (m, 1H), 7.60-7.46 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 149.3, 149.0, 139.8, 138.5, 130.3, 129.7, 129.6, 129.5, 129.0, 128.7, 128.5, 127.7, 126.5, 125.9, 125.8, 119.5; IR (neat) υ 3059,

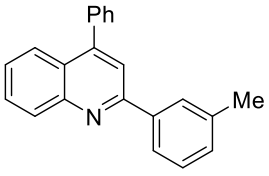
1590, 1547, 1489, 1406, 1358, 769, 698 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N$ 282.1283; Found 282.1287.



6ab

4-phenyl-2-(o-tolyl)quinoline (6ab)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 2-methylbenzyl alcohol **2b** (246.8 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100:1), **6ab** was obtained as colorless oil (51.1 mg, 86% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.7 Hz, 1H), 7.98 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.78-7.74 (m, 1H), 7.59-7.48 (m, 8H), 7.38-7.31 (m, 3H), 2.49 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.9, 148.6, 148.5, 140.7, 138.3, 136.2, 131.0, 130.1, 129.9, 129.7, 129.6, 128.7, 128.7, 128.6, 126.6, 126.1, 125.8, 125.4, 122.7, 20.6; IR (neat) υ 3058, 1590, 1547, 1489, 1406, 1355, 768, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1440.

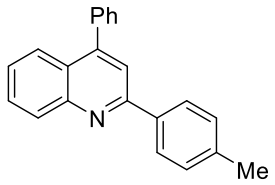


6ac

4-phenyl-2-(m-tolyl)quinoline (6ac)

: Following the general procedure A, **5a** (39.1 mg, 0.2 mmol), 3-methylbenzyl alcohol **2c** (243.6 μL, 2.0 mmol) were used as starting material. After purification by column

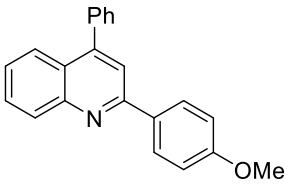
chromatography (hexane : EtOAc = 100:1), **6ac** was obtained as colorless oil (48.2 mg, 81% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 1H), 8.06 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.92 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.83 (s, 1H), 7.77-7.73 (m, 1H), 7.60-7.52 (m, 5H), 7.51-7.47 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 1H), 2.49 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.2, 149.2, 148.9, 139.7, 138.6, 138.6, 130.3, 130.2, 129.7, 129.6, 128.9, 128.7, 128.5, 128.4, 126.4, 125.9, 125.8, 124.9, 119.6, 21.7; IR (neat) IR (neat) υ 3059, 1590, 1574, 1450, 1405, 1357, 771, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1434.



6ad

3-phenyl-2-(p-tolyl)quinolin-4(1H)-one (6ad)

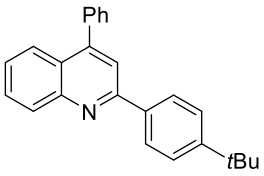
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-methylbenzyl alcohol **2d** (246.8 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ad** was obtained as white solid (58.1 mg, 87% yield); mp = 113-115 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.3 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 2H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.82 (s, 1H), 7.75-7.66 (m, 1H), 7.59-7.50 (m, 5H), 7.47 (td, *J* = 7.6, 1.4 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 2H), 2.45 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.9, 149.2, 148.9, 139.6, 138.6, 136.9, 130.2, 129.7, 129.6, 128.7, 128.5, 127.6, 126.3, 125.8, 125.7, 119.3, 21.5; IR (neat) υ 3059, 1591, 1544, 1490, 1419, 1357, 771, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1436.



6ae

2-(4-methoxyphenyl)-4-phenylquinoline (6ae)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-methoxybenzyl alcohol **2e** (251.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6ae** was obtained as yellow oil (41.2 mg, 66% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9.2 Hz, 1H), 8.18 (dt, *J* = 9.5, 2.5 Hz, 2H), 7.89 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.79 (s, 1H), 7.74-7.70 (m, 1H), 7.58-7.50 (m, 4H), 7.47-7.43 (m, 1H), 7.06 (dt, *J* = 9.6, 2.5 Hz, 2H), 3.89 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.0, 156.5, 149.1, 148.9, 138.6, 132.3, 130.0, 129.7, 129.6, 129.0, 128.7, 128.5, 126.1, 125.7, 125.6, 119.0, 114.3, 55.5; IR (neat) υ 3059, 1590, 1544, 1490, 1404, 1358, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1386.

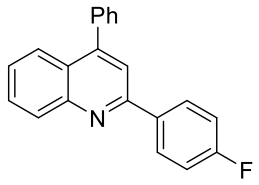


6af

2-(4-(tert-butyl)phenyl)-4-phenylquinoline (6af)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-*tert*-butylbenzyl alcohol **2f** (361.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6af** was obtained as colorless oil (47.6 mg, 71% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 1H), 8.16-8.13 (m, 2H),

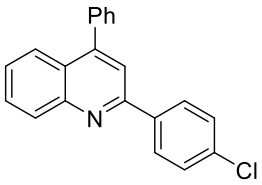
7.92 (dd, J = 8.3, 0.9 Hz, 1H), 7.83 (s, 1H), 7.76-7.72 (m, 1H), 7.59-7.51 (m, 7H), 7.50-7.45 (m, 1H), 1.40 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.1, 152.7, 149.1, 149.0, 138.6, 137.0, 130.2, 129.7, 129.6, 128.7, 128.5, 127.4, 126.3, 125.9, 125.8, 125.7, 119.4, 34.9, 31.4; IR (neat) υ 3060, 1590, 1543, 1490, 1416, 1363, 772, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}N$ 338.1909; Found 338.1914.



6ag

2-(4-fluorophenyl)-4-phenylquinoline (6ag)

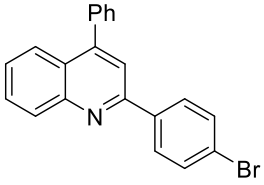
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-fluorobenzyl alcohol **2g** (291.5 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ag** was obtained as white solid (48.1 mg, 80% yield); mp = 111-113 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25-8.18 (m, 3H), 7.91 (d, J = 8.2 Hz, 1H), 7.78 (s, 1H), 7.76-7.72 (m, 1H), 7.57-7.51 (m, 5H), 7.50-7.46 (m, 1H), 7.24-7.19 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.1 (d, J_{CF} = 247.3 Hz), 162.7 (d, J_{CF} = 247.3 Hz), 155.9, 149.4, 148.8, 138.4, 135.9 (d, J_{CF} = 2.9 Hz), 135.9 (d, J_{CF} = 2.9 Hz), 130.1, 129.8, 129.7, 129.6 (d, J_{CF} = 8.7 Hz), 129.5 (d, J_{CF} = 8.7 Hz), 128.7, 128.6, 126.5, 125.8, 119.1, 116.0 (d, J_{CF} = 22.1 Hz), 115.8 (d, J_{CF} = 22.1 Hz); ^{19}F-NMR (376 MHz, $CDCl_3$) δ -112.25; IR (neat) υ 3060, 1591, 1547, 1490, 1401, 1357, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}FN$ 300.1189; Found 300.1193.



6ah

2-(4-chlorophenyl)-4-phenylquinoline (6ah)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-chlorobenzyl alcohol **2h** (288.0 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ah** was obtained as beige solid (45.3 mg, 72% yield); mp = 115-117 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.8 Hz, 1H), 8.16 (dt, *J* = 9.2, 2.2 Hz, 2H), 7.91 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.78 (s, 1H), 7.77-7.73 (m, 1H), 7.57-7.47 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.6, 149.6, 148.9, 138.4, 138.1, 135.7, 130.2, 129.8, 129.7, 129.1, 129.0, 128.8, 128.6, 126.7, 125.9, 125.8, 119.0; IR (neat) υ 3060, 1591, 1544, 1488, 1417, 1356, 772, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}ClN$ 316.0893; Found 316.0887.



6ai

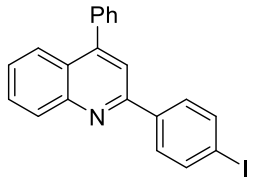
2-(4-bromophenyl)-4-phenylquinoline (6ai)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-bromobenzyl alcohol **2i** (377.86 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ai** was obtained as beige solid (44.7 mg, 62% yield); mp = 131-133 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.7 Hz, 1H), 8.09 (dt, *J* = 9.0, 2.1 Hz, 2H), 7.91 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.78 (s, 1H), 7.77-7.73 (m,

1H), 7.65 (dt, *J* = 8.9, 2.3 Hz, 2H), 7.59-7.52 (m, 5H), 7.51-7.48 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.7, 149.6, 148.9, 138.5, 138.3, 132.1, 130.2, 129.8, 129.7, 129.2, 128.8, 128.6, 126.7, 126.0, 125.8, 124.1, 119.0; IR (neat) υ 3059, 1589, 1543, 1487, 1416, 1357, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrN$ 360.0388; Found 360.0391.

*For the gram scale synthesis of **6ai***

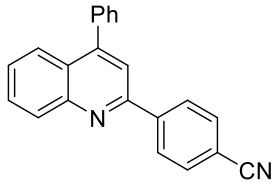
Substrate **5a** (1.11 g, 5.7 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (764.7 mg, 1.14 mmol, 20 mol%.) were added to an oven-dried 100 ml two-nected round bottom flask. The flask was capped with rubber septum and charged with N_2 balloon. DMSO (14.2 mL), 4-bromobenzyl alcohol **2i** (10.77 g, 57.0 mmol, 10.0 equiv) and DTBP (3.19 mL, 17.1 mmol, 3.0 equiv.) were added to the flask. The flask was equipped with reflux condenser and recharged with N_2 Balloon. The reaction mixture was stirred at 90 ℃ using oil bath and monitored by TLC. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (50 mL) and H_2O (30 mL). The mixture was extracted with EtOAc (50 mL x 2). Combined organic phase was washed with H_2O (2 x 50 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc : DCM = 200 : 1 : 1 to 100 : 1 1), **6ci** was obtained as beige solid (1.33 g, 65% yield).



6aj

2-(4-iodophenyl)-4-phenylquinoline (6aj)

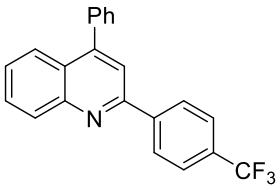
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-iodobenzyl alcohol **2j** (472.8 mg, 2.0 mmol) were used as starting material. by column chromatography (hexane : EtOAc = 100 : 1), **6aj** was obtained as white solid (55.9 mg, 69% yield); mp = 142-144 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.3 Hz, 1H), 7.95 (dt, *J* = 8.7, 2.1 Hz, 2H), 7.91 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.86 (dt, *J* = 8.7, 2.1 Hz, 2H), 7.77 (s, 1H), 7.76-7.72 (m, 1H), 7.56-7.52 (m, 5H), 7.51-7.47 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.7, 149.5, 148.8, 139.1, 138.3, 138.0, 130.2, 129.8, 129.6, 129.3, 128.7, 128.6, 126.7, 126.0, 125.8, 118.9, 96.1; IR (neat) υ 3058, 1588, 1541, 1484, 1415, 1356, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}IN$ 408.0249; Found: 408.0251.



6ak

4-(4-phenylquinolin-2-yl)benzonitrile (6ak)

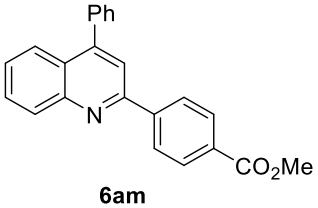
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-cyanobenzyl alcohol **2k** (269.0 mg, 2.0 mmol) were used as starting material. by column chromatography (hexane : EtOAc = 20 : 1), **6ak** was obtained as white solid (41.9 mg, 68% yield at 100 ℃); mp = 175-177 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 2H), 8.25 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.7 Hz, 1H), 7.81-7.75 (m, 4H), 7.61-7.51 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.5, 150.0, 148.9, 143.7, 138.1, 132.7, 130.4, 130.1, 129.6, 128.8, 128.2, 127.3, 126.2, 125.9, 119.1, 118.9, 112.9; IR (neat) υ 3060, 2226, 1588, 1542, 1490, 1417, 1358, 770, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}N_2$ 307.1235; Found 307.1236.



6al

4-phenyl-2-(4-(trifluoromethyl)phenyl)quinoline (6al)

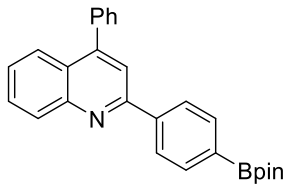
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-(trifluoromethyl)benzyl alcohol **2l** (355.8 mg, 2.0 mmol) were used as starting material. by column chromatography (hexane : EtOAc = 200 : 1), **6al** was obtained as white solid (57.4 mg, 82% yield at 100 ℃); mp = 123-125 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.3 Hz, 2H), 8.27 (d, *J* = 8.3 Hz, 1H), 7.94 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.84 (s, 1H), 7.80-7.75 (m, 3H), 7.58-7.54 (m, 5H), 7.54-7.50 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.3, 149.7, 148.9, 143.0, 138.2, 131.7 (q, J_{CF} = 32.6 Hz), 131.4 (q, J_{CF} = 32.6 Hz), 131.0 (q, J_{CF} = 32.6 Hz), 130.7 (q, J_{CF} = 32.6 Hz), 130.3, 130.3 (d, J_{CF} = 9.5 Hz), 130.2 (d, J_{CF} = 9.5 Hz), 130.0, 129.6, 129.0, 128.8, 128.7, 128.4 (q, J_{CF} = 270.0 Hz), 128.0 (q, J_{CF} = 2.9 Hz), 128.0 (q, J_{CF} = 2.9 Hz), 127.0 (q, J_{CF} = 2.9 Hz), 127.0 (q, J_{CF} = 2.9 Hz), 126.1, 125.8, 125.7 (q, J_{CF} = 270.0 Hz), 123.0 (q, J_{CF} = 270.0 Hz), 120.3 (q, J_{CF} = 270.0 Hz), 119.2; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -62.41; IR (neat) υ 3061, 1590, 1547, 1490, 1420, 1323, 770, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}F_3N$ 350.1157; Found 350.1150.



6am

methyl 4-(4-phenylquinolin-2-yl)benzoate (6am)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), methyl 4-(hydroxymethyl)benzoate **2m** (339.1 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 40 : 1), **6am** was obtained as white solid (45.8 mg, 67% yield); mp = 147-149 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29-8.25 (m, 3H), 8.19 (dd, *J* = 6.4, 1.8 Hz, 2H), 7.92 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.85 (s, 1H), 7.78-7.73 (m, 1H), 7.58-7.48 (m, 6H), 3.96 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.0, 155.6, 149.6, 148.9, 143.8, 138.3, 130.8, 130.3, 130.2, 129.9, 129.7, 128.8, 128.7, 127.6, 127.0, 126.1, 125.8, 119.4, 52.3 IR (neat) υ 3060, 1723, 1590, 1545, 1490, 1419, 1356, 772, 704 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{23}H_{18}NO_2$ 340.1338; Found 340.1344.



6an

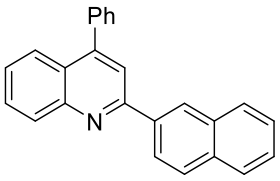
4-phenyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)quinoline (6an)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanol **2n** (447.8 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 4 : 1), **6an** was obtained as white solid (49.5 mg, 61% yield); mp = 96-98 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H), 8.23 (dd, *J* = 6.4, 1.8 Hz, 2H), 7.98 (dd, *J* = 6.4, 1.8 Hz, 2H), 7.91 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.86 (s, 1H), 7.76-7.72 (m, 1H), 7.59-7.51 (m, 5H), 7.51-7.46 (m, 1H), 1.39 (s, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.7, 149.4, 148.9, 142.1, 138.5, 135.4, 130.3, 129.7, 128.7, 128.6, 126.9, 126.6, 126.0, 125.8, 119.5, 84.1, 25.0; IR (neat) υ 3059, 1589, 1542, 1490, 1397, 1357, 774, 701 cm^{-1}; HRMS (FAB)

m/z: $[M + H]^+$ Calcd for $C_{27}H_{27}BNO_2$ 408.2135; Found 408.2145.

*For the 1.0 mmol scale synthesis of **6an***

Substrate **5a** (195.3 mg, 1.0 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (134.2 mg, 0.2 mmol, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (2.5 mL), (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanol **2n** (2.39 g, 10.0 mmol, 10.0 equiv.) and DTBP (0.56 mL, 3.0 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 90 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (20 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (20 mL x 2). Combined organic phase was washed with H_2O (20 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc = 20 : 1), **6an** was obtained as withe solid (242.9 mg, 60%).

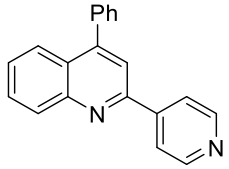


6ao

2-(naphthalen-2-yl)-4-phenylquinoline (6ao)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 2-naphthalenemethanol **2o** (319.6 mg, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ao** was obtained as beige solid (59.6 mg, 90% yield) ; mp = 118-120 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 1.4 Hz, 1H),

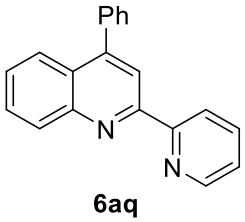
8.44 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 8.03-7.98 (m, 3H), 7.95 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.92-7.89 (m, 1H), 7.80-7.75 (m, 1H), 7.63-7.49 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.8, 149.4, 149.0, 138.5, 137.0, 134.0, 133.6, 130.2, 129.7, 129.0, 128.8, 128.7, 128.6, 127.9, 127.3, 126.8, 126.5, 126.5, 126.0, 125.8, 125.2, 119.6; IR (neat) υ 3058, 1590, 1548, 1491, 1407, 1347, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{25}H_{18}N$ 332.1439; Found 332.1444.



6ap

4-phenyl-2-(pyridin-4-yl)quinoline (6ap)

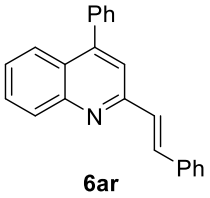
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 4-pyridinemethanol **2p** (220.5 mg, 1.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 1 : 1), **6ap** was obtained as white solid (45.7 mg, 80% yield at 110 ℃); mp = 149-151 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.1 Hz, 2H), 8.26 (d, *J* = 8.3 Hz, 1H), 8.09 (d, *J* = 6.0 Hz, 2H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.83 (s, 1H), 7.79-7.74 (m, 1H), 7.59-7.50 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.0, 150.5, 149.9, 148.9, 146.7, 138.0, 130.5, 130.0, 129.6, 128.8, 128.8, 127.4, 126.5, 125.9, 121.7, 118.9; IR (neat) υ 3058, 1587, 1541, 1489, 1415, 1361, 773, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2$ 283.1235; Found 283.1236.



6aq

4-phenyl-2-(pyridin-2-yl)quinoline (6aq)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 2-pyridinemethanol **2q** (195.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 4 : 1), **6aq** was obtained as white solid (29.7 mg, 53% yield at 110 ℃); mp = 143-145 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.1 Hz, 1H), 8.70 (d, *J* = 7.8 Hz, 1H), 8.53 (s, 1H), 8.27 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.89 (td, *J* = 7.8, 1.8 Hz, 1H), 7.77-7.73 (m, 1H), 7.60 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.56-7.47 (m, 4H), 7.36 (ddd, *J* = 7.5, 4.8, 0.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.4, 155.7, 149.4, 149.3, 148.6, 138.5, 137.1, 130.3, 129.8, 129.6, 128.6, 128.4, 126.9, 126.9, 125.9, 124.2, 122.0, 119.4; IR (neat) υ 3060, 1587, 1549, 1491, 1404, 1361, 772, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2$ 283.1235; Found 283.1231.

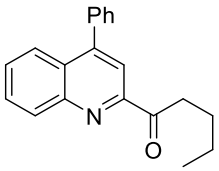


6ar

(E)-4-phenyl-2-styrylquinoline (6ar)

: Following the general procedure C, **1a** (39.1 mg, 0.2 mmol), cinnamyl alcohol **2r** (262.4 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6ar** was obtained as yellow oil (20.2 mg, 33% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.3 Hz, 1H), 7.88-7.85 (m, 1H),

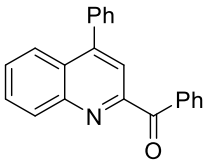
7.74-7.69 (m, 2H), 7.66-7.63 (m, 3H), 7.56-7.49 (m, 5H), 7.48-7.39 (m, 4H), 7.35-7.31 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.6, 148.9, 148.8, 138.4, 136.6, 134.7, 129.8, 129.7, 129.1, 128.9, 128.8, 128.7, 128.6, 127.4, 126.4, 126.1, 125.9, 119.6; IR (neat) υ 3058, 1587, 1541, 1489, 1415, 1361, 773, 702 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{23}H_{18}N$ 308.1439; Found 308.1438.



6as`

1-(4-phenylquinolin-2-yl)pentan-1-one (6as′)

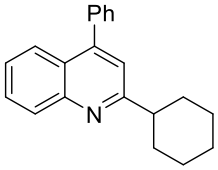
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 1-hexanol **2s** (512.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6as′** was obtained as brown oil (7.5 mg, 13% yield at 120 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.7 Hz, 1H), 8.07 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.81-7.77 (m, 1H), 7.61-7.57 (m, 1H), 7.57-7.48 (m, 5H), 3.43 (t, *J* = 7.3 Hz, 2H), 1.86-1.75 (m, 2H), 1.49 (td, *J* = 14.9, 7.5 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 203.1, 152.8, 149.5, 148.0, 138.0, 131.1, 129.9, 129.7, 128.8, 128.7, 128.6, 128.2, 126.0, 118.5, 37.4, 26.6, 22.7, 14.2; IR (neat) υ 3060, 1697, 1552, 1492, 1411, 1379, 772, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO$ 290.1545; Found 290.1536.



6at`

phenyl(4-phenylquinolin-2-yl)methanone (6at')

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), 1-hexanol **2s** (512.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6at′** was obtained as white solid (7.5 mg, 13% yield at 120 ℃); mp = 125-127 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29-8.27 (m, 3H), 8.06 (s, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.82-7.77 (m, 1H), 7.66-7.50 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 148.9, 148.3, 138.6, 129.7, 129.4, 129.3, 128.6, 128.4, 125.8, 125.7, 125.7, 120.0, 47.8, 33.0, 26.7, 26.2; IR (neat) υ 3060, 1658, 1586, 1490, 1361, 1258, 771, 701 cm^{-1};HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{16}NO$ 310.1232; Found 310.1235.

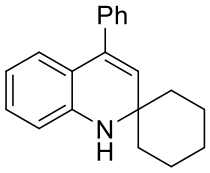


3au

2-cyclohexyl-4-phenylquinoline (6au)

: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), cyclohexaemethanol **2u** (503.0 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6au** was obtained as colorless oil (14.0 mg, 24% yield at 110 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.3 Hz, 1H), 7.86 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.71-7.66 (m, 1H), 7.55-7.46 (m, 5H), 7.43 (td, *J* = 7.6, 1.1

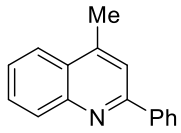
Hz, 1H), 7.27 (s, 1H), 2.97 (tt, *J* = 12.0, 3.0 Hz, 1H), 2.07 (dd, *J* = 13.3, 1.8 Hz, 2H), 1.90 (dt, *J* = 12.8, 3.2 Hz, 2H), 1.82-1.77 (m, 1H), 1.71-1.61 (m, 2H), 1.49 (qt, *J* = 12.8, 3.2 Hz, 2H), 1.33 (qt, *J* = 12.7, 3.6 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.5, 148.9, 148.3, 138.6, 129.7, 129.4, 129.3, 128.6, 128.4, 125.8, 125.7, 125.7, 120.0, 47.8, 33.0, 26.7, 26.2; IR (neat) υ 3058, 1592, 1542, 1490, 1414, 1339, 765, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}N$ 288.1752; Found 288.1755.



6av

4'-phenyl-1'H-spiro[cyclohexane-1,2'-quinoline] (6av)

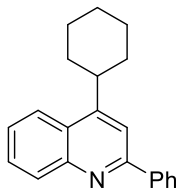
: Following the general procedure C, **5a** (39.1 mg, 0.2 mmol), cyclohexanol **2v** (425.5 μL, 4.0 mmol, 20 equiv.) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6av** was obtained as purple oil (6.5 mg, 12% yield at 100 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.31 (m, 5H), 7.01 (td, *J* = 7.6, 1.7 Hz, 1H), 6.88 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.61-6.56 (m, 2H), 5.62 (s, 1H), 1.81-1.77 (m, 2H), 1.69-1.63 (m, 2H), 1.61-1.51 (m, 4H), 1.49-1.43 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 143.8, 140.0, 136.6, 129.3, 129.2, 128.7, 128.3, 127.4, 126.2, 121.9, 117.5, 113.9, 53.3, 38.6, 29.9, 25.6, 21.5; IR (neat) υ 3057, 1593, 1556, 1490, 1445, 1361, 768, 702 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{20}H_{21}N$ 275.1674; Found 275.1684.



6ba

4-methyl-2-phenylquinoline (6ba)

: Following the general procedure C, **5b** (26.5 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ba** was obtained as colorless oil (30.8 mg, 70% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.2 Hz, 1H), 8.18-8.15 (m, 2H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.75-7.71 (m, 2H), 7.57-7.52 (m, 3H), 7.49-7.45 (m, 1H), 2.77 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.2, 148.1, 145.1, 139.8, 130.3, 129.5, 129.3, 128.9, 127.7, 127.3, 126.2, 123.7, 119.9, 19.2; IR (neat) υ 3061, 1599, 1550, 1495, 1452, 1364, 769, 696 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N$ 220.1126; Found 220.1123.

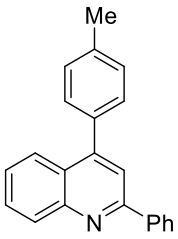


6ca

4-cyclohexyl-2-phenylquinoline (6ca)

: Following the general procedure C, **5c** (40.3 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ca** was obtained as white solid (39.8 mg, 69% yield); mp = 94-96 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 8.7, 0.9 Hz, 1H), 8.17-8.14 (m, 2H), 8.10 (d, *J* = 9.2 Hz, 1H), 7.77 (s, 1H), 7.73-7.69 (m, 1H), 7.56-7.52 (m, 3H), 7.49-7.45 (m, 1H), 3.41-3.35 (m, 1H), 2.09 (d, *J* = 10.5 Hz, 2H), 1.97 (dd, *J* = 9.6,

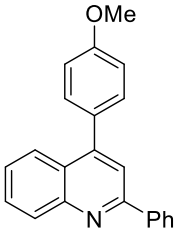
2.8 Hz, 2H), 1.91-1.87 (m, 1H), 1.69-1.53 (m, 4H), 1.38 (qt, *J* = 12.6, 3.6 Hz, 1H)^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.5, 154.1, 148.7, 140.4, 130.8, 129.2, 129.1, 128.9, 127.7, 126.0, 123.0, 115.6, 115.6, 39.2, 33.8, 27.1, 26.4; IR (neat) υ 3061, 1595, 1550, 1495, 1415, 1369, 768, 694 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}N$ 288.1752; Found 288.1751.



6da

2-phenyl-4-(p-tolyl)quinoline (6da)

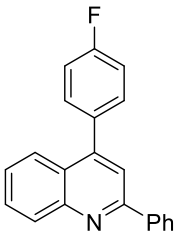
: Following the general procedure C, **5d** (41.9 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6da** was obtained as colorless oil (48.5 mg, 82% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H), 8.22-8.19 (m, 2H), 7.96 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.83 (s, 1H), 7.76-7.72 (m, 1H), 7.57-7.52 (m, 2H), 7.51-7.46 (m, 4H), 7.38 (d, *J* = 7.8 Hz, 2H), 2.50 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 149.4, 148.9, 139.8, 138.5, 135.6, 130.2, 129.6, 129.4, 129.0, 127.7, 126.4, 126.0, 125.8, 119.5, 21.4; IR (neat) υ 3059, 1591, 1546, 1492, 1402, 1359, 771, 695 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1433.



6ea

4-(4-methoxyphenyl)-2-phenylquinoline (6ea)

: Following the general procedure C, **5e** (45.1 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), 6**ea** was obtained as white solid (49.3 mg, 79% yield); mp = 106-108 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 9.2 Hz, 1H), 8.22-8.19 (m, 2H), 7.97 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.81 (s, 1H), 7.76-7.72 (m, 1H), 7.56-7.45 (m, 6H), 7.09 (dt, *J* = 9.3, 2.5 Hz, 2H), 3.92 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.0, 157.0, 149.0, 149.0, 139.8, 135.9, 130.9, 130.8, 130.2, 129.6, 129.4, 128.9, 127.7, 126.3, 126.1, 125.8, 119.4, 114.2, 55.5; IR (neat) υ 3060, 1591, 1545, 1493, 1419, 1359, 771, 695 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1399.

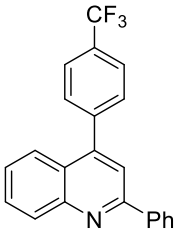


6fa

4-(4-fluorophenyl)-2-phenylquinoline (6fa)

: Following the general procedure C, **5f** (42.7 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column

chromatography (hexane : EtOAc = 100 : 1), **6fa** was obtained as white solid (47.1 mg, 79% yield); mp = 85-87 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.2 Hz, 1H), 8.21 (dd, *J* = 9.4, 2.5 Hz, 2H), 7.87 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.80 (s, 1H), 7.77-7.73 (m, 1H), 7.56-7.46 (m, 6H), 7.25 (tt, *J* = 9.0, 2.4 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 164.3 (d, J_{CF} = 246.3 Hz), 161.8 (d, J_{CF} = 246.3 Hz), 157.0, 148.9, 148.2, 139.6, 134.5 (d, J_{CF} = 3.8 Hz), 134.4 (d, J_{CF} = 3.8 Hz), 131.4 (d, J_{CF} = 7.6 Hz), 131.3 (d, J_{CF} = 7.6 Hz), 130.3, 129.7, 129.5, 129.0, 127.7, 126.6, 125.8, 125.5, 119.5, 115.9 (d, J_{CF} = 22.0 Hz), 115.7 (d, J_{CF} = 22.0 Hz); ^{19}F-NMR (376 MHz, $CDCl_3$) δ -113.14; IR (neat) υ 3061, 1607, 1546, 1494, 1415, 1358, 771, 694 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}FN$ 300.1189; Found 300.1189.

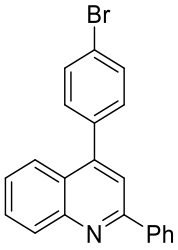


6ga

2-phenyl-4-(4-(trifluoromethyl)phenyl)quinoline (6ga)

: Following the general procedure C, **5g** (52.7 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ga** was obtained as white solid (29.9 mg, 43% yield at 100 °C); mp = 91-93 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.7 Hz, 1H), 8.21-8.19 (m, 2H), 7.82 (dd, *J* = 9.4, 7.6 Hz, 4H), 7.79-7.75 (m, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.57-7.47 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 148.9, 147.7, 142.2, 139.5, 131.3 (q, J_{CF} = 32.6 Hz), 131.0 (q, J_{CF} = 32.6 Hz), 130.6 (q, J_{CF} = 32.6 Hz), 130.4, 130.3 (q, J_{CF} = 32.6 Hz), 130.1, 130.0, 129.7, 129.1, 128.3 (q, J_{CF} = 271.2 Hz), 127.7,

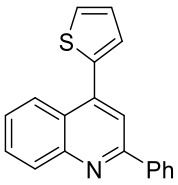
126.9, 125.8 (q, J_{CF} = 2.9 Hz), 125.8 (q, J_{CF} = 2.9 Hz), 125.7 (q, J_{CF} = 2.9 Hz), 125.7 (q, J_{CF} = 2.9 Hz), 125.6 (q, J_{CF} = 271.2 Hz), 125.5, 125.2, 122.9 (q, J_{CF} = 271.2 Hz), 120.2 (q, J_{CF} = 271.2 Hz), 119.4; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -62.43 IR (neat) υ 3061, 1607, 1546, 1494, 1415, 1358, 771, 694 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}F_3N$ 350.1157; Found 350.1150.



6ha

4-(4-bromophenyl)-2-phenylquinoline (6ha)

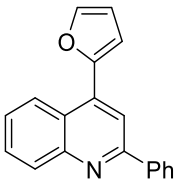
: Following the general procedure C, **5h** (54.8 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ha** was obtained as white solid (49.1 mg, 68% yield at 100 ℃); mp = 89-91 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 1H), 8.21-8.18 (m, 2H), 7.85 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.79 (s, 1H), 7.77-7.73 (m, 1H), 7.69 (dt, *J* = 8.6, 2.1 Hz, 2H), 7.56-7.46 (m, 4H), 7.44 (dt, *J* = 8.9, 2.2 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) 13C-NMR (101 MHz, CHLOROFORM-D) δ 157.0, 148.8, 148.0, 139.5, 137.3, 131.9, 131.3, 130.3, 129.8, 129.6, 129.0, 127.7, 126.7, 125.5, 125.4, 122.9, 119.3; IR (neat) υ 3060, 1597, 1546, 1486, 1409, 1357, 771, 693 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrN$ 360.0388; Found 360.0379.



6ia

2-phenyl-4-(thiophen-2-yl)quinoline (6ia)

: Following the general procedure C, **5i** (40.3 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ia** was obtained as white solid (49.9 mg, 87% yield); mp = 86-88 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.28 (t, *J* = 7.8 Hz, 2H), 8.22-8.20 (m, 2H), 7.94 (s, 1H), 7.79-7.74 (m, 1H), 7.57-7.53 (m, 4H), 7.50-7.47 (m, 1H), 7.44 (dd, *J* = 3.7, 0.9 Hz, 1H), 7.26 (dd, *J* = 4.8, 3.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 149.1, 141.7, 139.5, 139.3, 130.3, 129.8, 129.6, 129.0, 128.7, 127.9, 127.7, 127.3, 126.8, 125.5, 125.4, 119.9; IR (neat) υ 3061, 1584, 1546, 1493, 1405, 1360, 770, 694 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{19}H_{13}NS$ 288.0847; Found 288.0838.

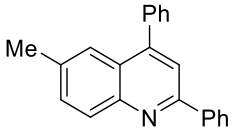


6ja

4-(furan-2-yl)-2-phenylquinoline (6ja)

: Following the general procedure C, **5j** (37.1 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ja** was obtained as beige solid (26.3 mg, 48% yield); mp = 122-124 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 8.7, 0.9 Hz, 1H), 8.25-8.20 (m, 3H), 8.12 (s, 1H), 7.78-7.73 (m, 1H), 7.71 (t, *J* = 0.9 Hz, 1H), 7.60-

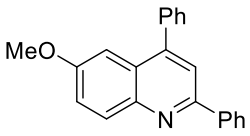
7.53 (m, 3H), 7.50-7.46 (m, 1H), 7.03-7.02 (m, 1H), 6.66 (q, *J* = 1.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.1, 151.4, 149.3, 144.0, 139.7, 136.6, 130.5, 129.7, 129.5, 129.0, 127.7, 126.9, 125.3, 123.6, 116.8, 112.2; IR (neat) υ 3062, 1596, 1561, 1495, 1405, 1376, 764, 706 cm^{-1}; HRMS (FAB) m/z: [M] Calcd for $C_{19}H_{14}NO$ 272.1075; Found 272.1073.



6ka

6-methyl-2,4-diphenylquinoline (6ka)

: Following the general procedure C, **5k** (41.9 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ka** was obtained as beige solid (31.5 mg, 53% yield); mp = 120-122 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21-8.16 (m, 3H), 7.79 (s, 1H), 7.67 (s, 1H), 7.60-7.51 (m, 8H), 7.49-7.44 (m, 1H), 2.49 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.1, 148.6, 147.4, 139.8, 138.7, 136.4, 131.9, 129.9, 129.7, 129.3, 128.9, 128.7, 128.4, 127.6, 125.8, 124.5, 119.6, 22.0; IR (neat) υ 3057, 1588, 1548, 1490, 1448, 1359, 761, 698 cm^{-1};HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1445.

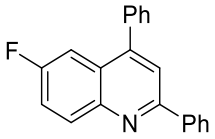


6la

6-methoxy-2,4-diphenylquinoline (6la)

: Following the general procedure C, **5l** (45.1 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column

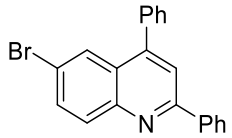
chromatography (hexane : EtOAc = 100 : 1), **6la** was obtained as beige solid (45.0 mg, 72% yield); mp = 109-111 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19-8.16 (m, 3H), 7.79 (s, 1H), 7.61-7.49 (m, 7H), 7.47-7.43 (m, 1H), 7.41 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.21 (d, *J* = 2.8 Hz, 1H), 3.80 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.9, 154.7, 147.9, 145.0, 139.8, 138.8, 131.7, 129.5, 129.1, 128.9, 128.8, 128.5, 127.4, 126.8, 122.0, 119.8, 103.8, 55.6; IR (neat) υ 3059, 1591, 1546, 1492, 1403, 1359, 771, 696 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}NO$ 312.1388; Found 312.1391.



6ma

6-fluoro-2,4-diphenylquinoline (6ma)

: Following the general procedure C, **5m** (42.7 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ma** was obtained as white solid (40.9 mg, 68% yield); mp = 93-95 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 9.2, 5.5 Hz, 1H), 8.20-8.17 (m, 2H), 7.85 (s, 1H), 7.60-7.46 (m, 10H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J_{CF} = 246.1 Hz), 159.5 (d, J_{CF} = 246.1 Hz), 156.4 (d, J_{CF} = 2.9 Hz), 156.4 (d, J_{CF} = 2.9 Hz), 148.9, 148.8, 146.0, 139.4, 138.1, 132.7, 132.6, 129.6, 129.5, 129.0, 128.9, 128.8, 127.6, 126.7 (d, J_{CF} = 9.5 Hz), 126.6 (d, J_{CF} = 9.5 Hz), 120.0, 119.9 (d, J_{CF} = 24.9 Hz), 119.7 (d, J_{CF} = 24.9 Hz), 109.3, 109.1; ^{19}F-NMR (376 MHz, $CDCl_3$) δ -112.83; IR (neat) IR (neat) υ 3060, 1593, 1549, 1491, 1390, 1359, 779, 698 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}FN$ 300.1189; Found 300.1192.



6na

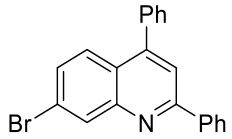
6-bromo-2,4-diphenylquinoline (6na)

: Following the general procedure C, **5n** (54.8 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6na** was obtained as white solid (51.1 mg, 71% yield at 100 ℃); mp = 96-98 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20-8.17 (m, 2H), 8.11 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 2.3 Hz, 1H), 7.84 (s, 1H), 7.80 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.61-7.46 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.3, 148.5, 147.5, 139.3, 137.8, 133.2, 132.0, 129.8, 129.6, 129.1, 129.0, 128.9, 127.9, 127.7, 127.1, 120.6, 120.2; IR (neat) υ 3060, 1589, 1544, 1491, 1419, 1355, 771, 700 cm^{-1};HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrN$ 360.0388; Found 360.0394.

*For the 1.0 mmol scale synthesis of **6na***

Substrate **5n** (247.2 mg, 1.0 mmol, 1.0 equiv.) and $Fe(OTs)_3.6H_2O$ (134.2 mg, 0.2 mmol, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (2.5 mL), benzyl alcohol **2a** (1.09 mL, 10.0 mmol, 10.0 equiv.) and DTBP (0.56 mL, 3.0 mmol, 3.0 equiv.) were added to the reaction tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred at 100 ℃ using oil bath. After stirring for 20 h, the reaction mixture was cooled to room temperature and diluted with EtOAc (20 mL) and H_2O (15 mL). The mixture was extracted with EtOAc (20 mL x 2). Combined organic phase was washed with H_2O (20 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6na** was

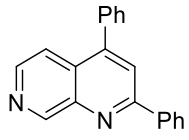
obtained as withe solid (234.4 mg, 65%).



6oa

7-bromo-2,4-diphenylquinoline (6oa)

: Following the general procedure C, **5o** (54.8 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6oa** was obtained as white solid (49.3 mg, 68% yield at 100 ℃); mp = 110-112 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 1.8 Hz, 1H), 8.19 (dt, *J* = 8.2, 1.7 Hz, 2H), 7.83 (s, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.59-7.47 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.9, 149.7, 149.4, 139.3, 138.0, 132.5, 129.8, 129.6, 129.0, 128.9, 128.8, 127.7, 127.2, 124.6, 123.9, 119.6; IR (neat) υ 3060, 1592, 1541, 1485, 1418, 1358, 765, 697 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrN$ 360.0388; Found 360.0387.

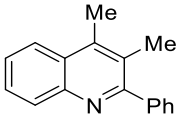


6pa

2,4-diphenyl-1,7-naphthyridine (6pa)

: Following the general procedure C, **1p** (39.5 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 5 : 1), **6pa** was obtained as white solid (5.4 mg, 10% yield at 110 ℃); mp = 116-118 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 8.56 (d, *J* = 5.9 Hz, 1H), 8.22 (dt, *J* = 6.6, 1.6 Hz, 2H), 8.03 (s, 1H), 7.75 (d, *J* = 5.0 Hz, 1H), 7.62-

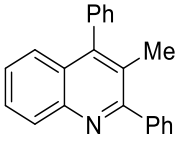
7.49 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.6, 154.9, 148.3, 144.0, 143.8, 138.9, 136.9, 130.1, 129.5, 129.2, 129.1, 129.0, 127.7, 122.8, 117.9; IR (neat) υ 3059, 1593, 1535, 1483, 1406, 1369, 767, 698 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}N_2$ 283.1235; Found 283.1238.



6qa

3-methyl-2,4-diphenylquinoline (6qa)

: Following the general procedure C, **5q** (29.4 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **6qa** was obtained as white solid (11.7 mg, 25% yield at 110 ℃); mp = 68-70 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 1H), 7.69-7.65 (m, 1H), 7.63 (dt, *J* = 6.6, 1.6 Hz, 2H), 7.58-7.42 (m, 6H), 7.41 (d, *J* = 3.7 Hz, 2H), 7.32 (dt, *J* = 6.4, 1.6 Hz, 2H), 2.17 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 146.3, 141.5, 137.8, 129.5, 129.4, 129.1, 128.8, 128.7, 128.4, 128.2, 128.0, 127.2, 126.9, 126.4, 126.1, 18.7; IR (neat) υ 3059, 1576, 1494, 1443, 1398, 1351, 757, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}N$ 234.1283; Found 234.1278.

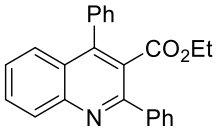


6ra

3-methyl-2,4-diphenylquinoline (6ra)

: Following the general procedure C, **5r** (41.9 mg, 0.2 mmol), benzyl alcohol **2a** (209.0

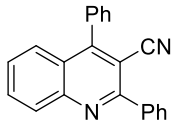
μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 40 : 1), **6ra** was obtained as white solid (43.8 mg, 74% yield at 110 ℃); mp = 151-153 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 1H), 7.69-7.65 (m, 1H), 7.63 (dt, *J* = 6.6, 1.6 Hz, 2H), 7.58-7.42 (m, 6H), 7.41 (d, *J* = 3.7 Hz, 2H), 7.32 (dt, *J* = 6.4, 1.6 Hz, 2H), 2.17 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.9, 148.0, 146.3, 141.5, 137.8, 129.5, 129.4, 129.1, 128.8, 128.7, 128.4, 128.2, 128.0, 127.2, 126.9, 126.4, 126.1, 18.7; IR (neat) υ 3059, 1572, 1556, 1485, 1396, 1352, 765, 701 cm^{-1} HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}N$ 296.1439; Found 296.1445.



6sa

ethyl 2,4-diphenylquinoline-3-carboxylate (6sa)

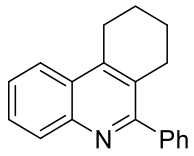
: Following the general procedure C, **5s** (53.5 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **6sa** was obtained as white solid (55.5 mg, 79% yield at 110 ℃); mp = 87-89 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.7 Hz, 1H), 7.79-7.75 (m, 3H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.53-7.41 (m, 9H), 3.88 (q, *J* = 7.2 Hz, 2H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.3, 156.1, 147.9, 147.3, 140.3, 135.7, 130.6, 129.9, 129.5, 129.0, 128.7, 128.6, 128.5, 128.3, 127.3, 127.2, 126.7, 125.7, 61.4, 13.5; IR (neat) υ 3060, 1730, 1552, 1485, 1400, 1298, 768, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}NO_2$ 354.1494; Found 354.1497.



6ta

2,4-diphenylquinoline-3-carbonitrile (6ta)

: Following the general procedure C, **5t** (39.5 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 5 : 1), **6ta** was obtained as pale yellow solid (7.5 mg, 12% yield at 110 ℃); mp = 159-161 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.2 Hz, 1H), 8.00 (dd, *J* = 7.5, 1.6 Hz, 2H), 7.89-7.85 (m, 1H), 7.70 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.65-7.51 (m, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.7, 156.6, 148.7, 138.3, 134.7, 132.7, 130.2, 130.1, 129.9, 129.6, 129.4, 129.0, 128.8, 128.1, 127.1, 124.9, 117.4, 105.8; IR (neat) υ 3060, 2223, 1546, 1483, 1393, 1350, 750, 697 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}N_2$ 307.1235; Found 307.1239.

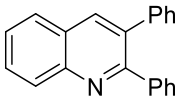


6ua

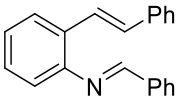
6-phenyl-7,8,9,10-tetrahydrophenanthridine (6ua)

: Following the general procedure C, **5u** (34.7 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6ua** was obtained as brown solid (23.5 mg, 45% yield); mp = 85-87 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.98 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.68-7.63 (m, 1H), 7.56-7.52 (m, 3H), 7.49-7.45 (m, 2H), 7.44-7.40 (m, 1H), 3.22 (t, *J* = 6.4 Hz, 2H), 2.73 (t, *J* = 6.2 Hz, 2H), 1.98 (tt, *J* = 9.2, 3.1

Hz, 2H), 1.79 (tt, *J* = 8.9, 3.1 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.9, 145.7, 142.2, 141.3, 130.2, 128.8, 128.6, 128.4, 128.1, 127.1, 126.3, 122.5, 28.9, 25.9, 22.9, 22.4; IR (neat) υ 3059, 1686, 1580, 1493, 1404, 1327, 768, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}N$ 260.1439; Found 260.1434.



6va



6va″

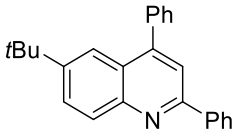
2,3-diphenylquinoline (6va)

: Following the general procedure C, **5v** (54.8 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 25 : 1), **6va** was obtained as yellow oil (3.3 mg, 6% yield at 110 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.7 Hz, 1H), 8.18 (s, 1H), 7.88 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.76-7.72 (m, 1H), 7.59-7.55 (m, 1H), 7.47-7.44 (m, 2H), 7.32-7.24 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.6, 147.4, 140.5, 140.1, 137.7, 134.7, 130.2, 129.9, 129.8, 129.6, 128.4, 128.1, 128.1, 127.6, 127.4, 127.3, 126.9; IR (neat) υ 3057, 1592, 1555, 1484, 1409, 1373, 768, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N$ 282.1283; Found 282.1284.

(E)-1-phenyl-N-(2-((E)-styryl)phenyl)methanimine (6va″)

: Following the general procedure C, **5v** (54.8 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 200 : 1), **6va″** was obtained as yellow oil (9.3 mg, 16% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.98 (q, *J* = 3.0 Hz, 2H), 7.72 (d, *J* = 6.9 Hz, 1H), 7.64 (d, *J* = 16.5 Hz, 1H), 7.52 (t, *J* = 3.2 Hz, 5H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.31-7.22 (m, 3H), 7.14 (d, *J* = 16.5 Hz, 1H), 7.00 (dd, *J* = 7.8, 0.9 Hz, 1H); ^{13}C-

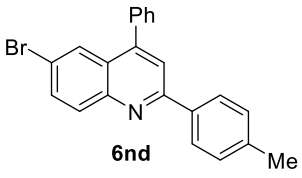
NMR (100 MHz, $CDCl_3$) δ 160.3, 150.2, 138.0, 136.5, 131.6, 131.3, 129.8, 129.0, 129.0, 128.7, 128.6, 127.6, 126.7, 126.1, 125.9, 125.4, 118.7; IR (neat) υ 3062, 1716, 1542, 1490, 1451, 1271, 757, 692 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{18}N$ 284.1439; Found 284.1447.



6wa

6-(tert-butyl)-2,4-diphenylquinoline (6wa)

: Following the general procedure C, **5w** (50.3 mg, 0.2 mmol), benzyl alcohol **2a** (209.0 μL, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6wa** was obtained as white solid (50.2 mg, 74% yield); mp = 133-135 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24-8.18 (m, 3H), 7.91 (d, *J* = 1.8 Hz, 1H), 7.86 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.82 (s, 1H), 7.63-7.51 (m, 7H), 7.49-7.45 (m, 1H), 1.38 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.5, 149.3, 149.1, 147.5, 140.0, 138.7, 129.8, 129.7, 129.2, 128.9, 128.7, 128.5, 127.6, 125.4, 120.6, 119.6, 35.2, 31.3; IR (neat) υ 3060, 1588, 1547, 1491, 1393, 1358, 771, 694 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}N$ 338.1909; Found 338.1906.

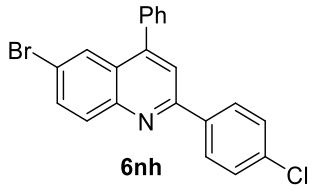


6nd

6-bromo-4-phenyl-2-(p-tolyl)quinoline (6md)

: Following the general procedure C, **5n** (54.8 mg, 0.2 mmol), 4-methylbenzyl alcohol **2d** (246.8 mg, 2.0 mmol) were used as starting material. After purification by column

chromatography (hexane : EtOAc = 100 : 1), **6nd** was obtained as white solid (64.4 mg, 80% yield at 100 ℃); mp = 116-118 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.7, 2.7 Hz, 3H), 8.03 (d, *J* = 2.3 Hz, 1H), 7.82 (s, 1H), 7.78 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.61-7.51 (m, 5H), 7.34 (d, *J* = 8.2 Hz, 2H), 2.44 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.2, 148.3, 147.5, 139.9, 137.9, 136.4, 133.0, 131.9, 129.8, 129.6, 128.9, 128.8, 127.9, 127.5, 127.0, 120.3, 119.9, 21.5; IR (neat) υ 3059, 1590, 1541, 1484, 1410, 1354, 770, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{22}H_{17}BrN$ 374.0544; Found 374.0542.



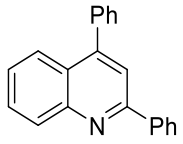
6nh

6-bromo-2-(4-chlorophenyl)-4-phenylquinoline (6nh)

: Following the general procedure C, **5n** (54.8 mg, 0.2 mmol), 4-chlorobenzyl alcohol **2h** (288.0 mg, 2.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6nh** was obtained as white solid (47.7 mg, 60% yield at 100 ℃); mp = 171-173 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (dt, *J* = 8.9, 2.3 Hz, 2H), 8.08 (d, *J* = 9.2 Hz, 1H), 8.03 (d, *J* = 1.8 Hz, 1H), 7.81-7.78 (m, 2H), 7.60-7.52 (m, 5H), 7.49 (dt, *J* = 9.2, 2.2 Hz, 2H)^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.9, 148.7, 147.5, 137.7, 136.0, 133.3, 131.9, 129.5, 129.2, 129.0, 129.0, 128.9, 127.9, 127.1, 120.8, 119.7; IR (neat) υ 3059, 1588, 1540, 1480, 1406, 1354, 830, 700 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{14}BrClN$ 393.9998; Found 393.9982.

4.2.2. General procedure D using methyl arenes

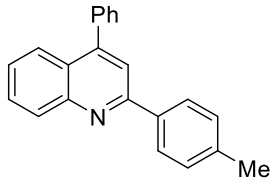
Substrate **5** (0.2 mmol, 1.0 equiv.), $Fe(OTs)_3.6H_2O$ (26.8 mg, 20 mol%.) were added to an oven-dried Borosilicate Glass Tube. The tube was capped with rubber septum and charged with N_2 balloon. DMSO (0.5 mL), methyl arene **4** (18 mmol, 90 equiv.) and DTBP (112.0 μL, 0.6 mmol, 3.0 equiv.) were added Borosilicate Glass Tube. The reaction vessel was recharged with N_2 Balloon, and then the mixture was stirred for 40 h 110 ℃ using oil bath. Reaction mixture was cooled to room temperature and diluted with EtOAc (10 mL) and H_2O (10 mL). The mixture was extracted with EtOAc (10 mL x 2). Combined organic phase was washed with H_2O (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated in *vacuo*. The residues were purified by flash column chromatography on silica gel.



6aa

2,4-diphenylquinoline (6aa)

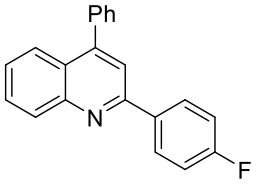
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc 100 : 1), **6aa** was obtained as white solid (31.1 mg, 55% yield).



6ad

4-phenyl-2-(p-tolyl)quinoline (6ad)

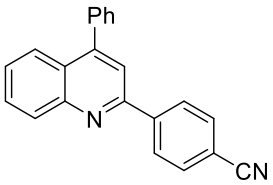
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), *p*-xylene **4d** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ad** was obtained as white solid (39.0 mg, 66% yield).



6ag

2-(4-fluorophenyl)-4-phenylquinoline (6ag)

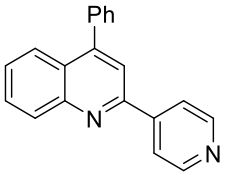
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), 4-fluorotoluene **4g** (2.0 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ag** was obtained as white solid (26.5 mg, 44% yield).



6ak

4-(4-phenylquinolin-2-yl)benzonitrile (6ak)

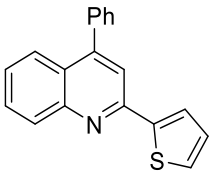
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), *p*-tolunitrile **4k** (2.2 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 20 : 1), **6ak** was obtained as white solid (20.7 mg, 34% yield).



6ao

4-phenyl-2-(pyridin-4-yl)quinoline (6ao)

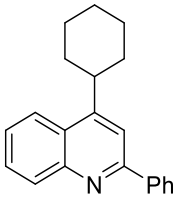
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), 4-picoline **4o** (1.8 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 5 : 1), **6ag** was obtained as white solid (25.2 mg, 45% yield).



6aw

4-phenyl-2-(thiophen-2-yl)quinoline (6aw)

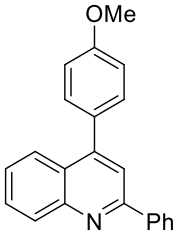
: Following the general procedure D, **5a** (39.1 mg, 0.2 mmol), 2-methylthiophene **4w** (1.8 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6aw** was obtained as brown oil (34.5 mg, 60% yield); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.3 Hz, 1H), 7.85 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.75 (d, *J* = 5.5 Hz, 2H), 7.73-7.69 (m, 1H), 7.59-7.51 (m, 5H), 7.49-7.47 (m, 1H), 7.46-7.42 (m, 1H), 7.16 (dd, *J* = 5.0, 3.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.0, 149.2, 148.7, 145.5, 138.2, 129.8, 129.7, 129.6, 128.7, 128.6, 128.2, 126.3, 126.0, 126.0, 125.8, 118.0; IR (neat) υ 3064, 1590, 1542, 1489, 1427, 1339, 770, 701 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}NS$ 288.0847; Found 288.0844.



6ca

4-cyclohexyl-2-phenylquinoline (6ca)

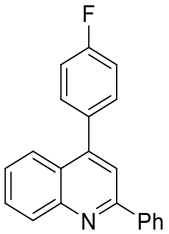
: Following the general procedure D, **5c** (40.3 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ca** was obtained as white solid (25.7 mg, 45% yield).



6ea

4-(4-methoxyphenyl)-2-phenylquinoline (6ea)

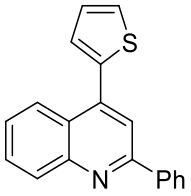
: Following the general procedure D, **5e** (45.1 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6ea** was obtained as white solid (33.3 mg, 53% yield).



6fa

4-(4-fluorophenyl)-2-phenylquinoline (6fa)

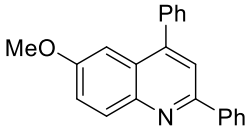
: Following the general procedure D, **5f** (42.7 mg, 0.2 mmol), toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6fa** was obtained as white solid (29.4 mg, 49% yield).



6ha

2-phenyl-4-(thiophen-2-yl)quinoline (6ha)

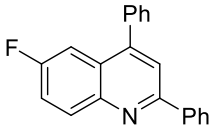
: Following the general procedure D, **5h** (40.3 mg, 0.2 mmol toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6ha** was obtained as white solid (28.6 mg, 50% yield).



6ka

6-methoxy-2,4-diphenylquinoline (6ka)

: Following the general procedure D, **5k** (45.1 mg, 0.2 mmol toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1), **6ka** was obtained as white solid (28.8 mg, 46% yield).



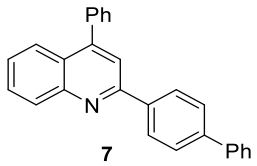
6la

6-fluoro-2,4-diphenylquinoline (6la)

: Following the general procedure D, **5l** (42.7 mg, 0.2 mmol toluene **4a** (1.9 mL, 18.0 mmol) were used as starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1), **6la** was obtained as white solid (28.0 mg, 47% yield).

4.3. Synthesis of poly-aryl substituted quinolines

Aryl halide (1.0 equiv.), Aryl boron (1.5 equiv.), anhydrous K_2CO_3 (4.0 equiv.), PPh_3 (15 mol%.), $Pd(OAc)_2$ (5 mol%.), and toluene : EtOH : H_2O (2.0 mL : 0.5 mL : 1.0 mL) were added to an oven-dried Borosilicate Glass Tube. The reaction vessel was charged with argon and sealed. The mixture was heated to 100 ℃ using oil bath and stirred for 24 h. The mixture was diluted with EtOAc (5.0 mL) and H_2O (5.0 mL), and extracted with EtOAc (2 x 10.0 mL). The organic layer was washed with H_2O (10.0 mL) and brine (10.0 mL), dried over anhydrous Mg_2SO_4, concentrated, and then residues were purified by flash column chromatography on silica gel using hexane and EtOAc or filtered and washed with EtO_2.



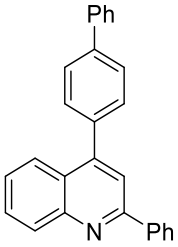
7

2-([1,1'-biphenyl]-4-yl)-4-phenylquinoline (7)

: Following the above procedure (using Br-quinoline), **6ai** (43.2 mg, 0.12 mmol, 1.0 equiv.), phenyl boronic acid (22.2 mg, 0.18 mmol, 1.5 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3 (4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1). **7** was obtained as white solid (33.4 mg, 78% yield).

: Following the above procedure (using Bpin-quinoline), **6an** (73.3 mg, 0.18 mmol, 1.5 equiv.), iodobenzene (25.0 mg, 0.12 mmol, 1.0 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3 (4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1). **7** was obtained as white solid (38.4 mg, 90% yield).

m.p = 175-177 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33-8.28 (m, 3H), 7.94 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.89 (s, 1H), 7.80-7.74 (m, 3H), 7.70 (dt, *J* = 8.1, 1.6 Hz, 2H), 7.61-7.52 (m, 5H), 7.52-7.47 (m, 3H), 7.42-7.37 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.5, 149.3, 149.0, 142.2, 140.7, 138.6, 138.5, 130.2, 129.7, 129.0, 128.7, 128.6, 128.1, 127.7, 127.7, 127.3, 126.5, 125.9, 125.8, 119.3; IR (neat) υ 3058, 1589, 1542, 1487, 1415, 1358, 768, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{27}H_{20}N$ 358.1596; Found 358.1589.

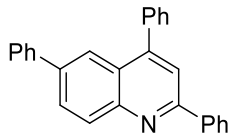


8

4-([1,1'-biphenyl]-4-yl)-2-phenylquinoline (8)

: Following the above procedure, **6ha** (43.2 mg, 0.12 mmol, 1.0 equiv.), phenyl boronic acid (22.2 mg, 0.18 mmol, 1.5 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3 (4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 50 : 1). **8** was obtained as white solid (47.1 mg, 99% yield); mp = 150-152 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.3 Hz, 1H), 8.24 (dt, *J* = 6.7, 1.5 Hz, 2H), 8.02 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.89 (s, 1H), 7.80 (dd, *J* = 10.5, 1.8 Hz, 2H), 7.78-7.71 (m, 3H), 7.68-7.65 (m, 2H), 7.58-7.47 (m, 6H), 7.45-7.41 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 148.9, 141.4, 140.5, 139.7, 137.4, 130.3, 130.2, 129.7, 129.5, 129.1, 129.0, 127.8, 127.7, 127.4, 127.3, 126.5, 125.8, 125.7, 119.5; IR (neat) υ 3059, 1590, 1545, 1487, 1411, 1359, 769, 695 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{27}H_{20}N$ 358.1596; Found

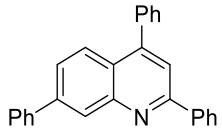
358.1602.



9

2,4,6-triphenylquinoline (9)

: Following the above procedure, **6na** (43.2 mg, 0.12 mmol, 1.0 equiv.), phenyl boronic acid (22.2 mg, 0.18 mmol, 1.5 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3 (4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1). **9** was obtained as white solid (35.7 mg, 83% yield); mp = 174-176 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.7 Hz, 1H), 8.24 (d, *J* = 7.3 Hz, 2H), 8.12 (s, 1H), 8.02 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.87 (s, 1H), 7.66-7.45 (m, 12H), 7.40-7.36 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.9, 149.5, 148.2, 140.8, 139.6, 139.2, 138.5, 130.6, 129.7, 129.6, 129.4, 129.0, 128.8, 128.6, 127.7, 127.6, 126.1, 123.5, 119.9; IR (neat) υ 3058, 1589, 1546, 1485, 1392, 1358, 763, 698 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{27}H_{20}N$ 358.1596; Found 358.1595.

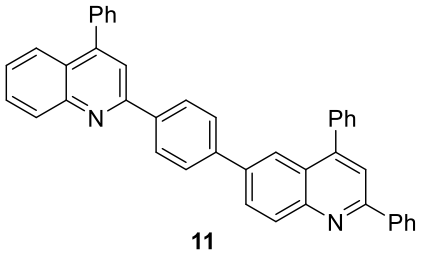


10

2,4,7-triphenylquinoline (10)

: Following the above procedure, **6oa** (43.2 mg, 0.12 mmol, 1.0 equiv.), phenyl boronic acid (22.2 mg, 0.18 mmol, 1.5 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3

(4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by column chromatography (hexane : EtOAc = 100 : 1). **10** was obtained as white solid (30.5 mg, 71% yield); mp = 131-133 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 1.8 Hz, 1H), 8.23 (dt, *J* = 8.5, 1.6 Hz, 2H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.84-7.80 (m, 3H), 7.77 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.63-7.48 (m, 10H), 7.45-7.41 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.5, 149.3, 149.1, 142.3, 140.4, 139.8, 138.5, 129.7, 129.5, 129.1, 129.0, 128.8, 128.7, 128.0, 127.9, 127.7, 127.6, 126.3, 126.0, 125.0, 119.4; IR (neat) υ 3032, 1705, 1621, 1508, 1489, 1339, 761, 695 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{27}H_{20}N$ 358.1596; Found 358.1592.



11

2,4-diphenyl-6-(4-(4-phenylquinolin-2-yl)phenyl)quinoline (11)

: Following the above procedure, **6na** (43.2 mg, 0.12 mmol, 1.0 equiv.), **6an** (73.3 mg, 0.18 mmol, 1.5 equiv.), K_2CO_3 (71.6 mg, 0.48 mmol, 4.0 equiv.), PPh_3 (4.67 mg,0.018, 15 mol%.), $Pd(OAc)_2$ (1.36 mg, 0.006 mmol, 5 mol%.) were used as a starting material. After purification by filtration using Et_2O, **11** was obtained as white solid (44.7 mg, 67% yield); mp = 251-253 ℃; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.7 Hz, 1H), 8.29 (dd, *J* = 8.0, 6.2 Hz, 3H), 8.24-8.19 (m, 3H), 8.09 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.89-7.84 (m, 2H), 7.80-7.73 (m, 3H), 7.65-7.47 (m, 14H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.0, 156.2, 149.6, 149.5, 148.8, 148.4, 141.6, 139.6, 138.7, 138.5, 138.4, 138.4, 130.7, 130.1, 129.8, 129.7, 129.7, 129.6, 129.2, 129.0, 128.9, 128.8, 128.7,

128.6, 128.2, 127.9, 127.7, 126.6, 126.1, 125.9, 125.8, 123.7, 120.0, 119.3; IR (neat) υ 3054, 1588, 1540, 1488, 1403, 1358, 825, 699 cm^{-1}; HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{42}H_{29}N_2$ 561.2331; Found 561.2329.

4.4. Fluorescence assay

Each quinoline compounds (10.0 µL, 1.0 mM solution in DMSO, final concentration: 5.0 µM) were added to EtOH (1990.0 µL). Excitation spectra of **6aa**, **7**-**11** were recorded from 200 - 400 nm and then, the emission spectra were measured by entering maximum excitation. All spectra were measured in either quartz or dis-posable acrylic 1.0 cm optical cuvettes.

국문 초록

질소를 포함하는 헤테로고리 화합물은 다양한 생리활성을 가지거나 또는 천연물에서 주로 발견되는 구조로 알려져 있다. 상용화된 저분자 의약품들 중에 *N*-헤테로고리 화합물구조가 핵심 골격으로 사용되는 것을 볼 수 있는데, 이는 *N*-헤테로고리 화합물이 타겟 단백질의 아미노산과 중요한 상호작용을 형성하여 다양한 생리활성을 나타낼 수 있기 때문이다. 이러한 타겟 단백질의 생리활성을 조절할 수 있는 특징으로 인해 *N*-헤테로고리 화합물의 연구가 의약화학뿐만 아니라 유기합성에서도 중요함을 시사하고 있다. 최근에 *N*-헤테로고리 화합물의 합성 방법으로 전이금속을 이용한 새로운 논문들이 많이 보고 되고 있다. 전이금속 중에서 철 촉매는 값이 저렴하고 친환경적이며 독성이 적고 지구상에 풍부하다고 알려져 있다. 이러한 철 촉매와 산화제를 함께 사용해 낮은 산화 수준의 기질인 alcohol과 methyl arene을 반응 중에 aldehyde로 산화시켜 *N*-헤테로고리 화합물의 합성에 적용하려 한다.

일반적인 *N*-헤테로고리 화합물의 합성은 질소를 포함한 친핵체와 aldehyde와 같은 친전자체를 이용하여 축합반응을 통해 합성된다. 하지만 aldehyde의 경우 불안정하여 상업적으로 구하기 어렵기 때문에 기질 범위를 확장하는데 제한이 된다. 이러한 단점을 보완하고자 낮은 산화 레벨의 기질인 alcohol과 methyl arene을 철 촉매와 산화제를 함께 사용하여 산화적 고리화 반응을 통해 *N*-헤테로고리 화합물을 합성하는 방법을 연구해 왔다. 철 촉매는 단일 전자 이동 (Single Electron Transfer)을 유도하여 라디칼 반응을 통해 화학 반응이 진행한다고 보고 되고 있으며, 산화제와 함께 이용하면 반응에서 산화과정을 조절하여 alcohol과 methyl arene을 쉽게 aldehyde로 산화시킬 수 있다. 이렇게 형성된 중간체의 aldehyde와 2-amino aryl ketone 또는 2-amino styrene를 산화적 고리화 반응을 통해 각각의 4-quinolone과 quinoline의

합성에 적용할 수 있었다. 이 합성 방법은 다양한 종류의 작용기에 적용 가능하였고, 총 47 종의 4-quinolone과 총 58 종의 quinoline을 합성하였다.

주요어 : *N*-헤테로고리 화합물, alcohol, methyl arene, 철 촉매, 산화제, 산화적 고리화 반응, 4-quinolone, quinoline

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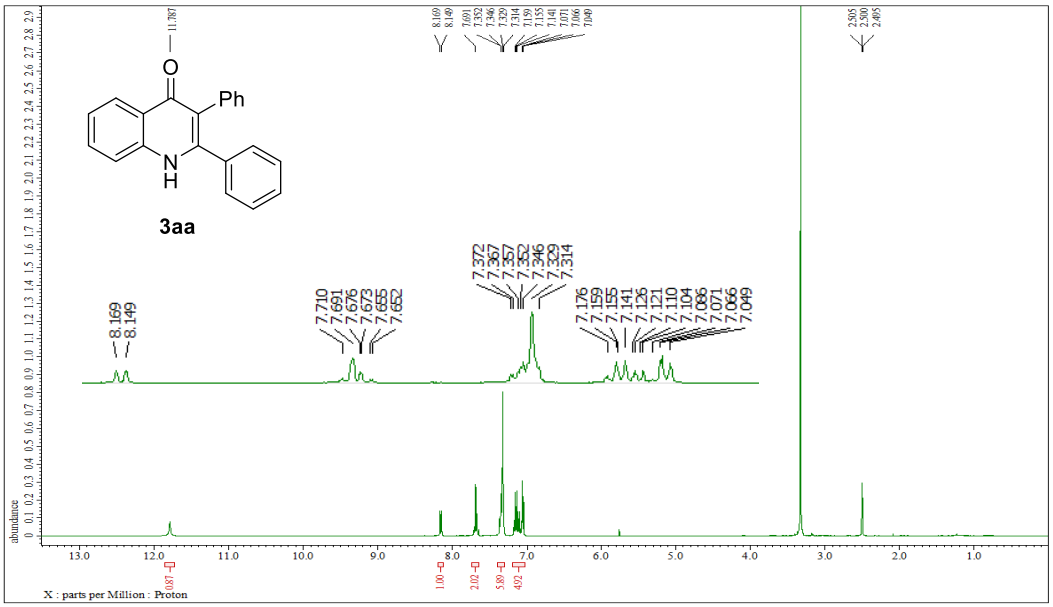
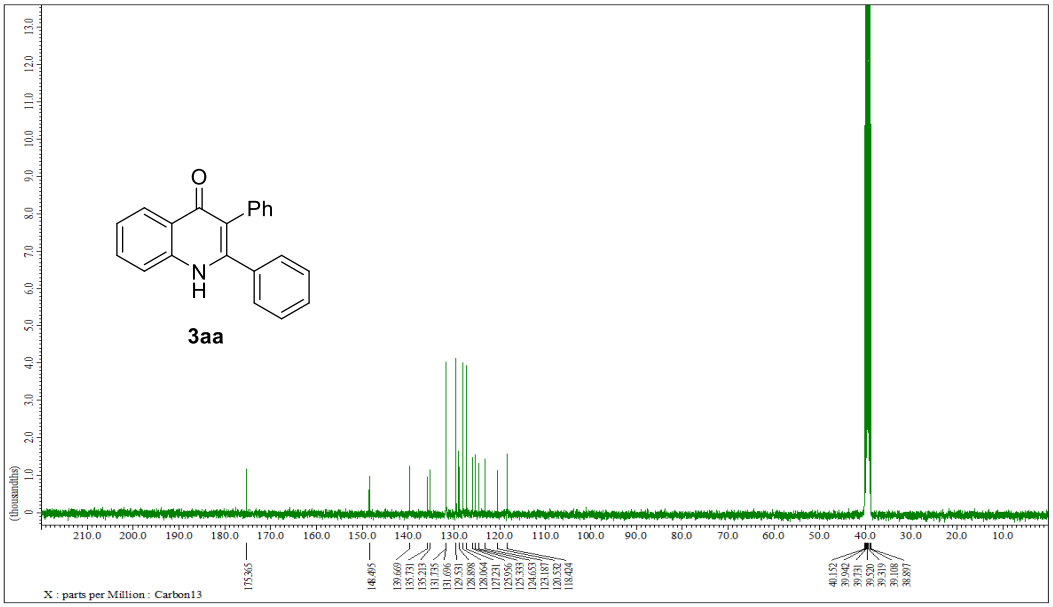
APPENDIX

3aa ^{1}H-NMR (400 MHz, DMSO)



3aa ^{13}C-NMR (100 MHz, DMSO)



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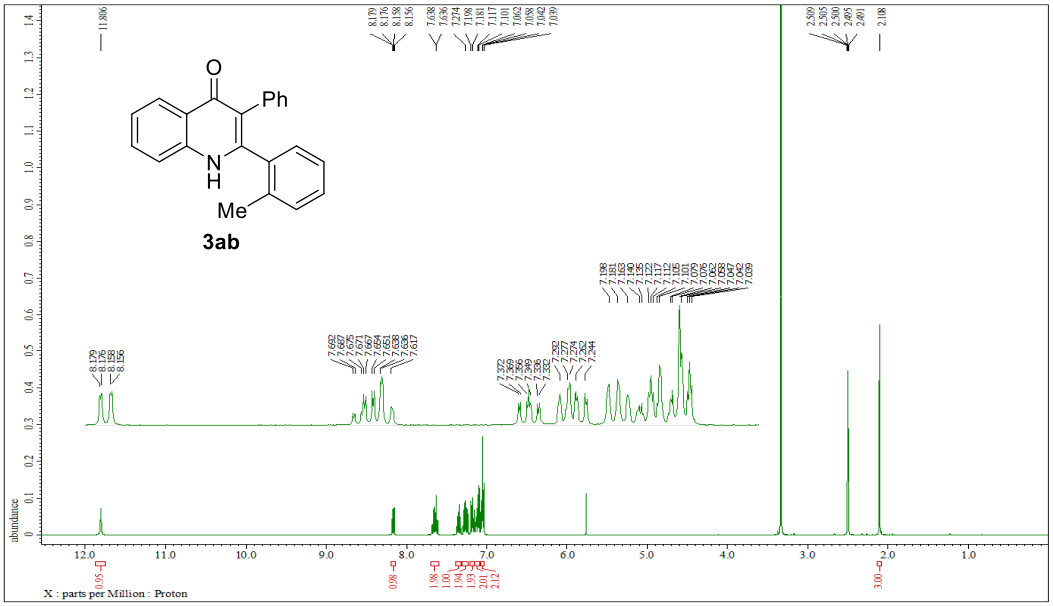

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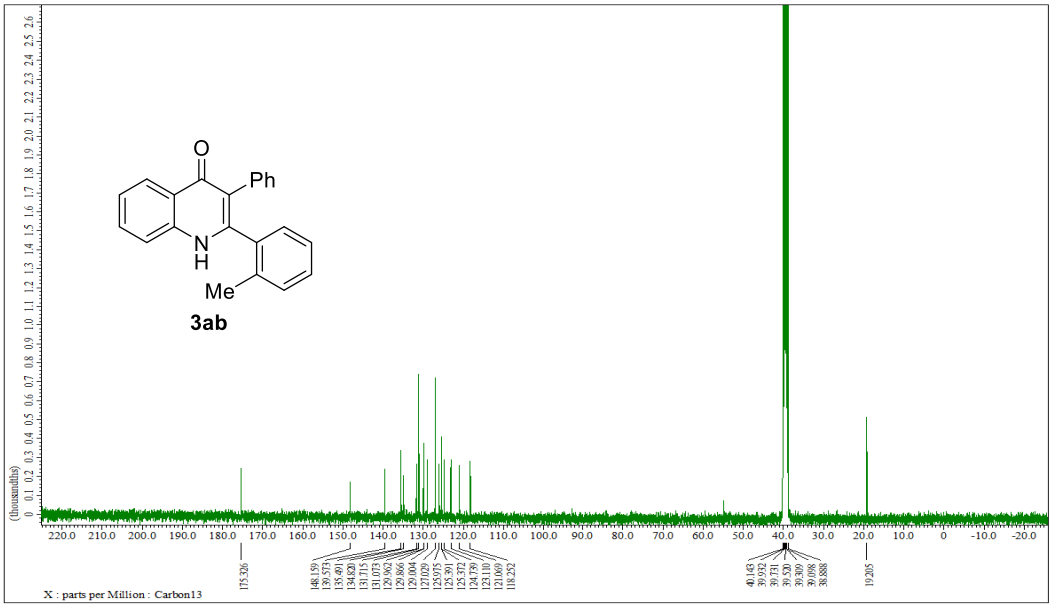

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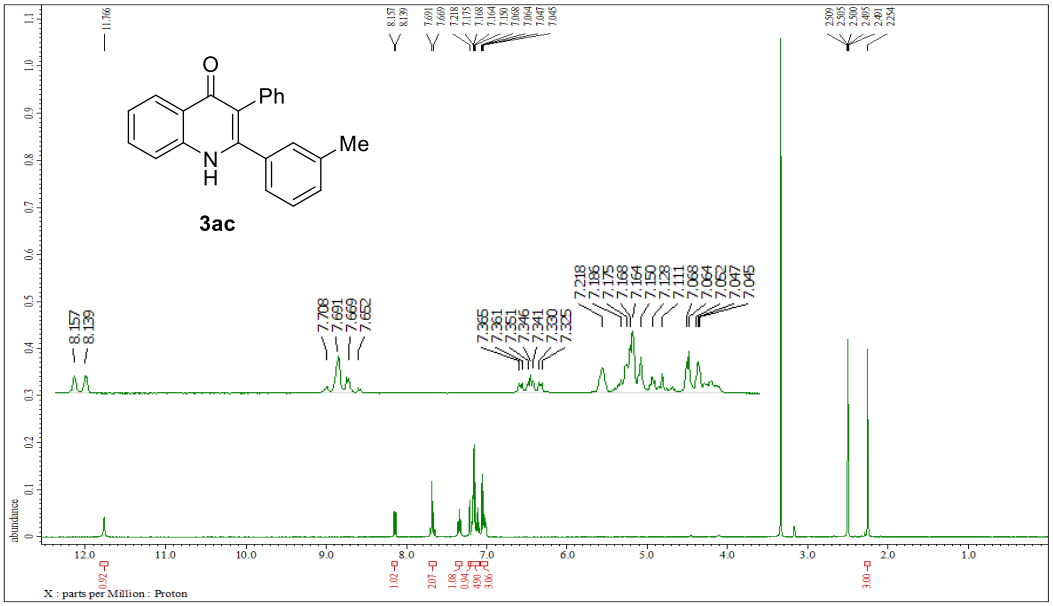

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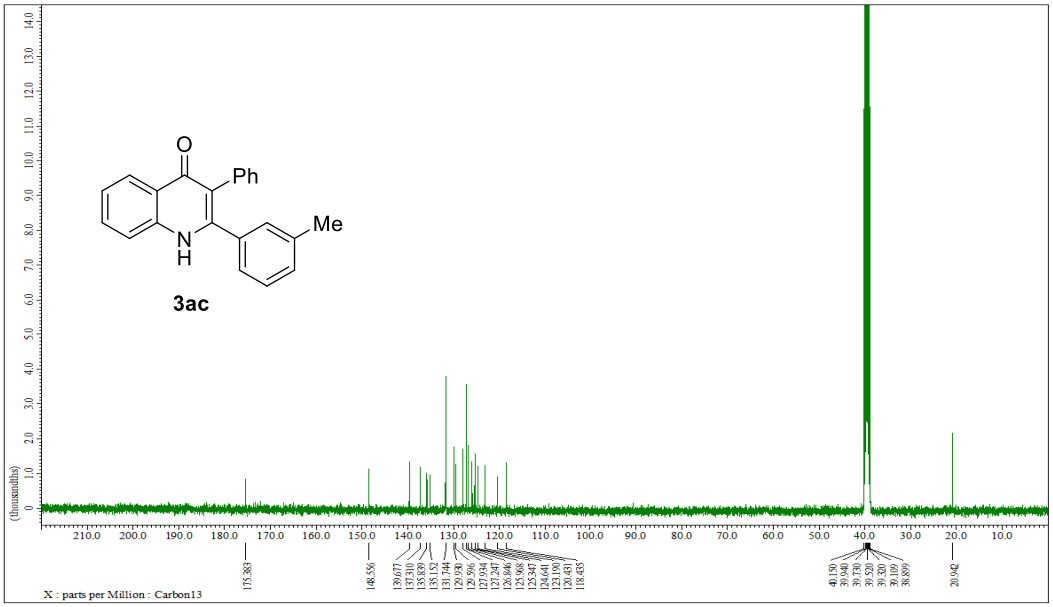

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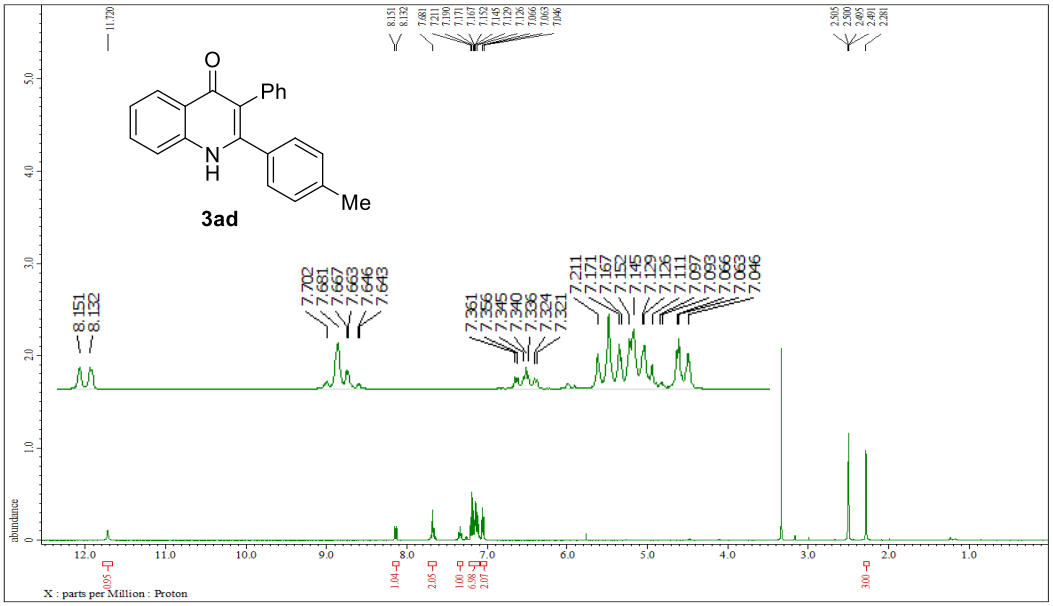

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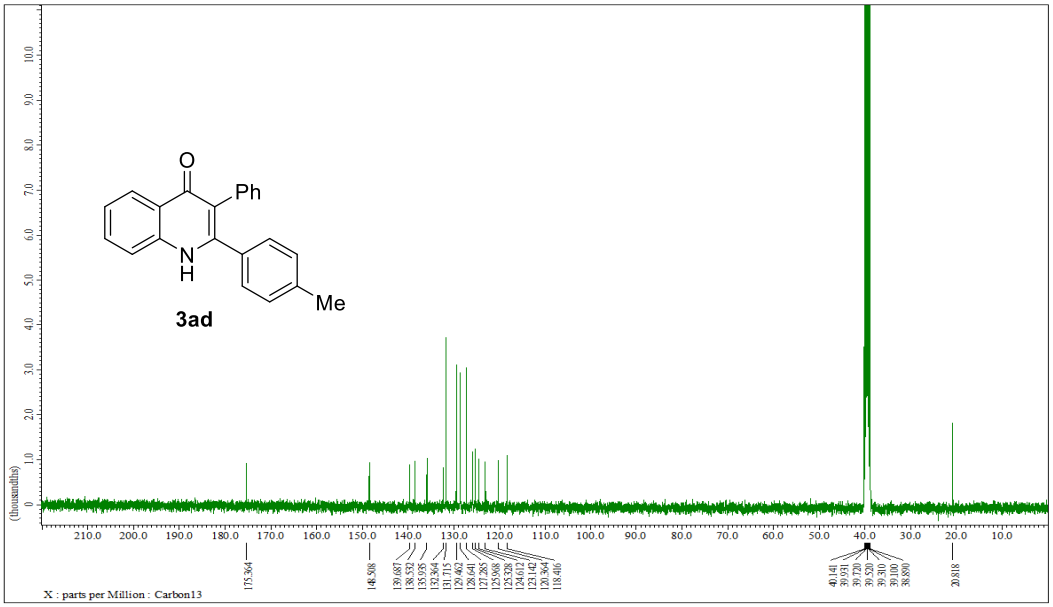
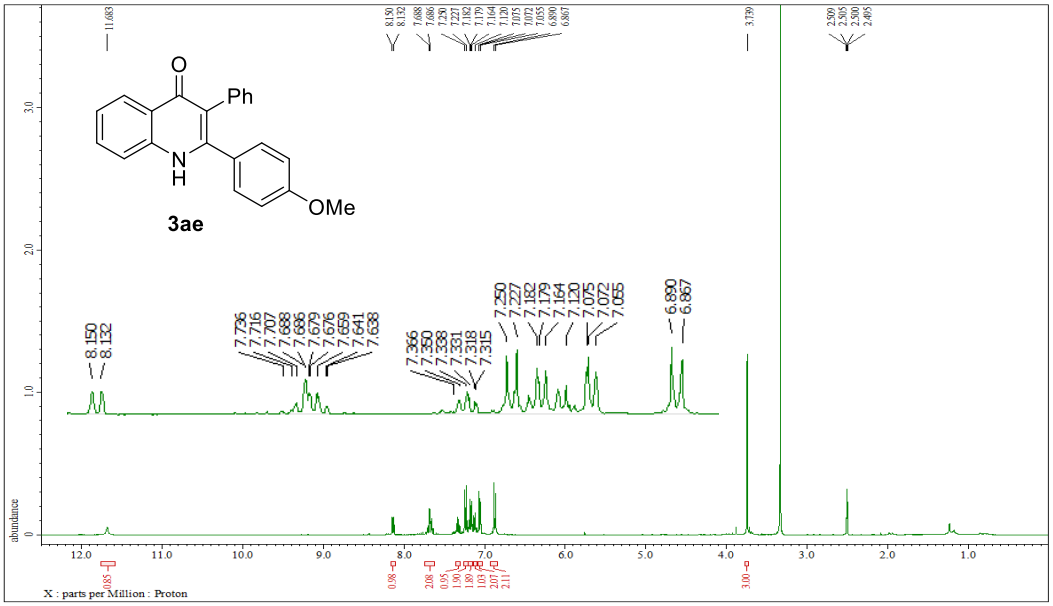


3ae ^{1}H-NMR (400 MHz, DMSO)



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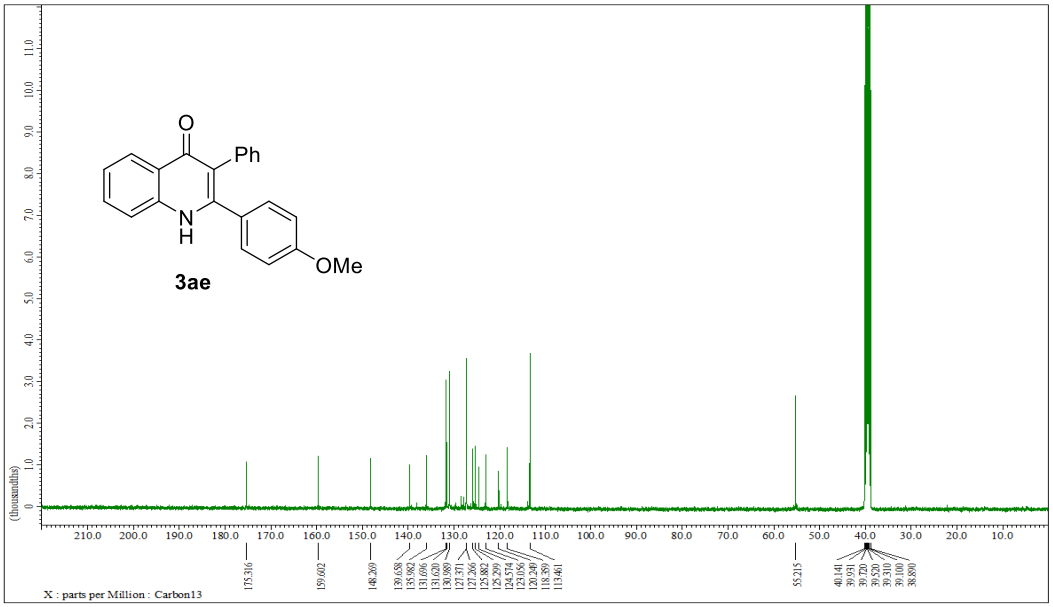

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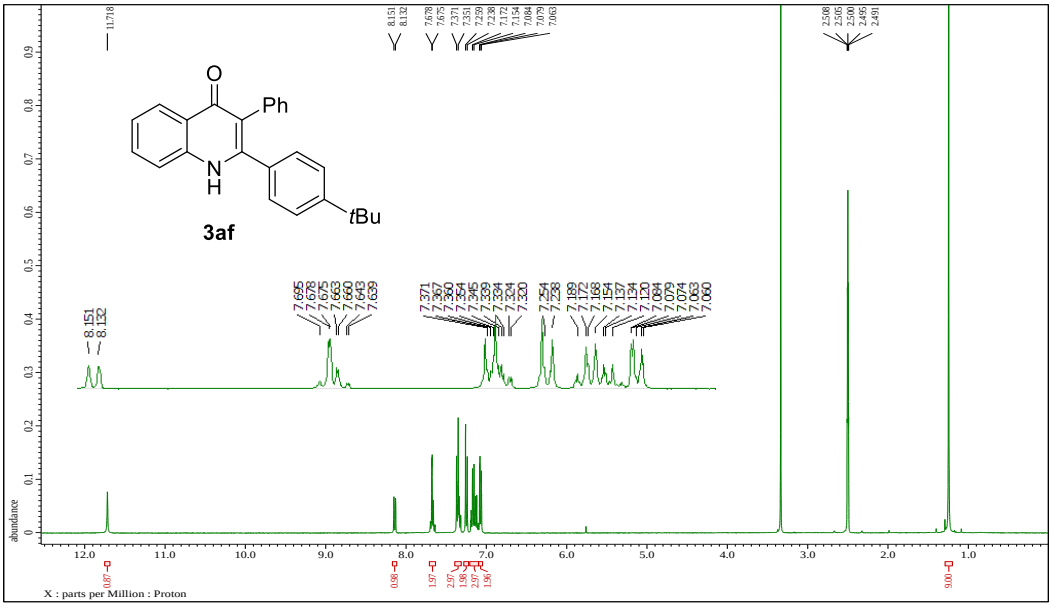

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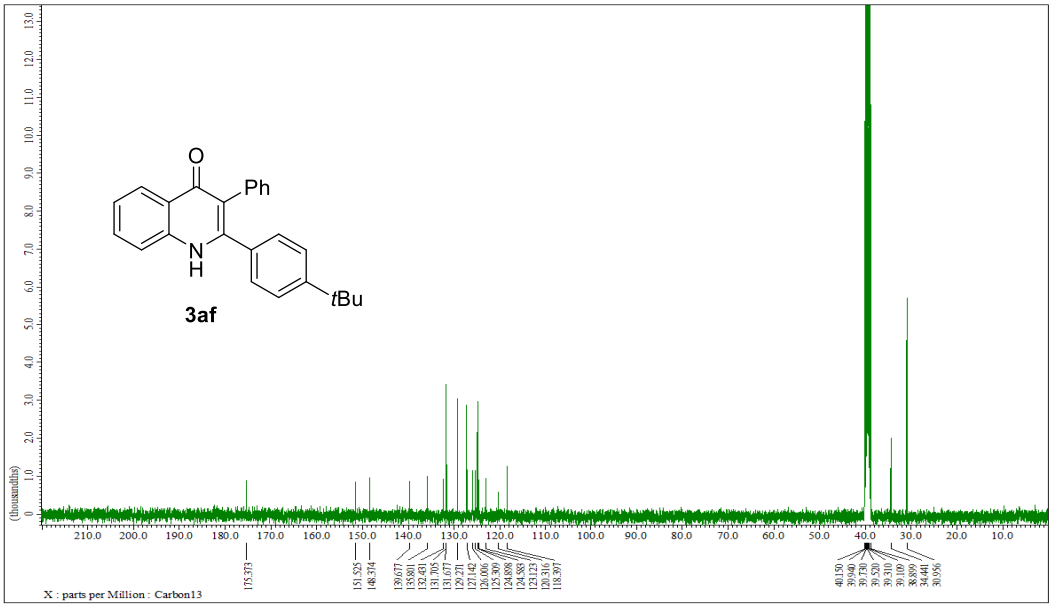

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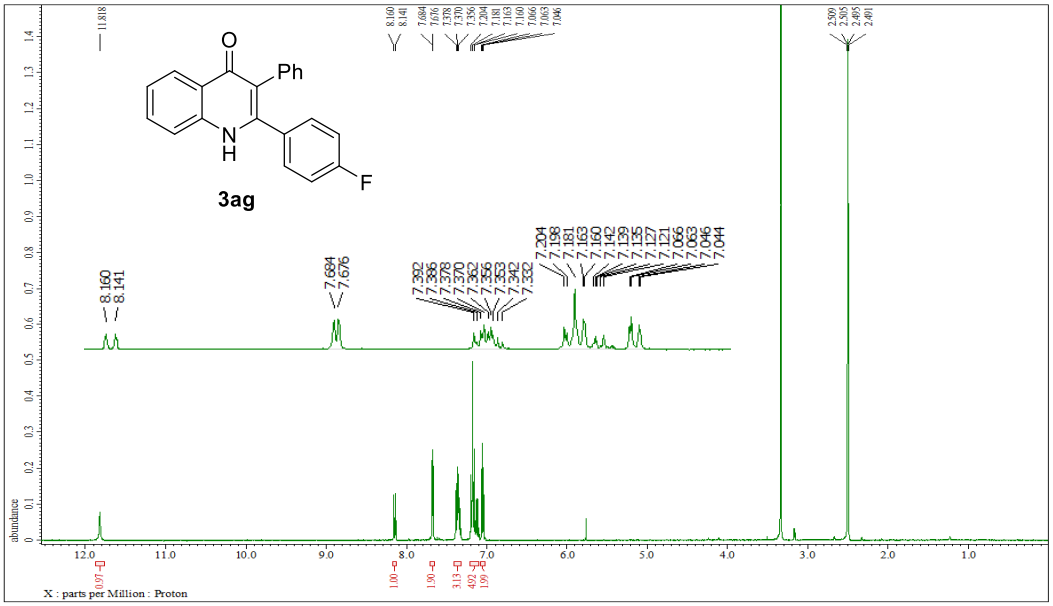

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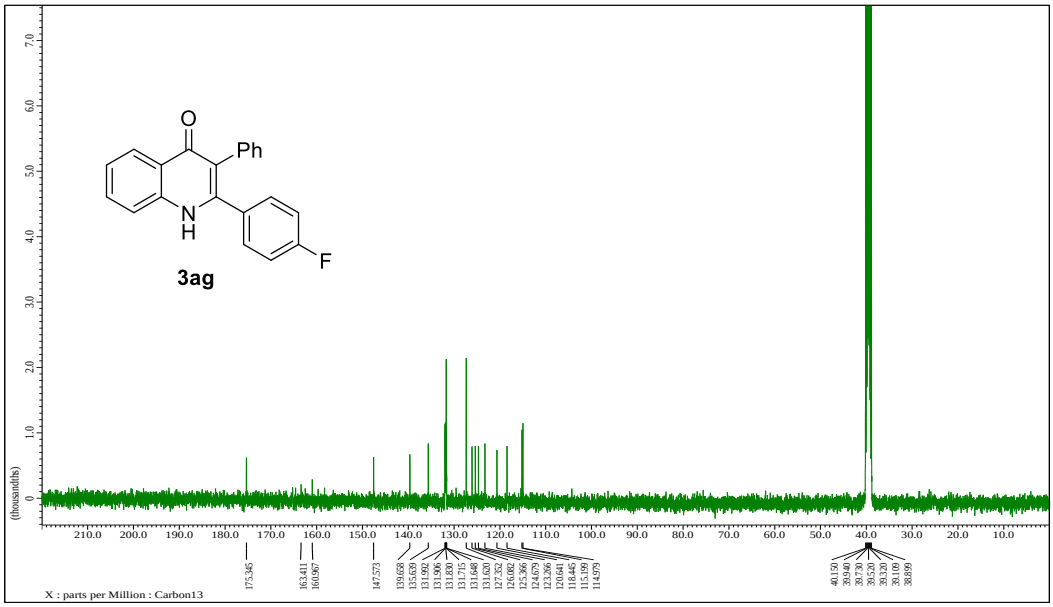
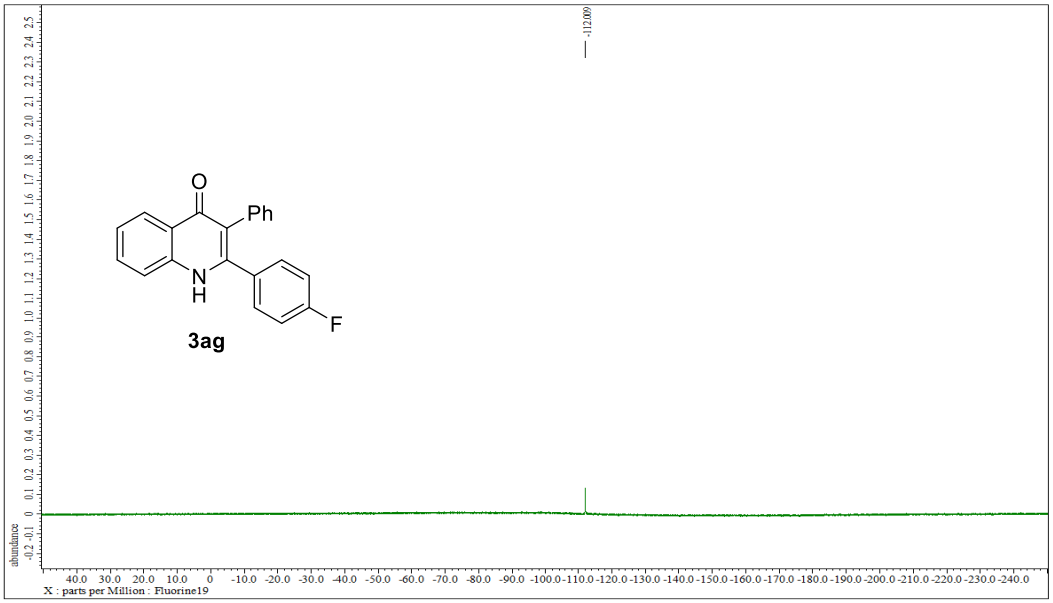


3ag ^{19}F-NMR (376 MHz, DMSO)



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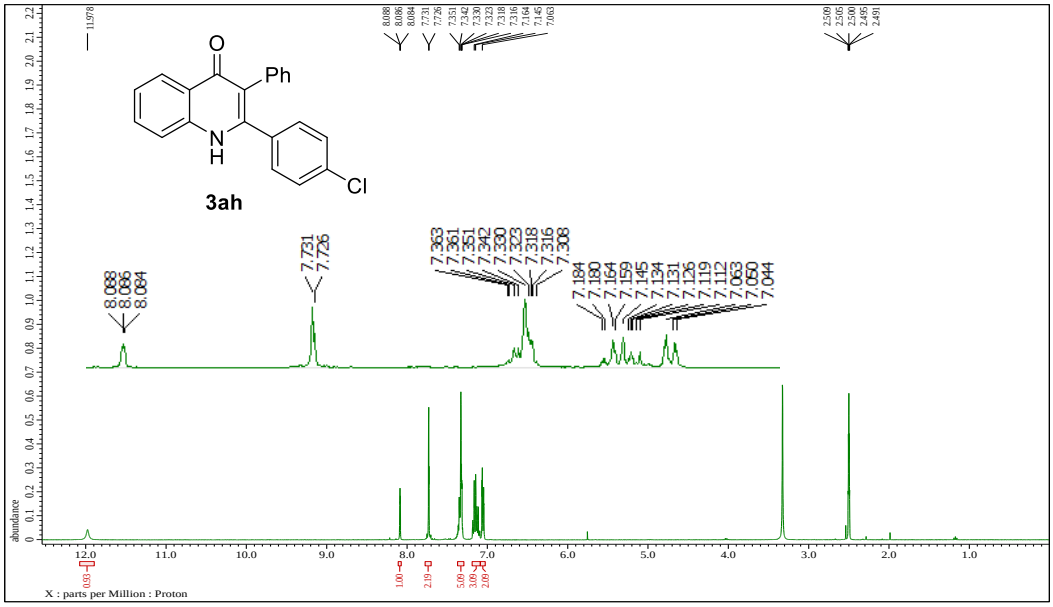

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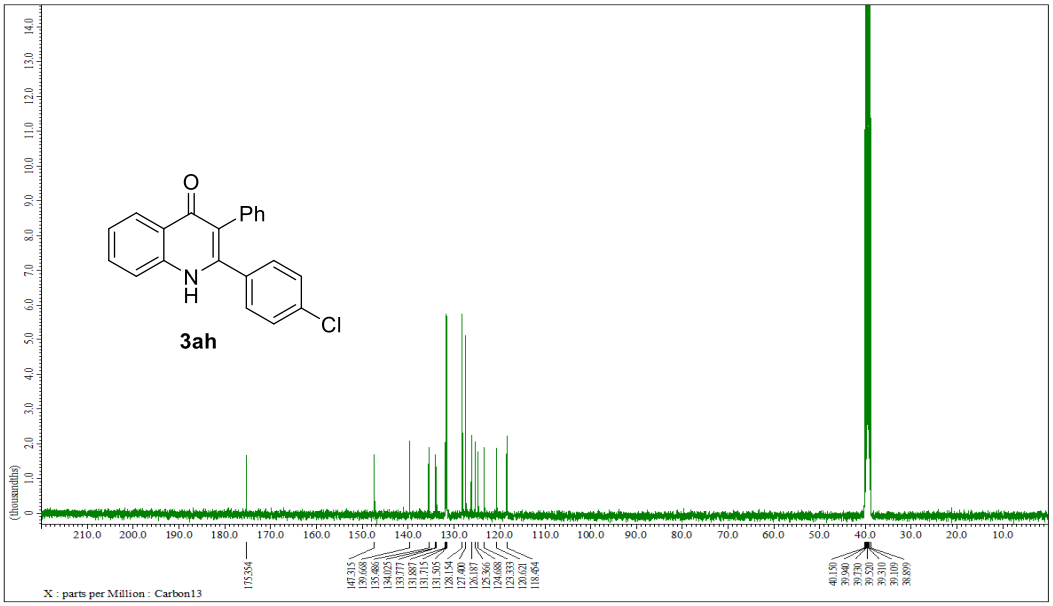

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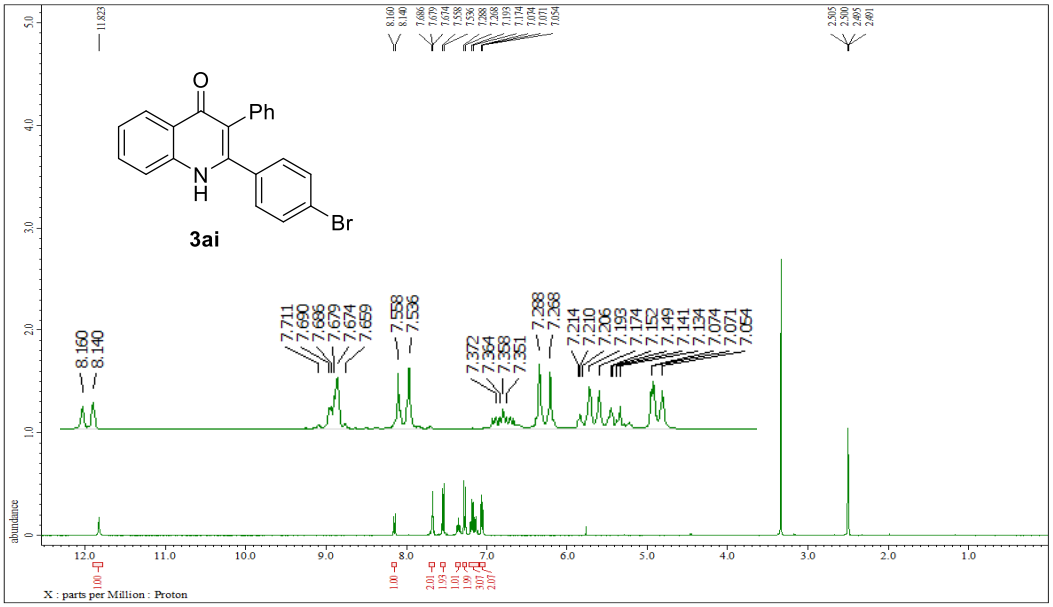

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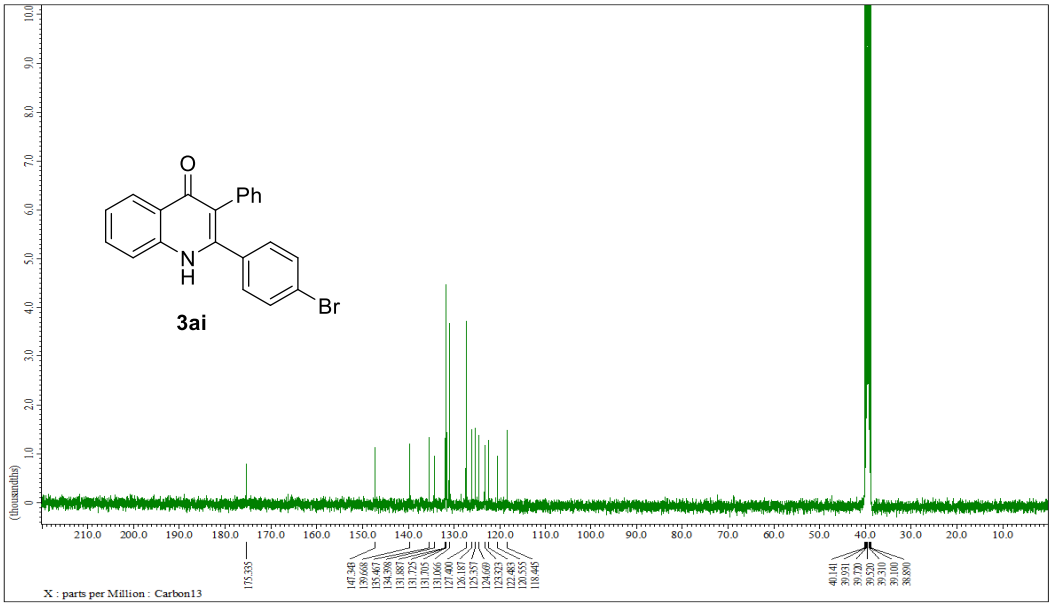

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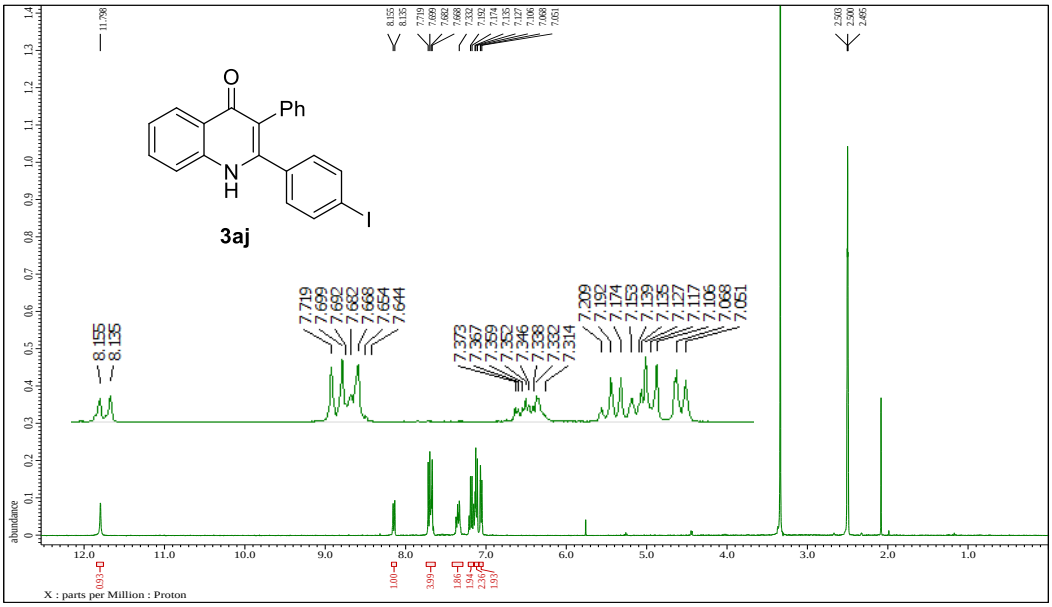

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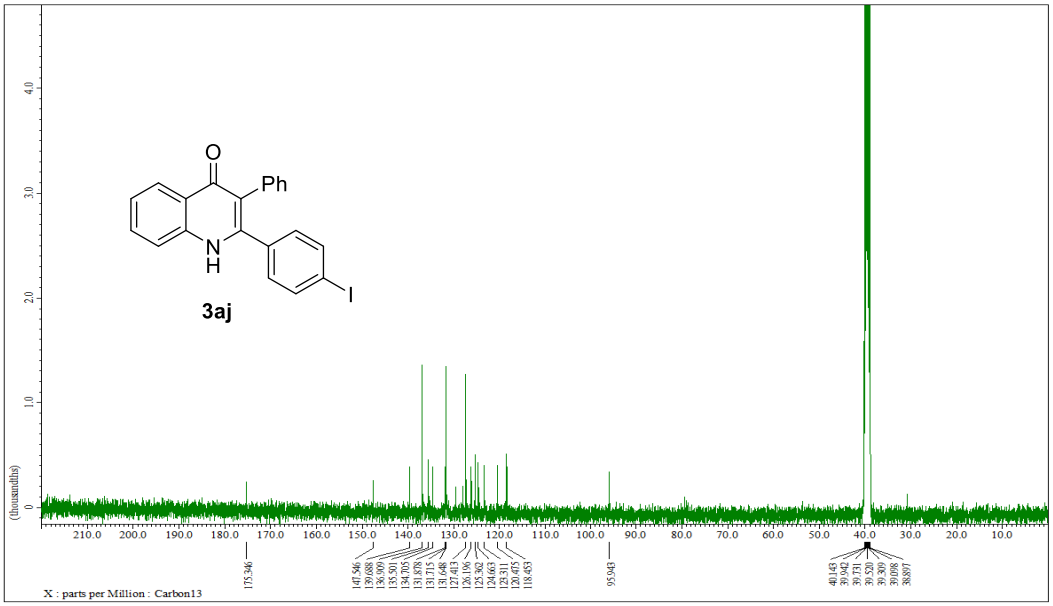

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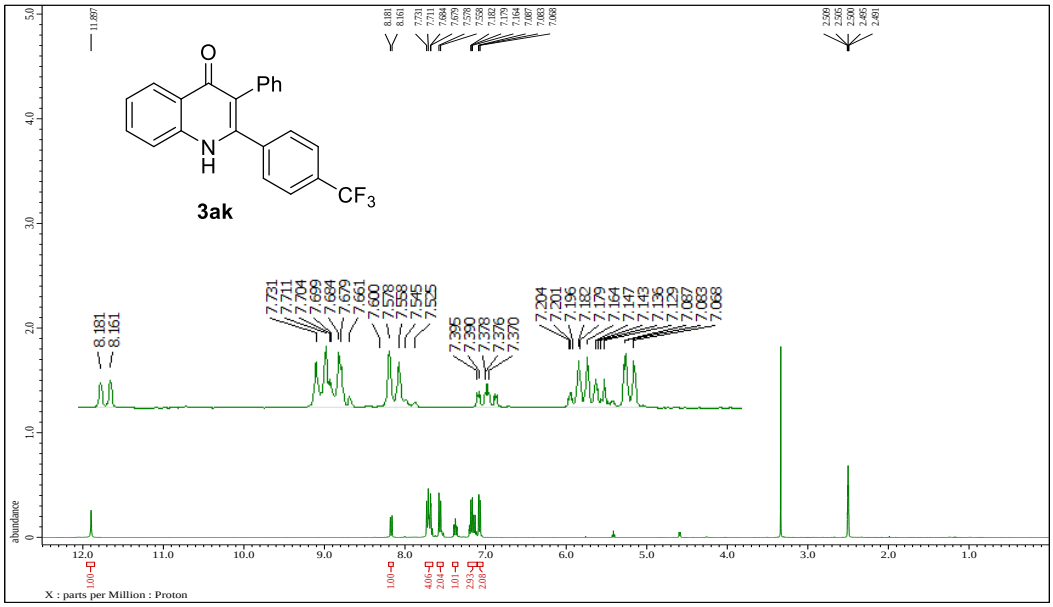

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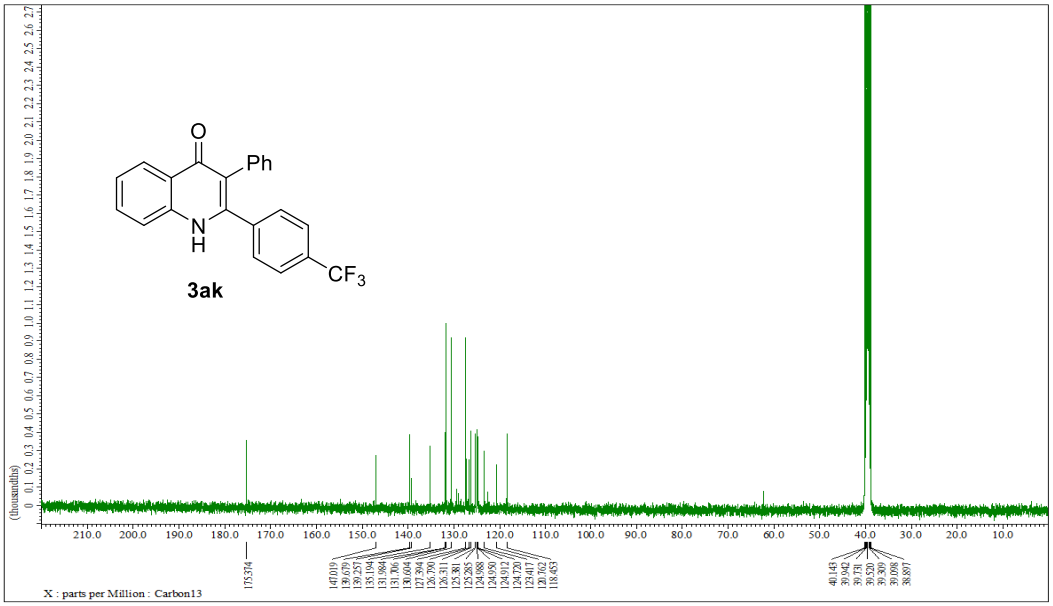
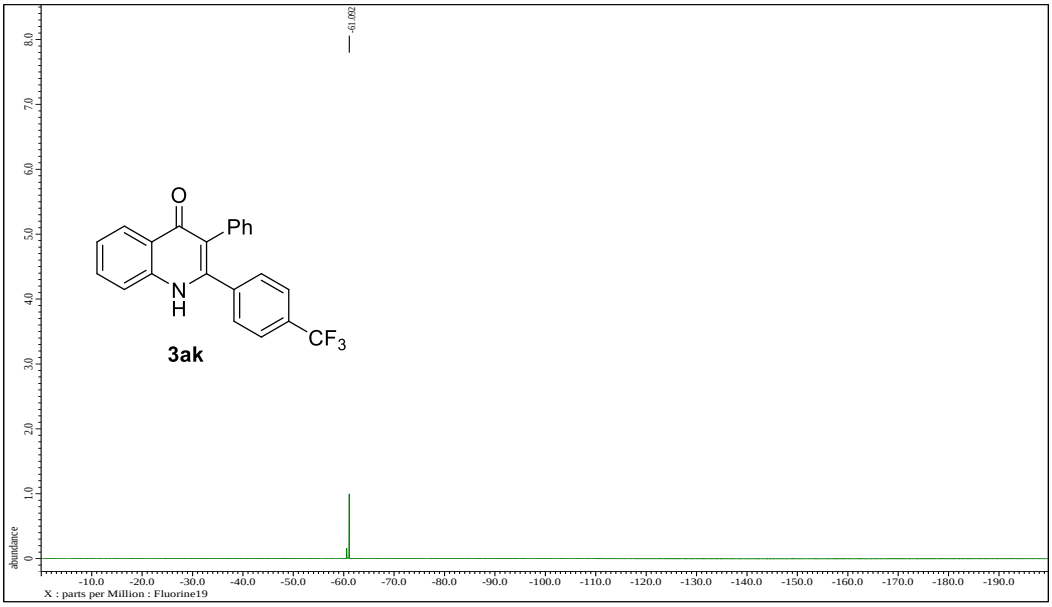


3ak ^{19}F-NMR (376 MHz, DMSO)



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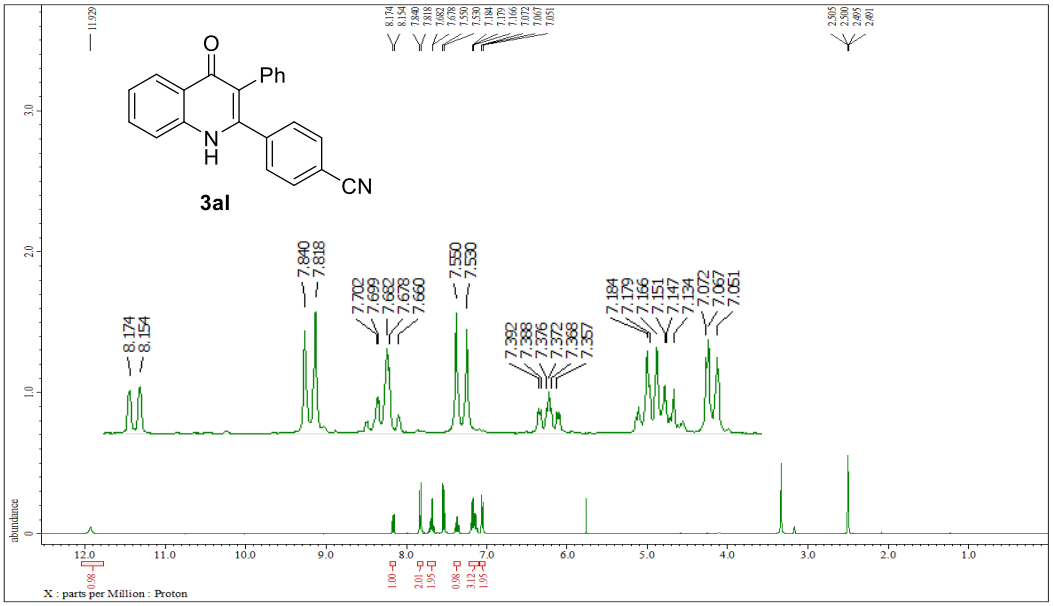

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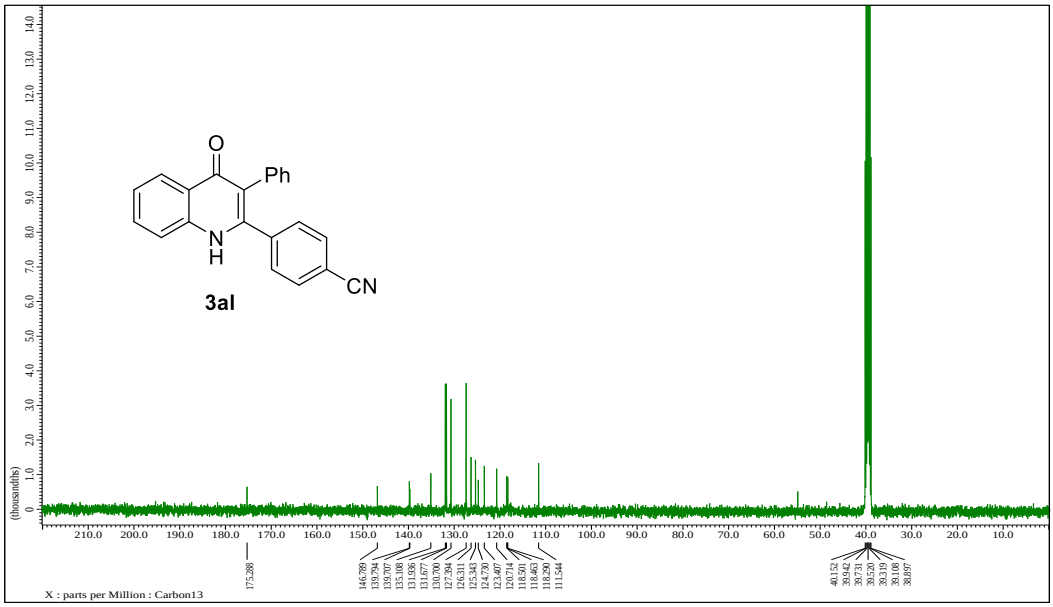

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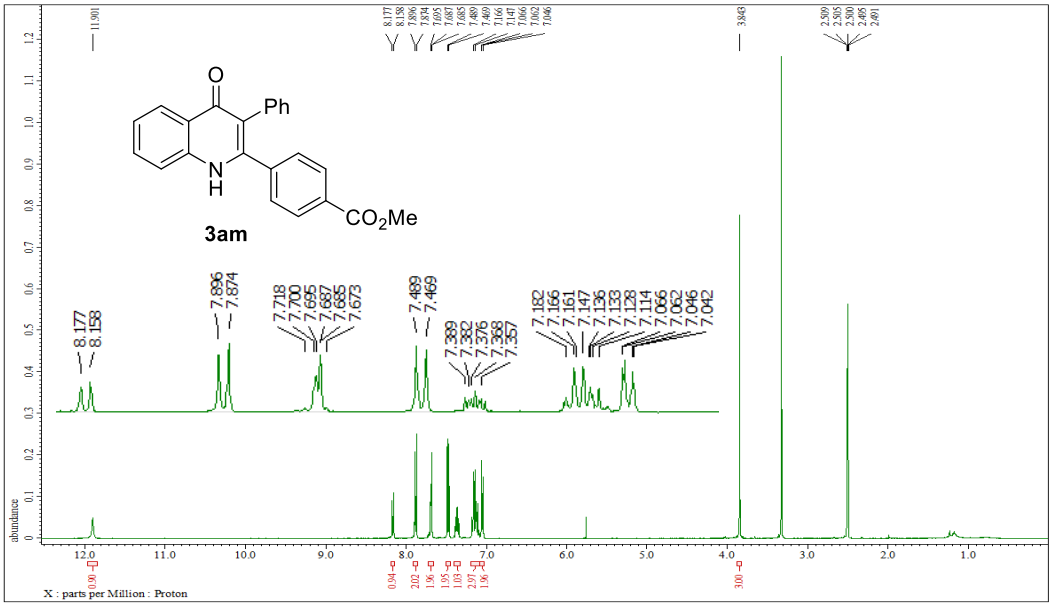

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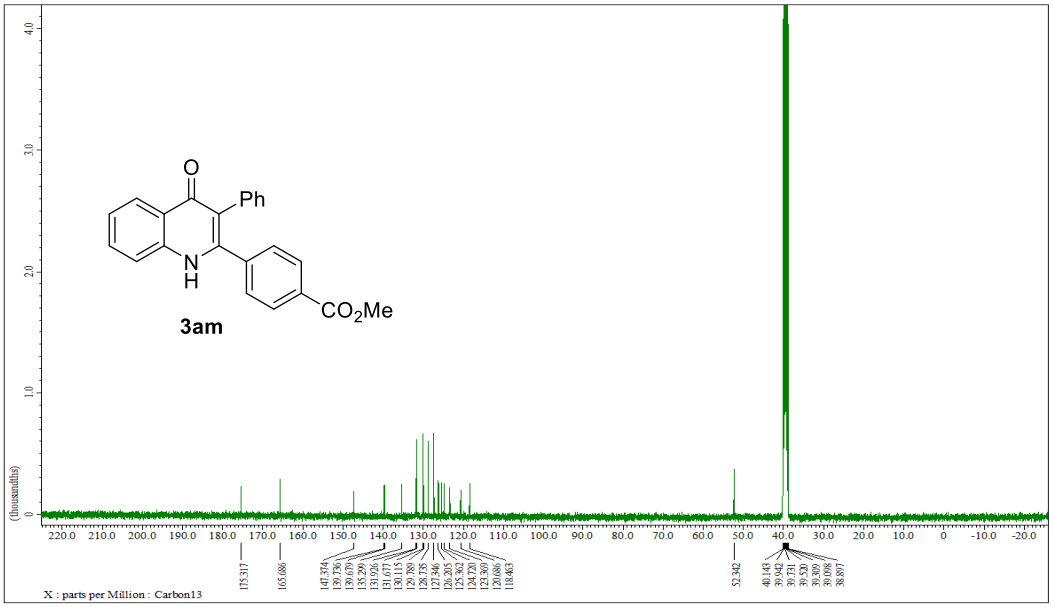

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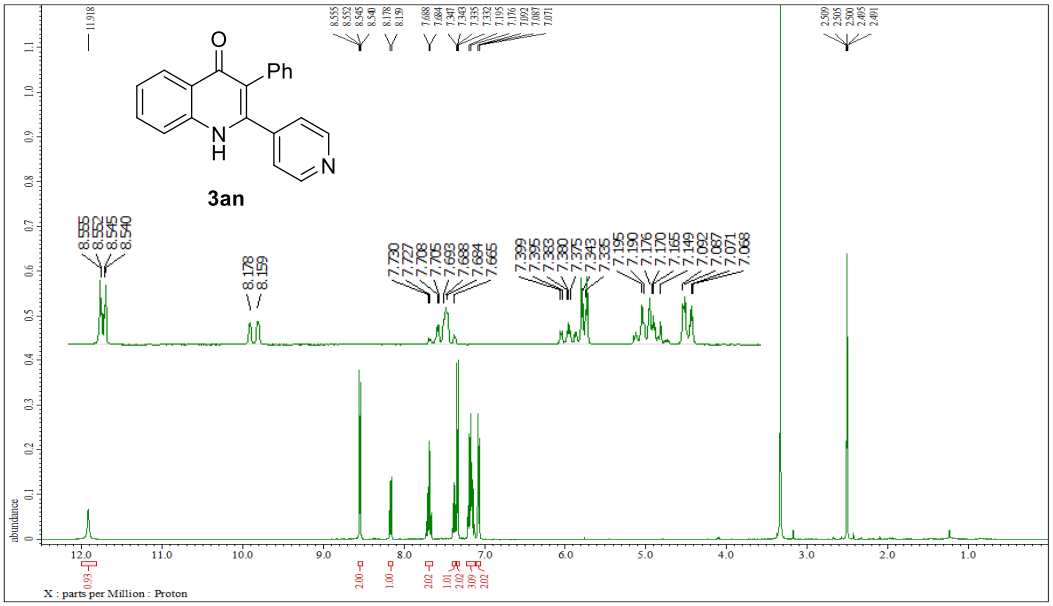

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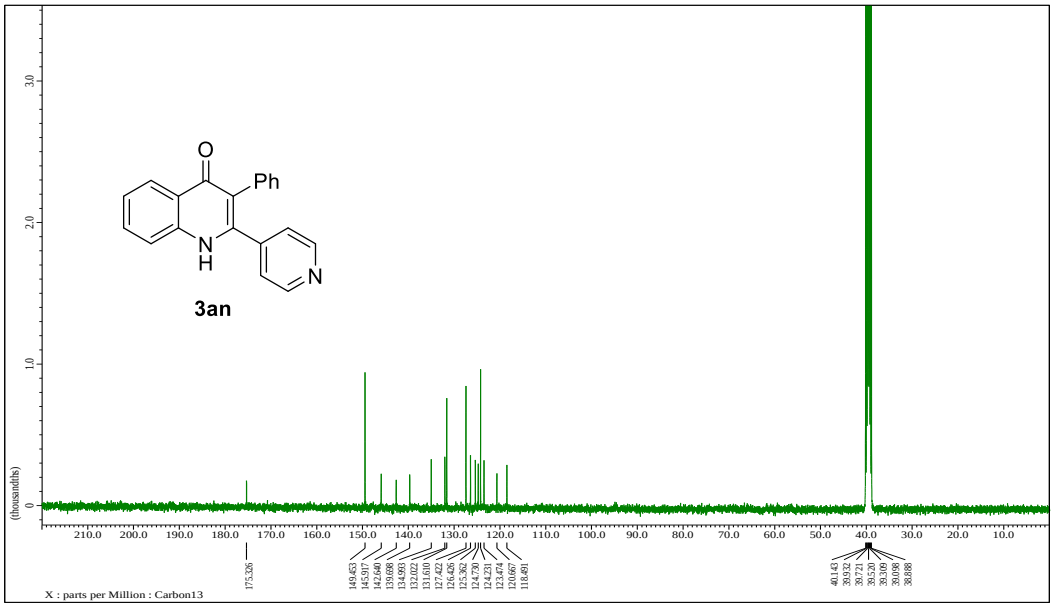

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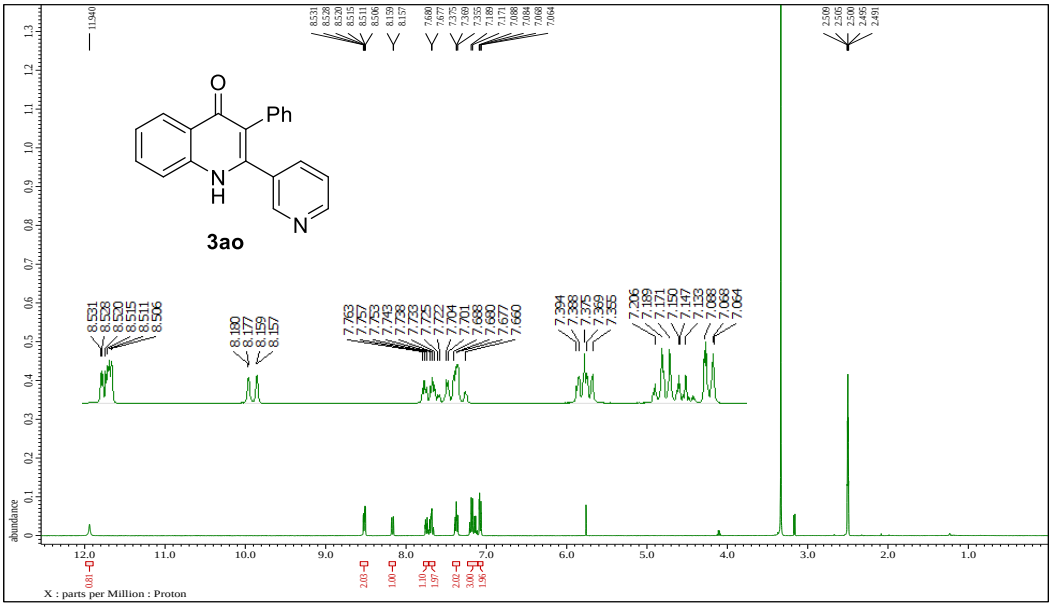

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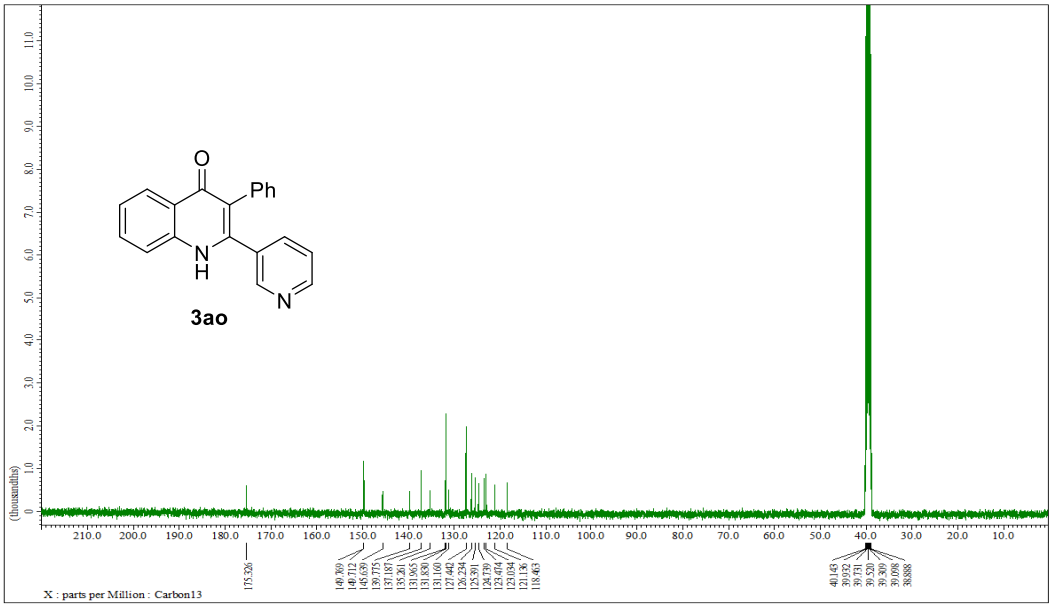
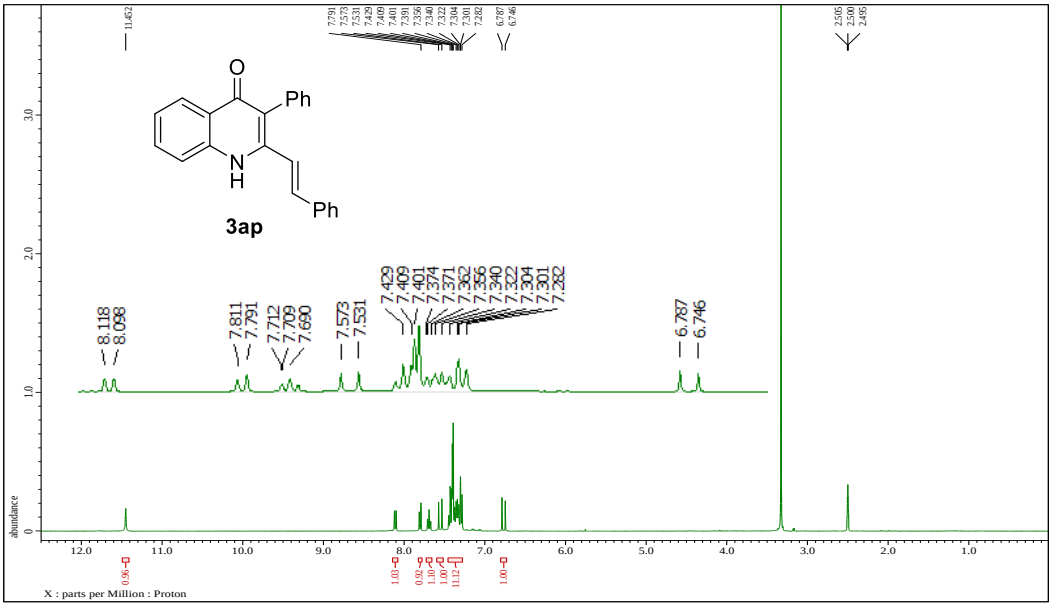


3ap ^{1}H-NMR (400 MHz, DMSO)



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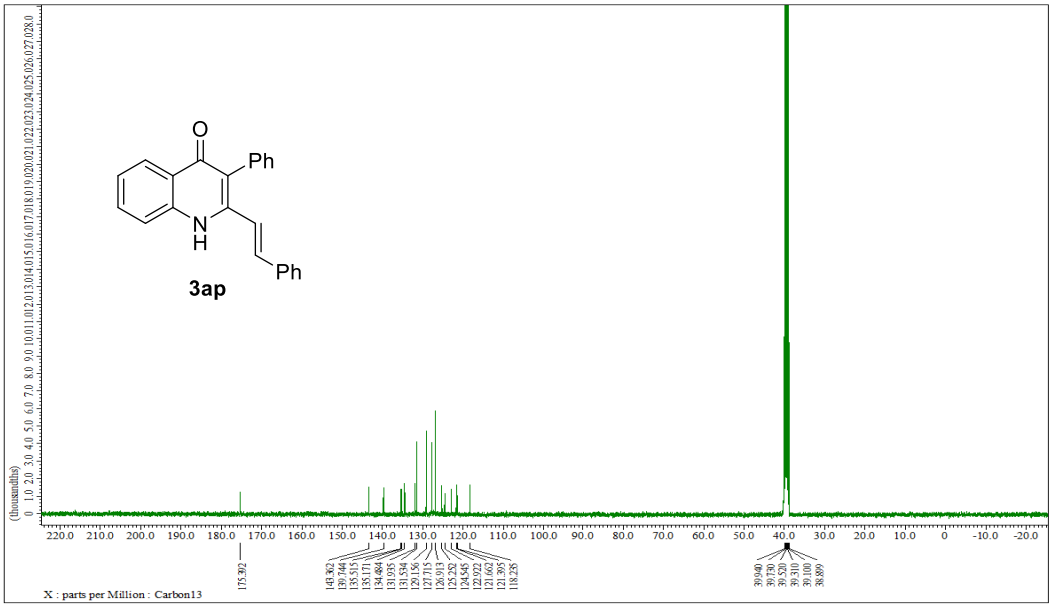
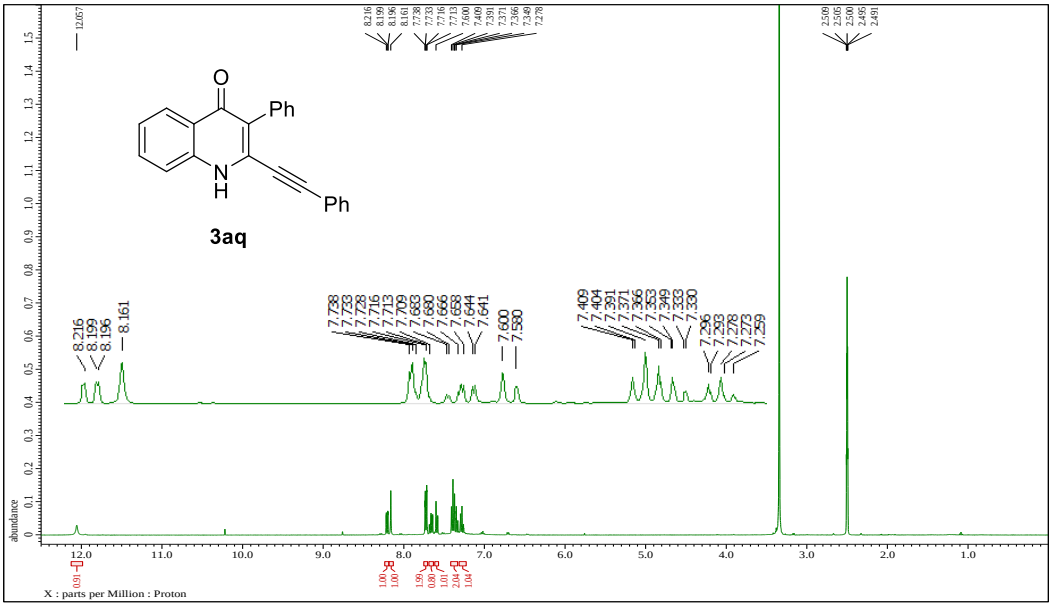


3aq ^{1}H-NMR (400 MHz, DMSO)



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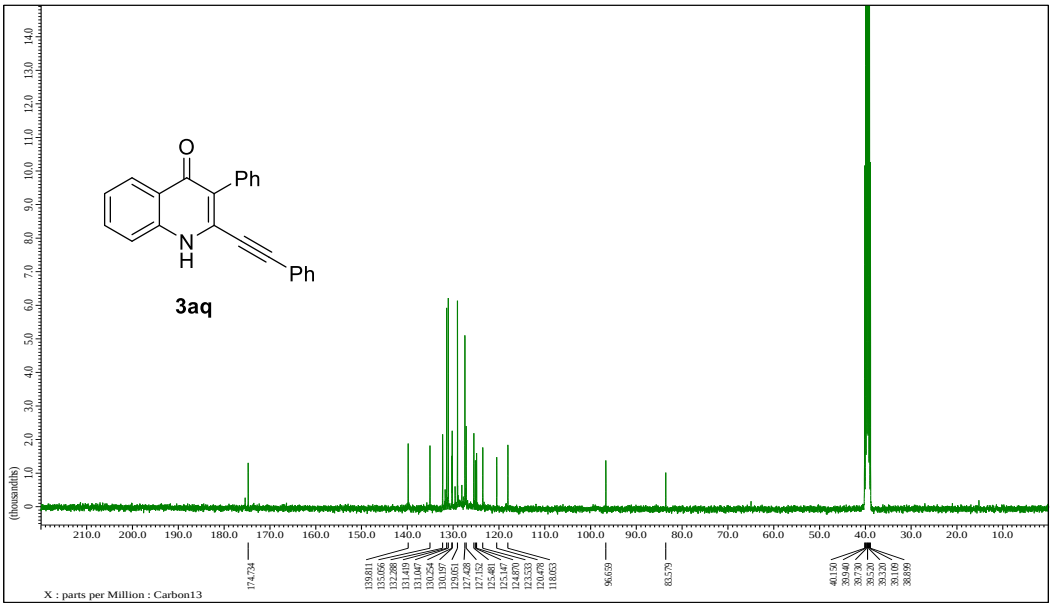

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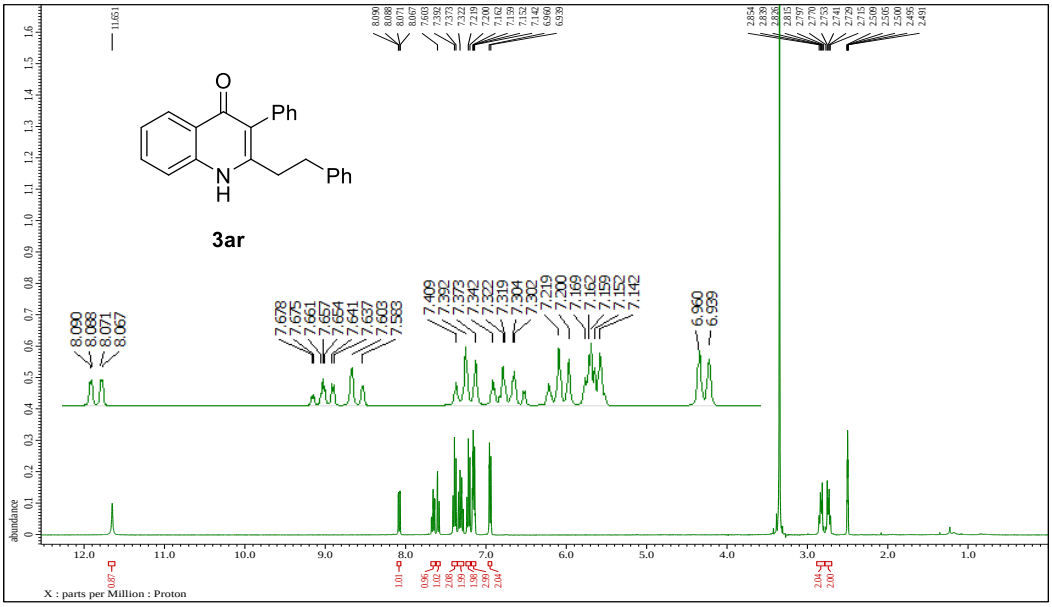

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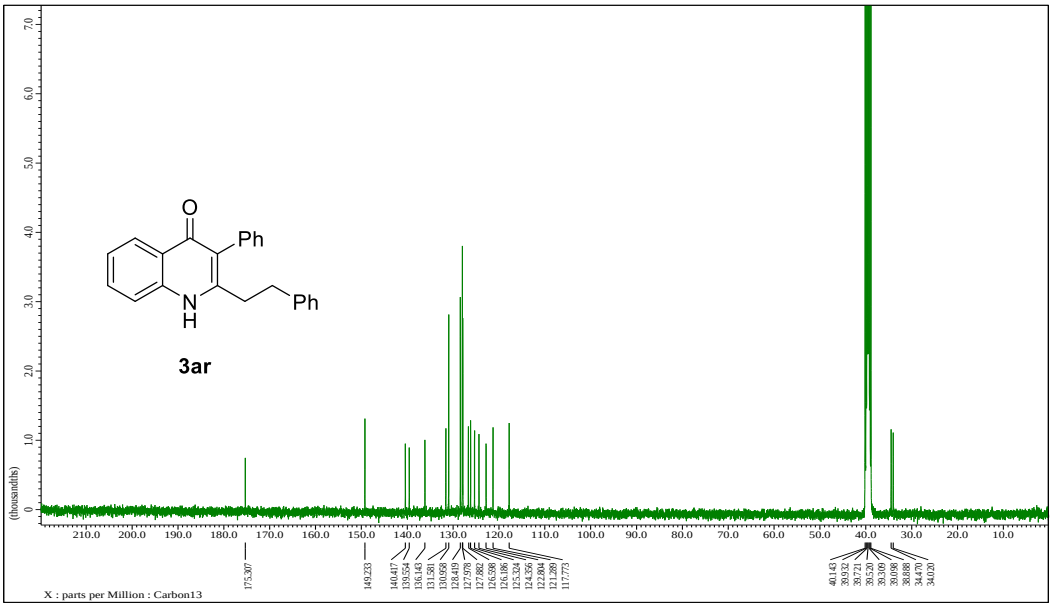

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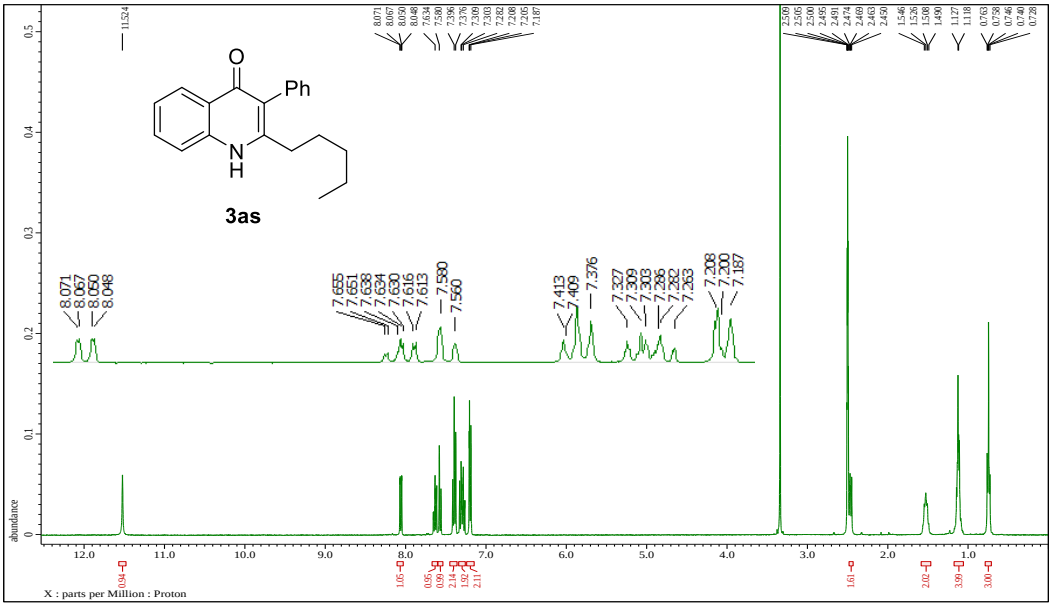

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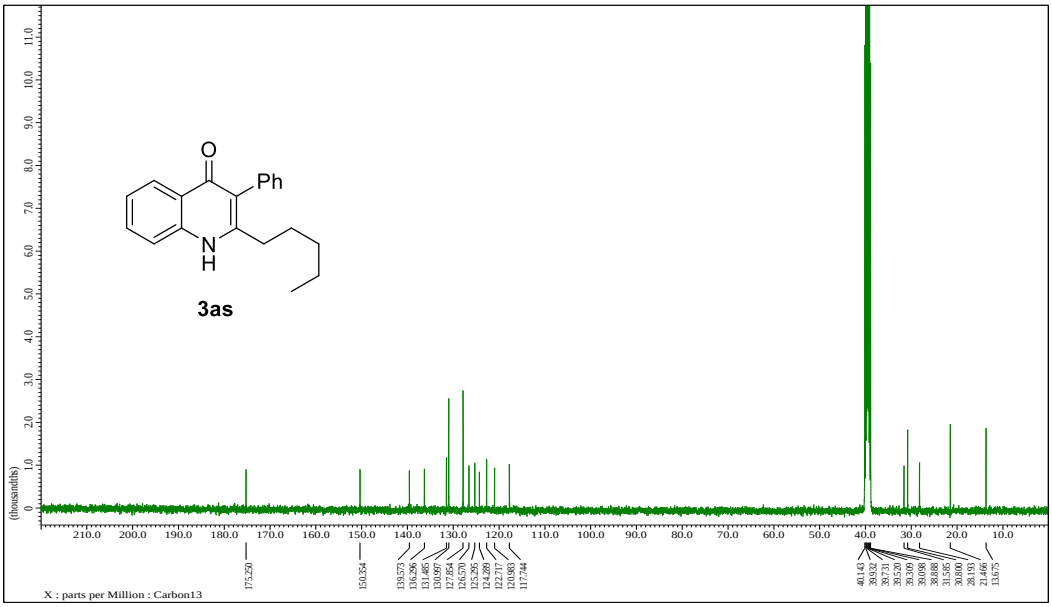
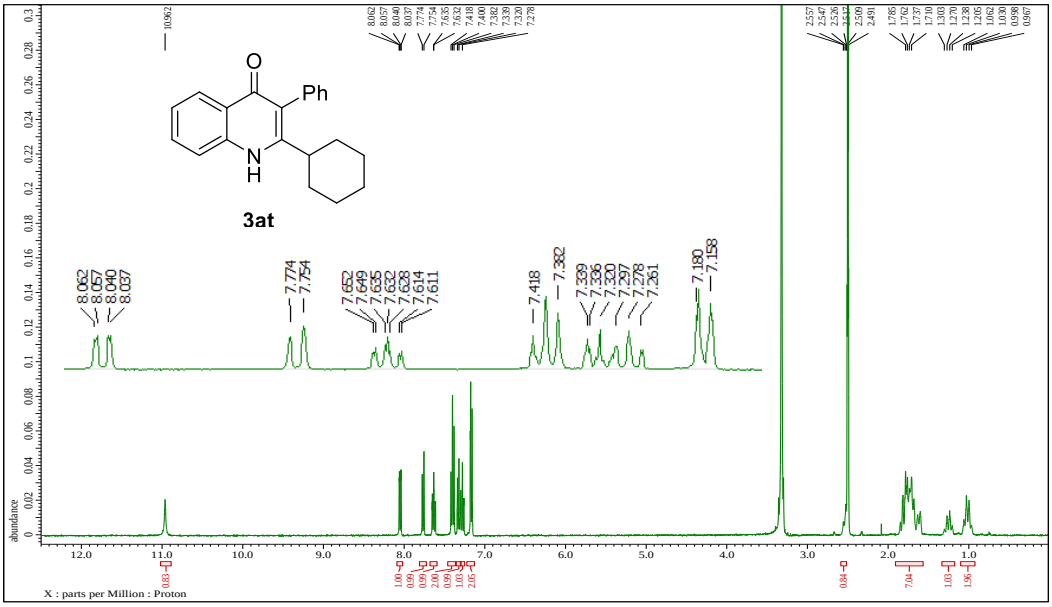
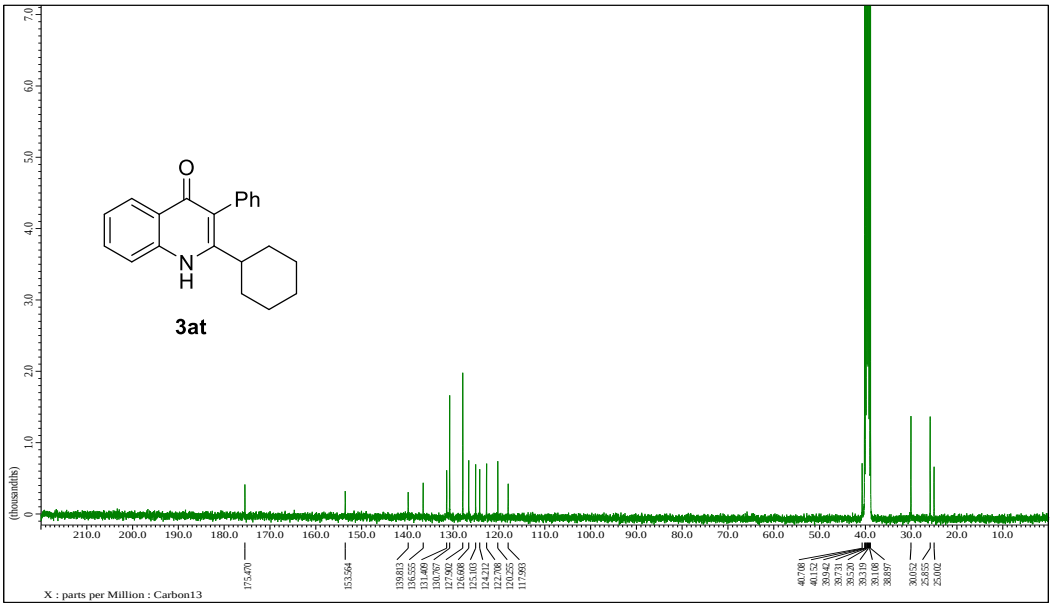


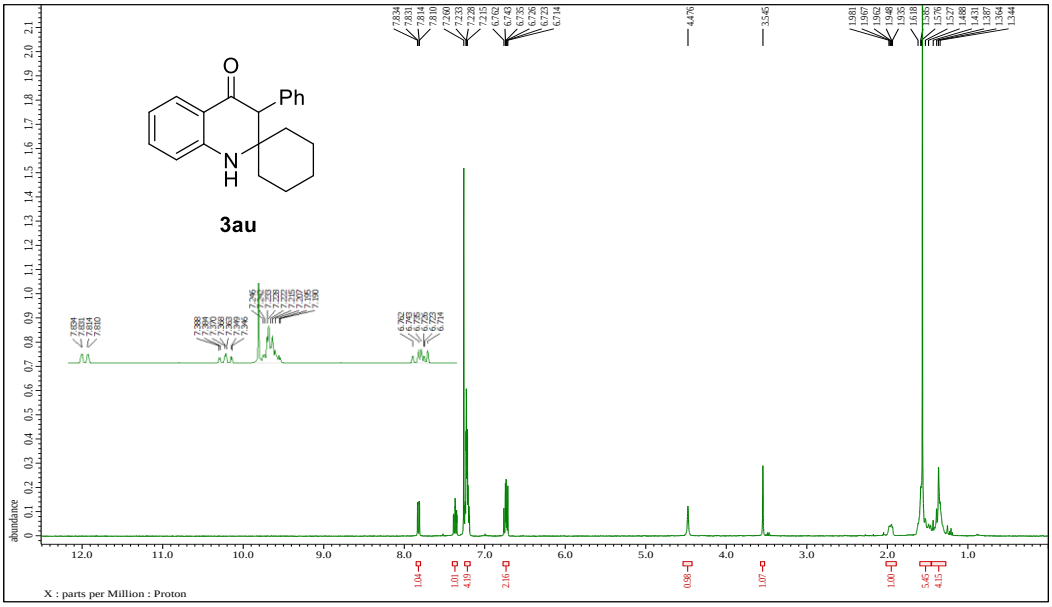
3at ^{1}H-NMR (400 MHz, DMSO)



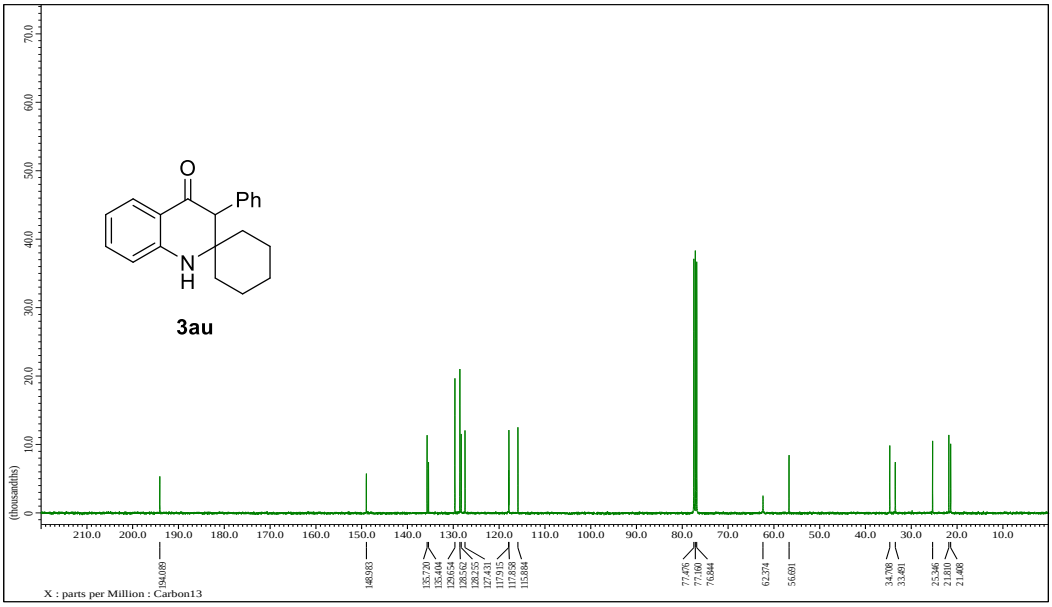
3at ^{13}C-NMR (100 MHz, DMSO)



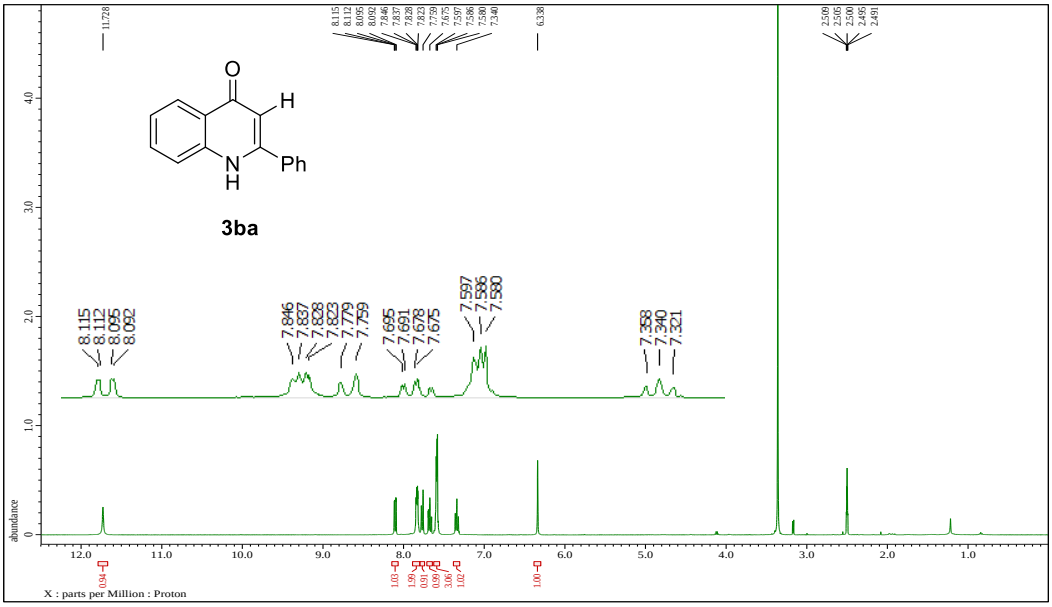
3au ^{1}H-NMR (400 MHz, $CDCl_3$)



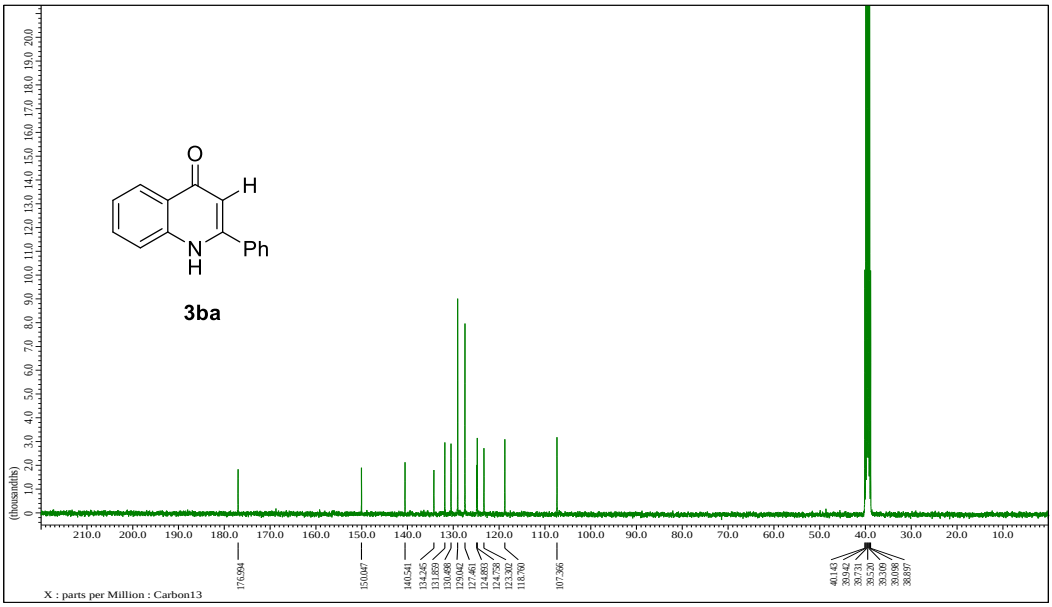
3au ^{13}C-NMR (100 MHz, $CDCl_3$)



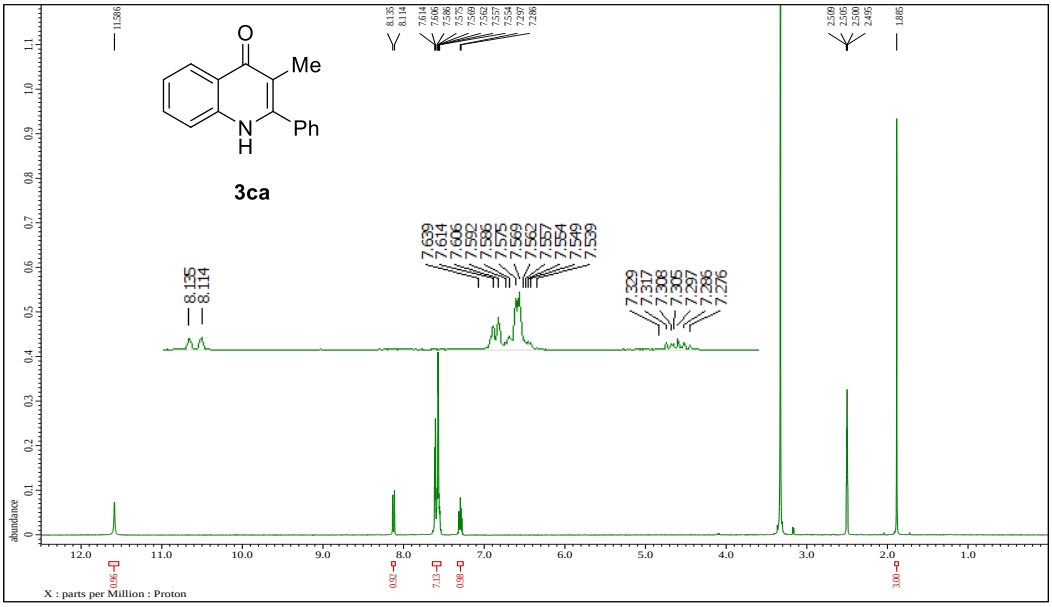
3ba ^{1}H-NMR (400 MHz, DMSO)



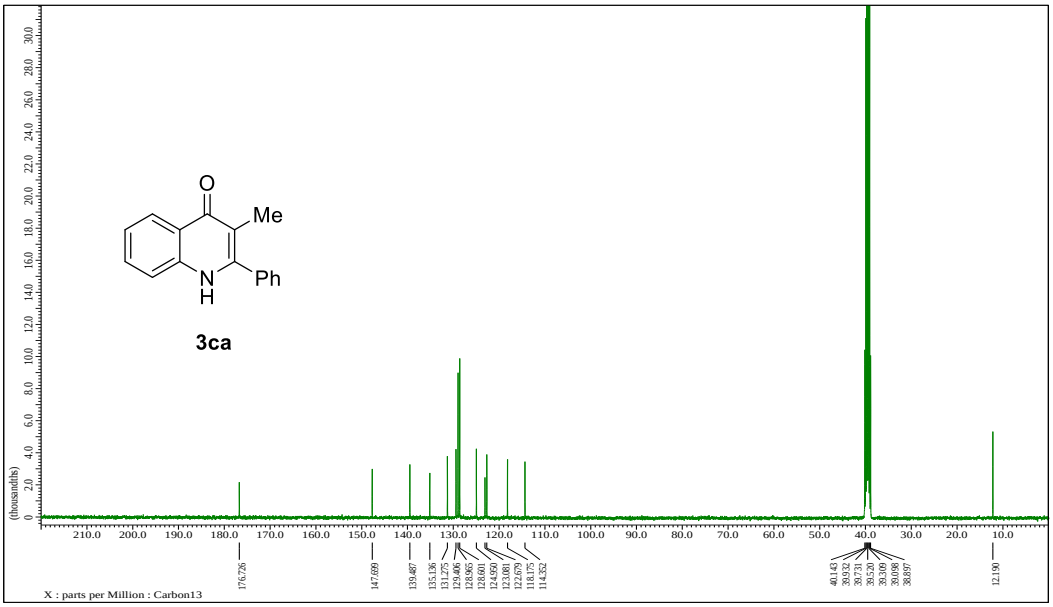
3ba ^{13}C-NMR (100 MHz, DMSO)



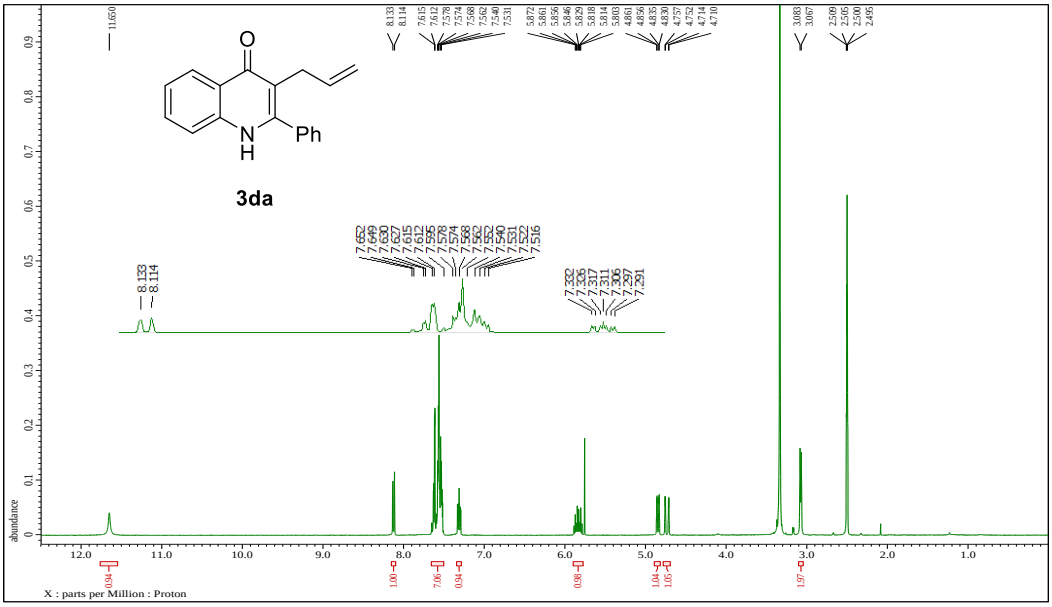
3ca ^{1}H-NMR (400 MHz, DMSO)



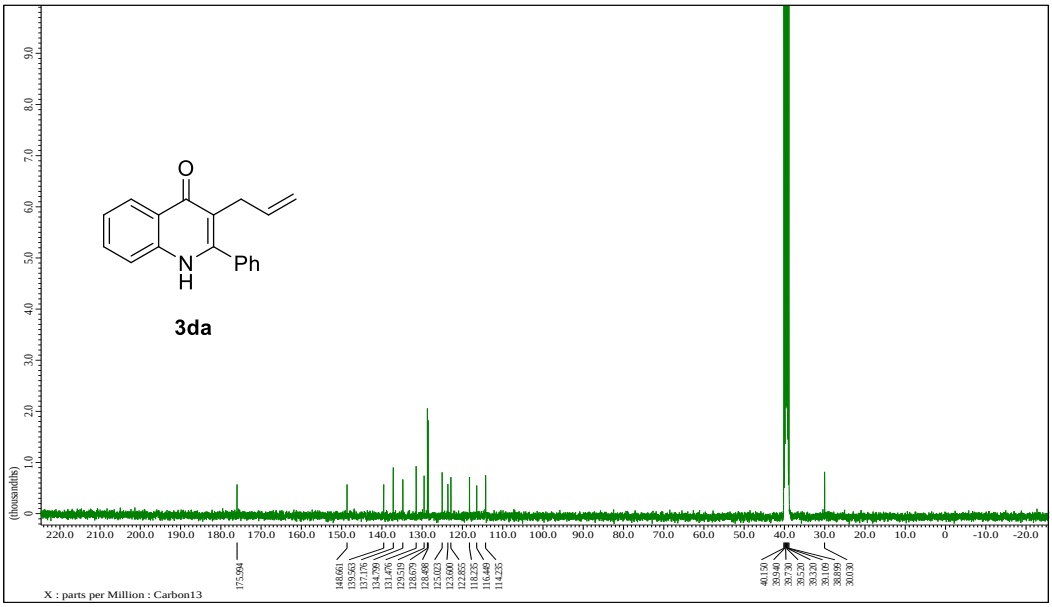
3ca ^{13}C-NMR (100 MHz, DMSO)



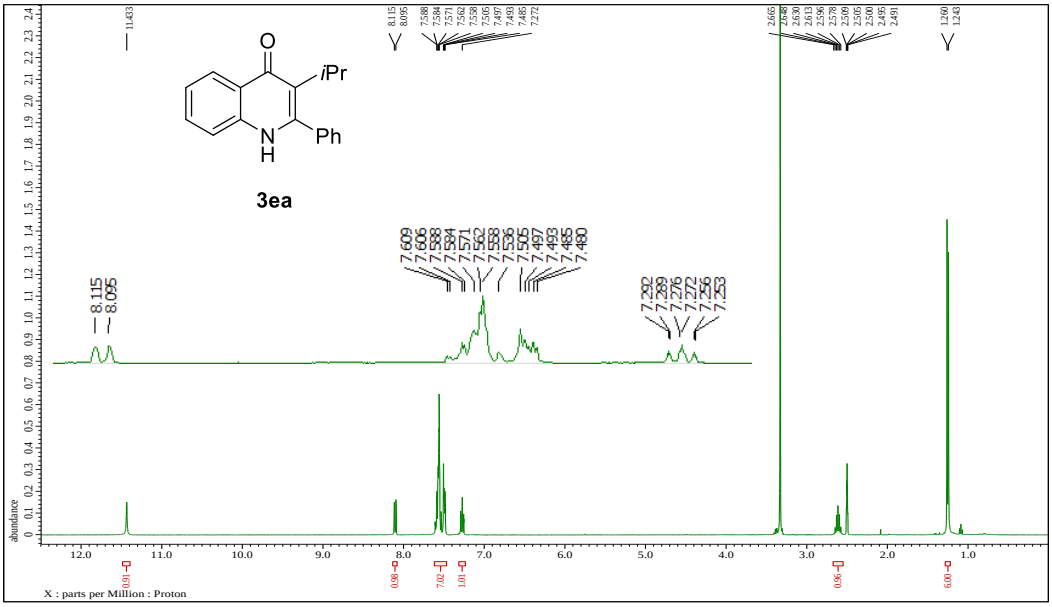
3da ^{1}H-NMR (400 MHz, DMSO)



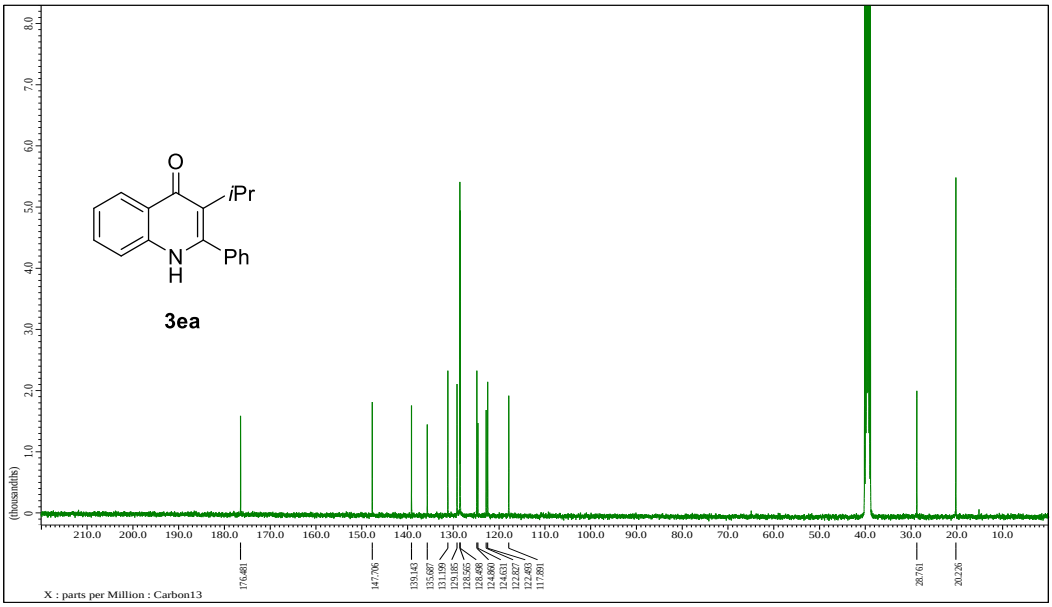
3da ^{13}C-NMR (100 MHz, DMSO)



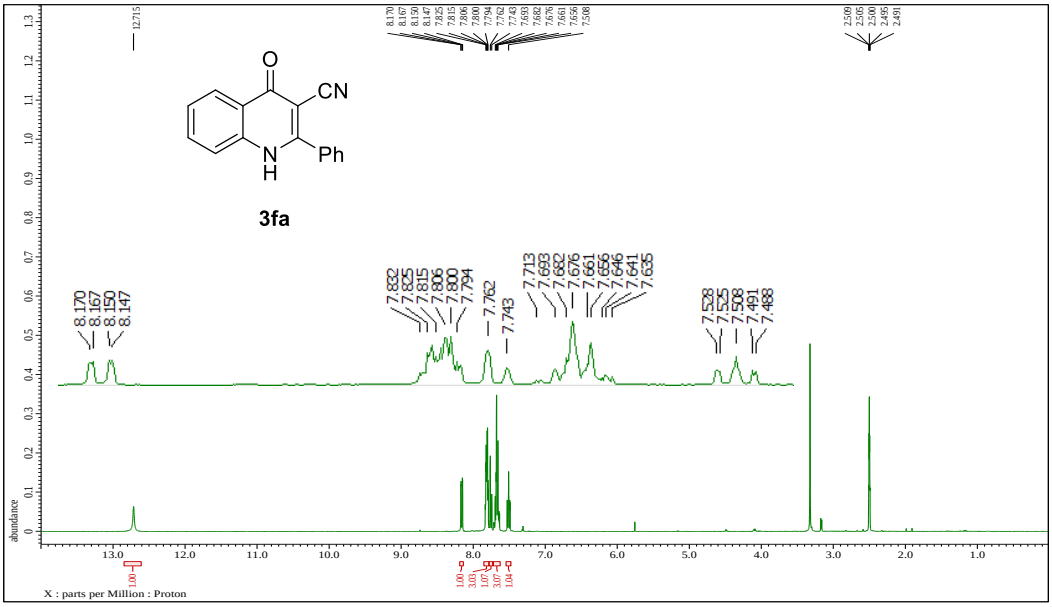
3ea ^{1}H-NMR (400 MHz, DMSO)



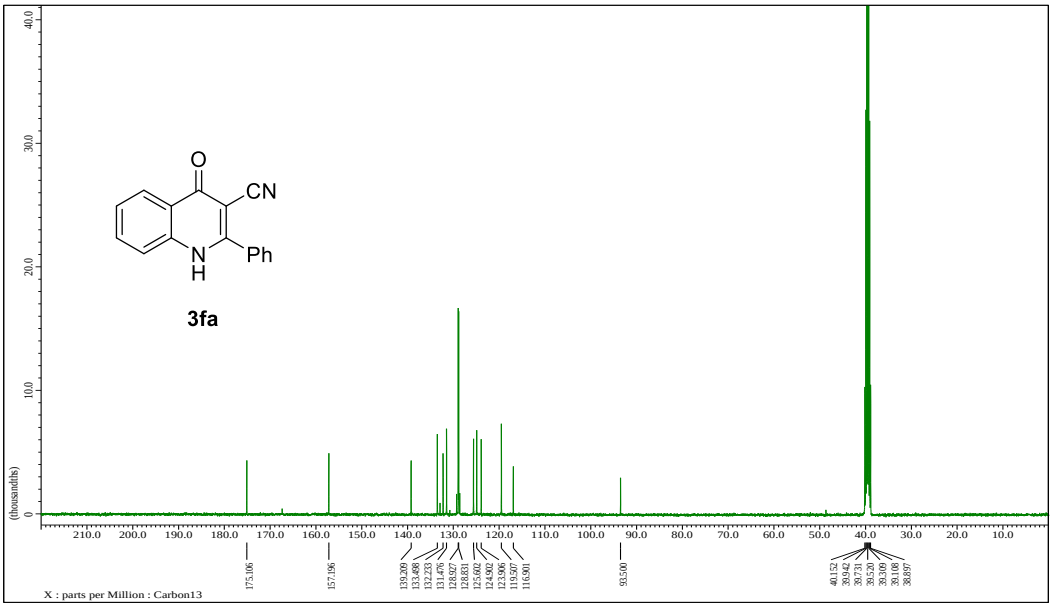
3ea ^{13}C-NMR (100 MHz, DMSO)



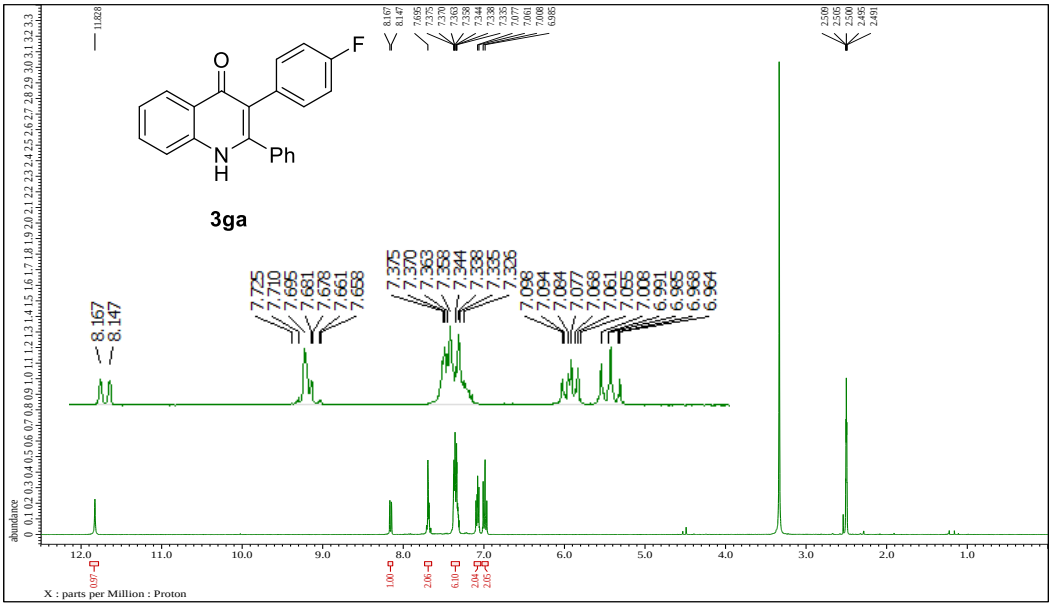
3fa ^{1}H-NMR (400 MHz, DMSO)



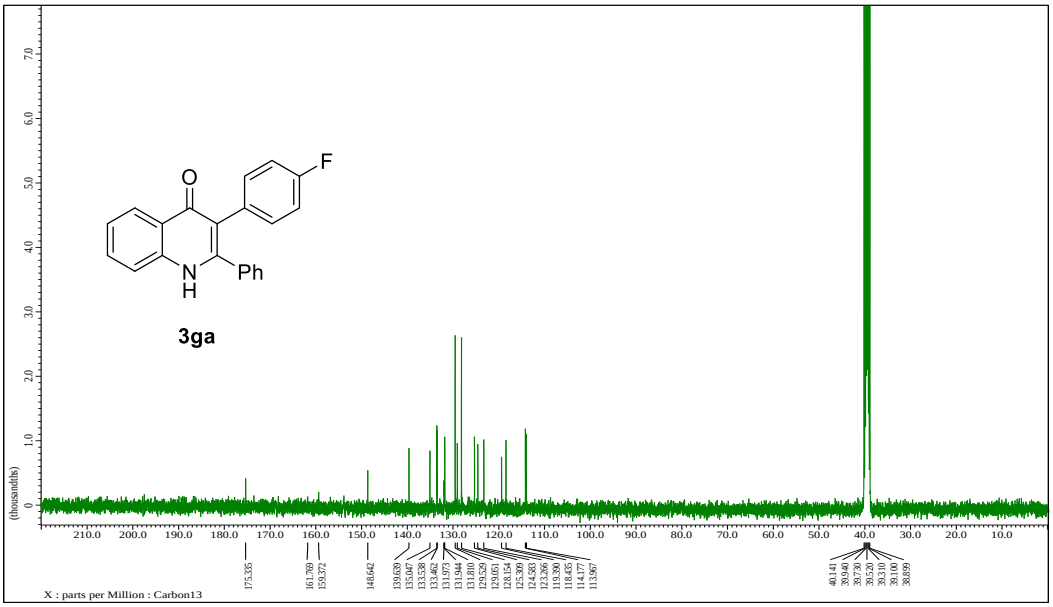
3fa ^{13}C-NMR (100 MHz, DMSO)



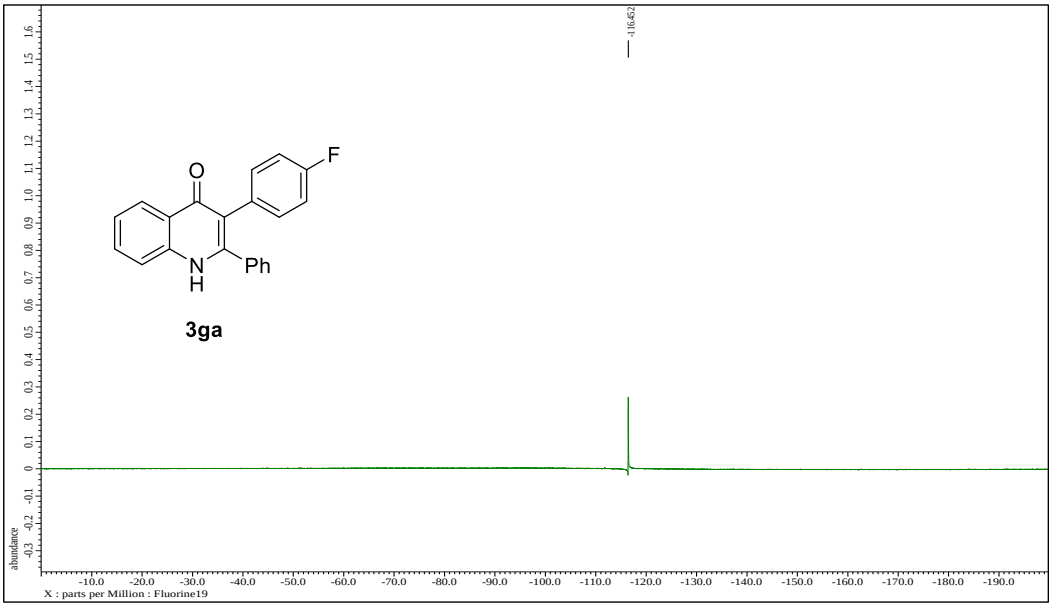
3ga ^{1}H-NMR (400 MHz, DMSO)



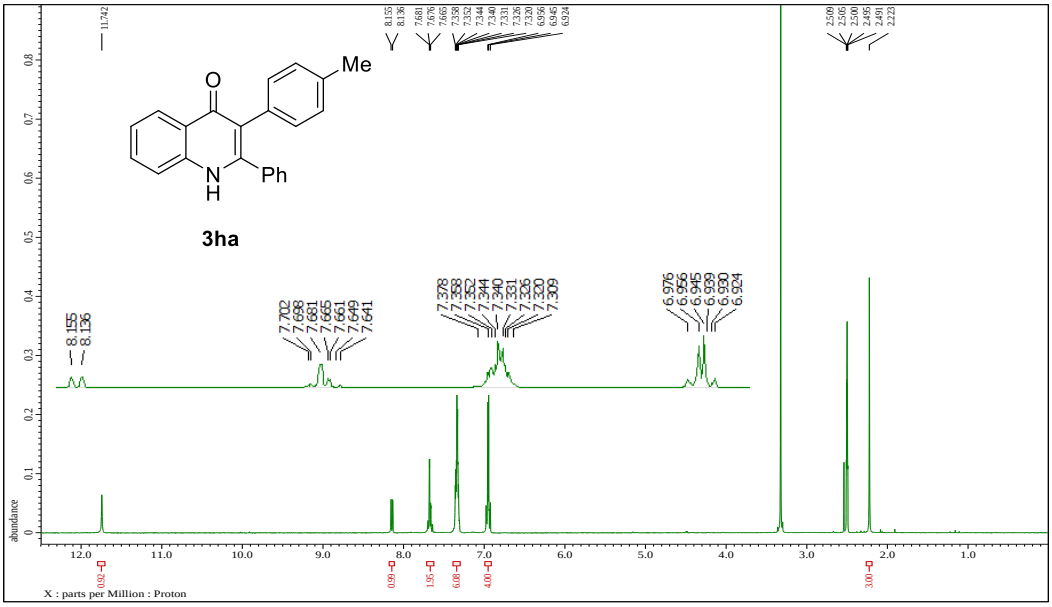
3ga ^{13}C-NMR (100 MHz, DMSO)



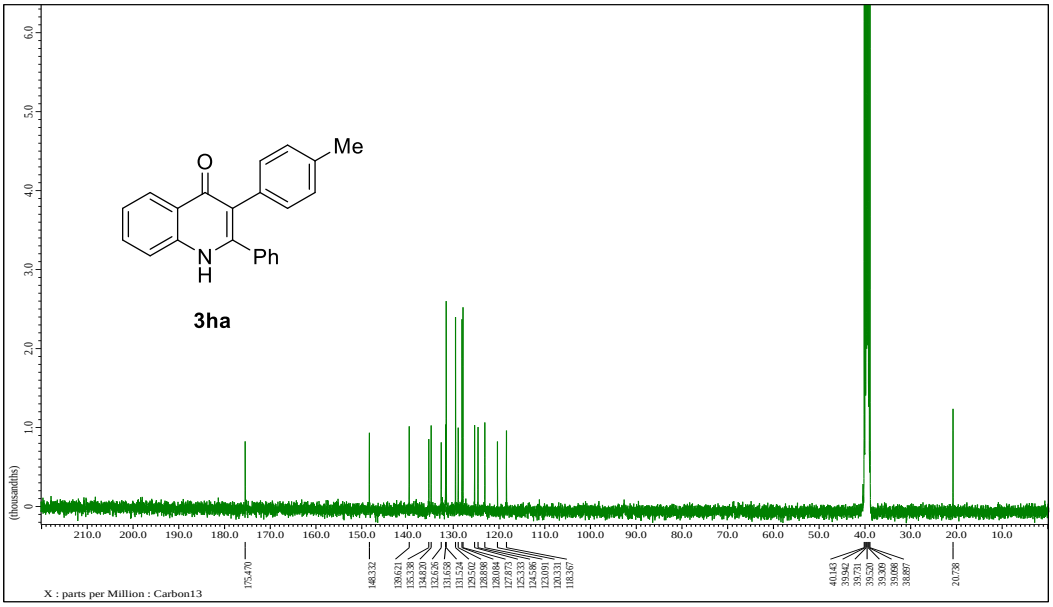
3ga ^{19}F-NMR (376 MHz, DMSO)



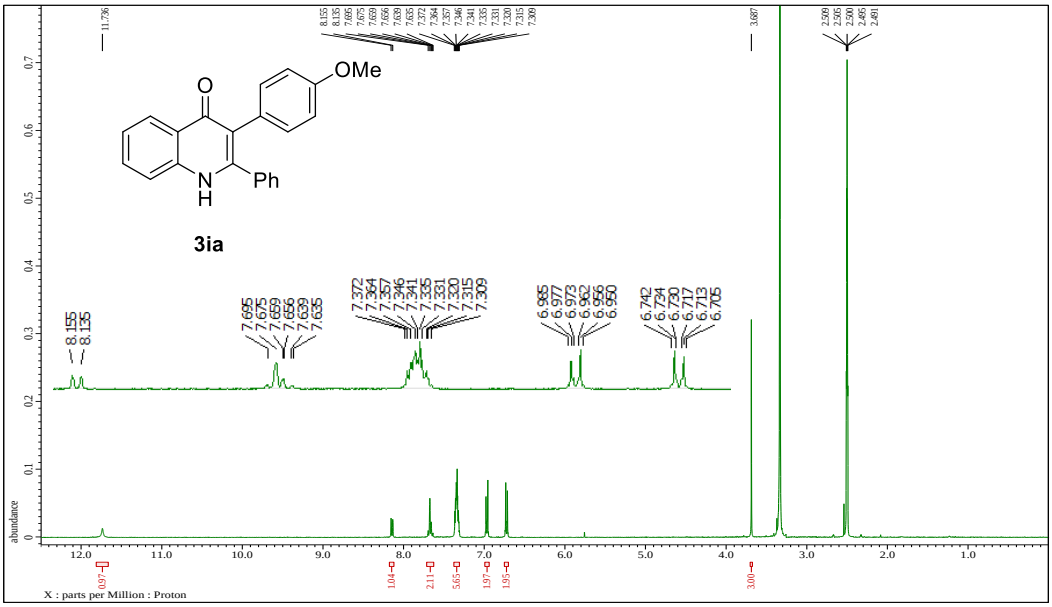
3ha ^{1}H-NMR (400 MHz, DMSO)



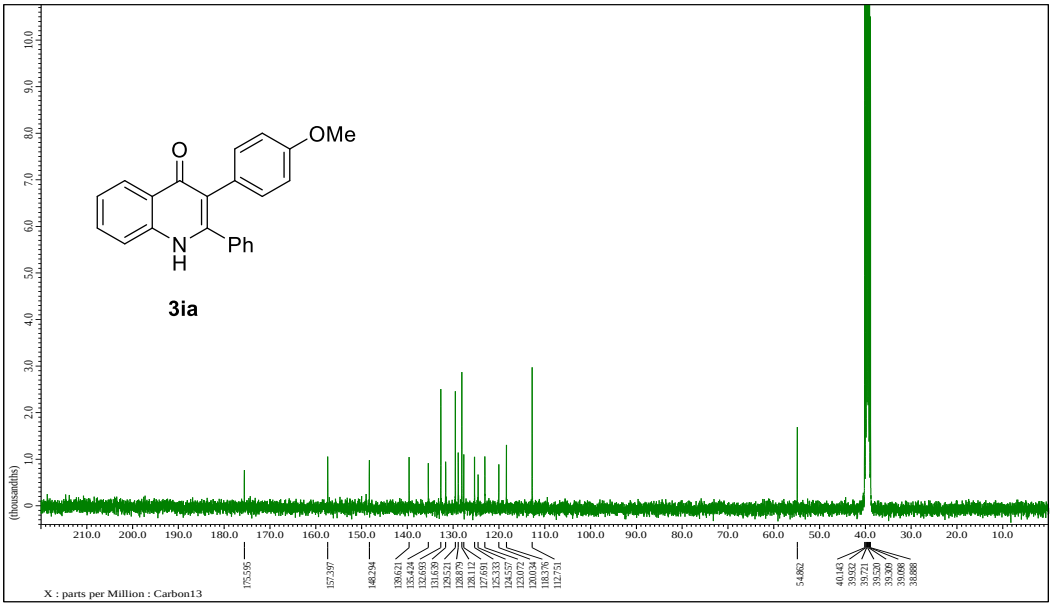
3ha ^{13}C-NMR (100 MHz, DMSO)



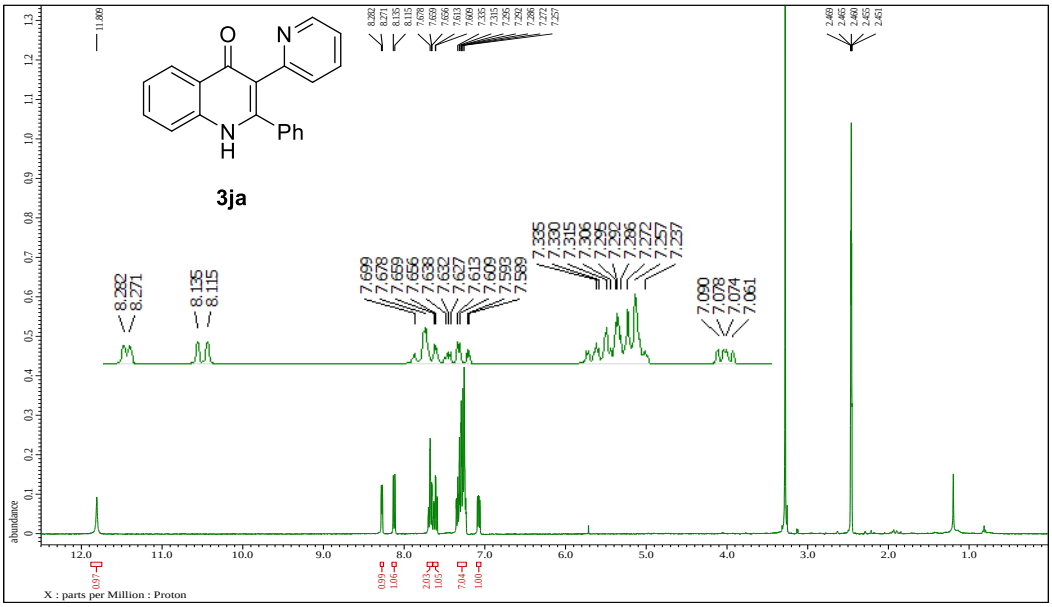
3ia ^{1}H-NMR (400 MHz, DMSO)



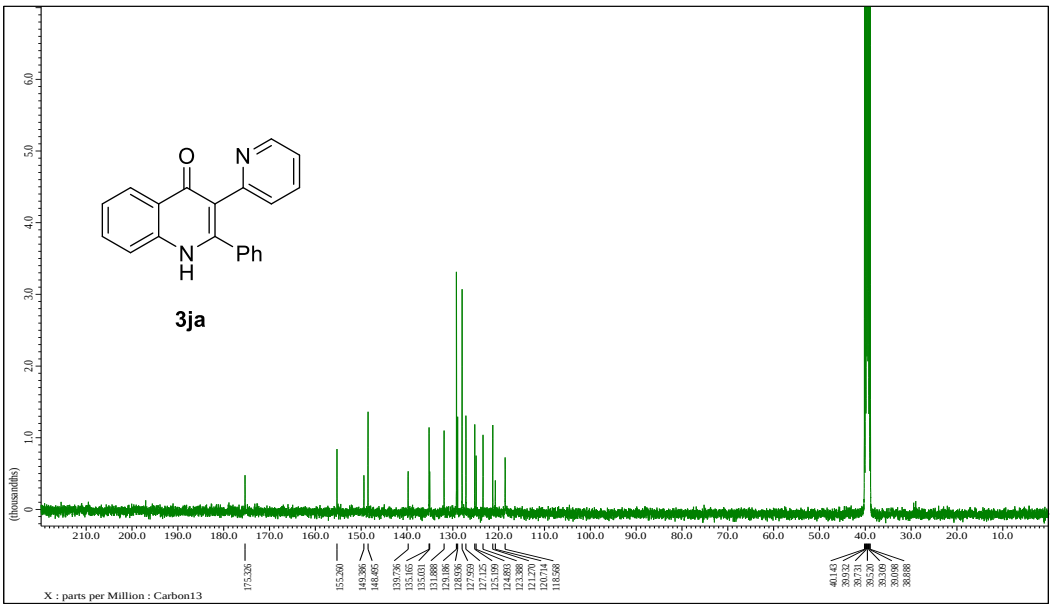
3ia ^{13}C-NMR (100 MHz, DMSO)



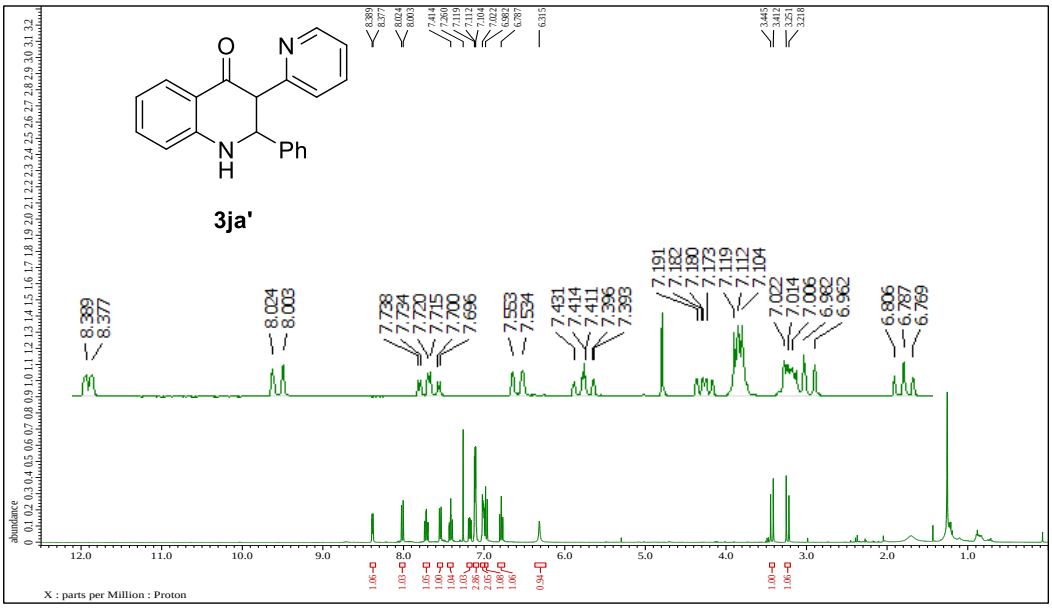
3ja ^{1}H-NMR (400 MHz, DMSO)



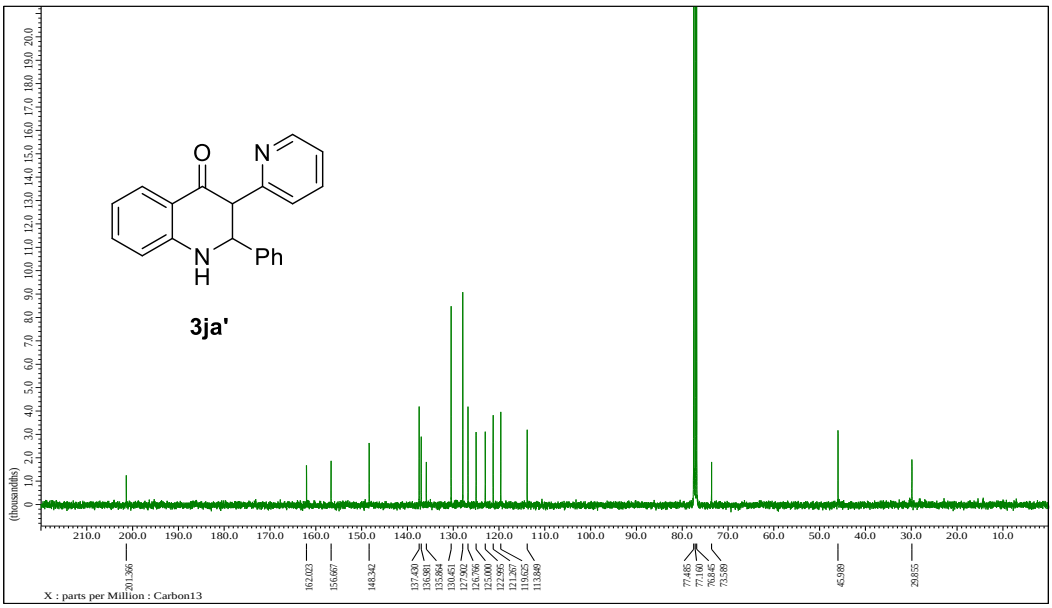
3ja ^{13}C-NMR (100 MHz, DMSO)



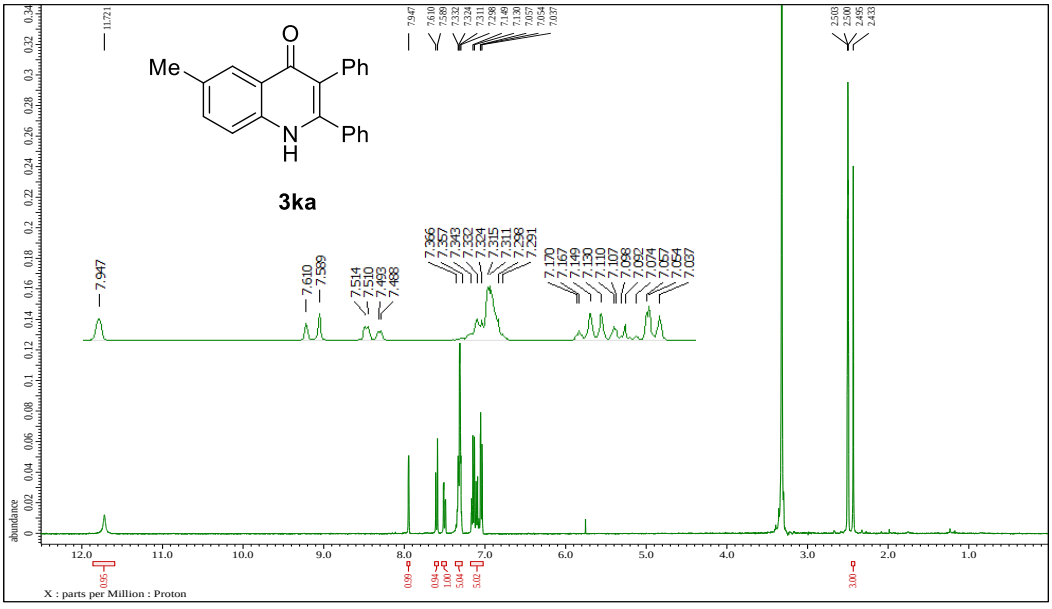
3ja´ ^{1}H-NMR (400 MHz, DMSO)



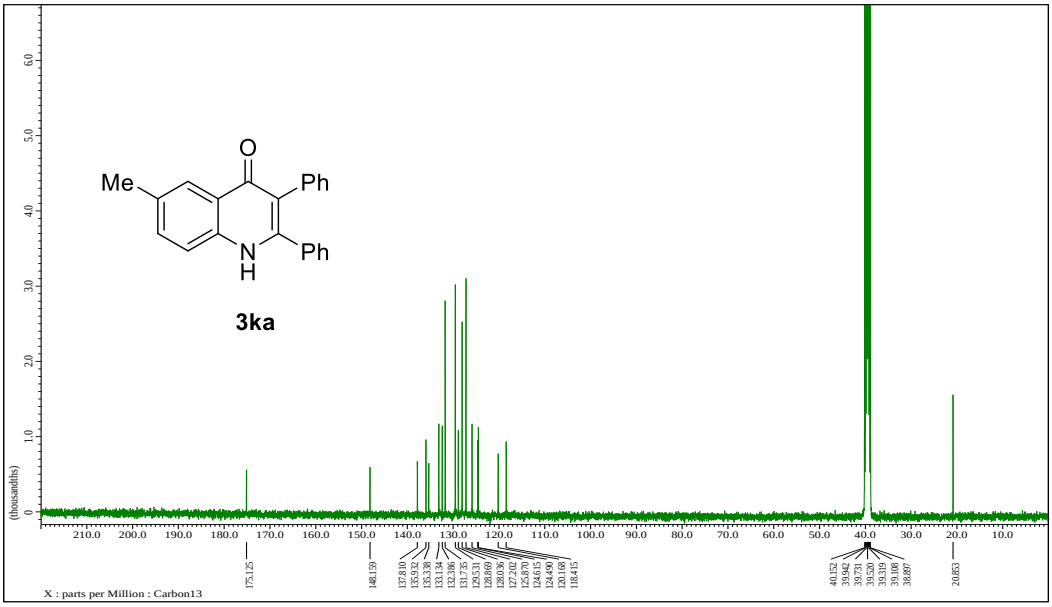
3ja´ ^{13}C-NMR (100 MHz, DMSO)



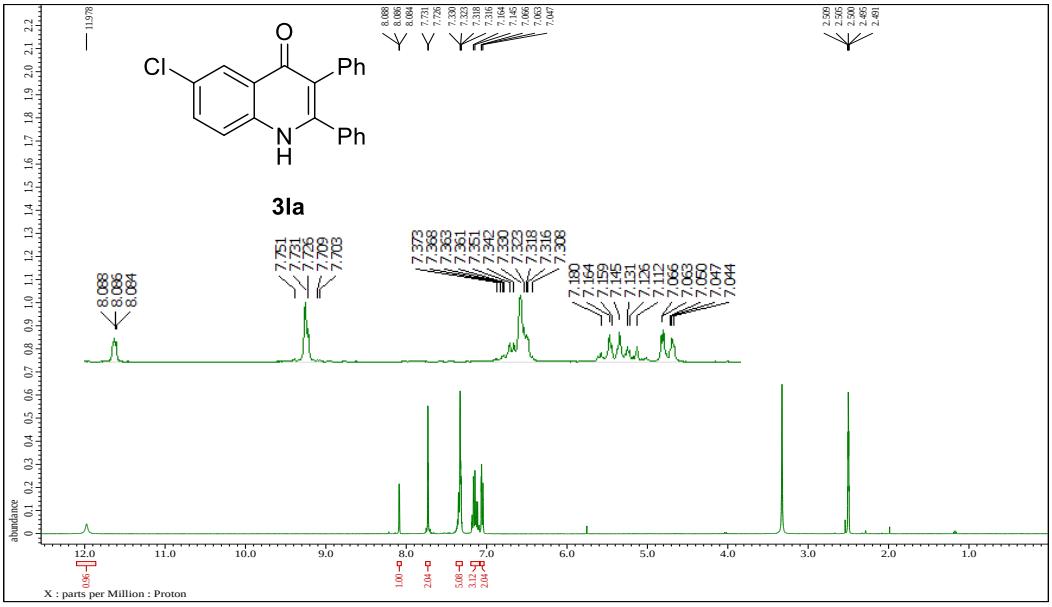
3ka ^{1}H-NMR (400 MHz, DMSO)



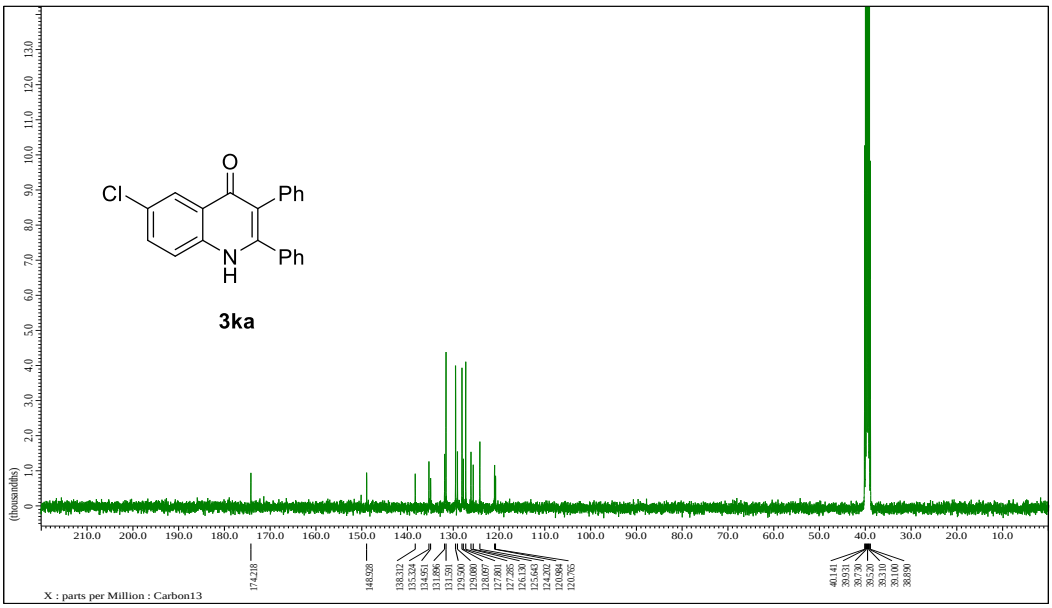
3ka ^{13}C-NMR (100 MHz, DMSO)



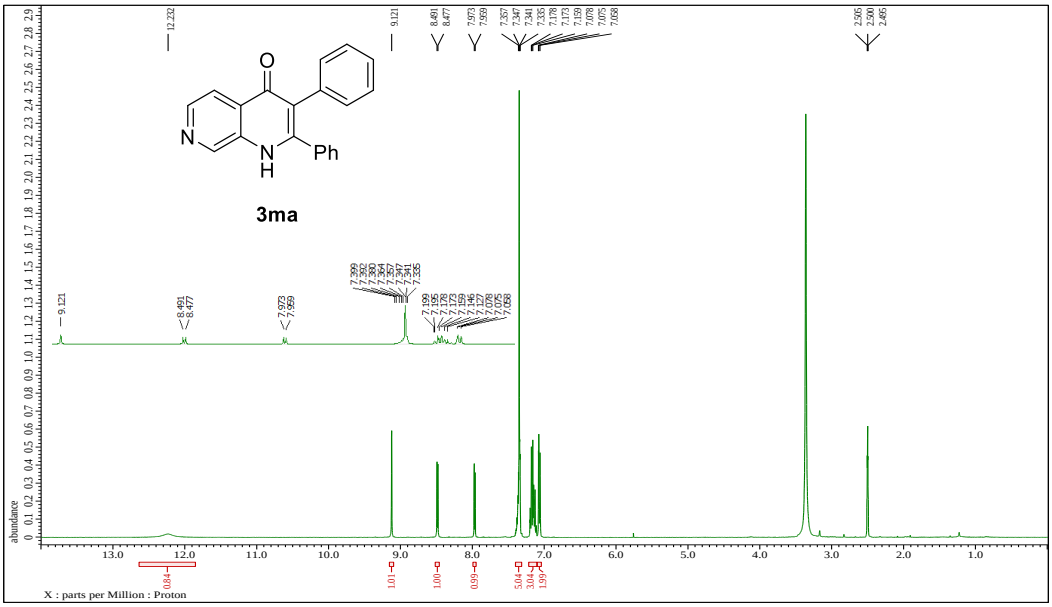
3la ^{1}H-NMR (400 MHz, DMSO)



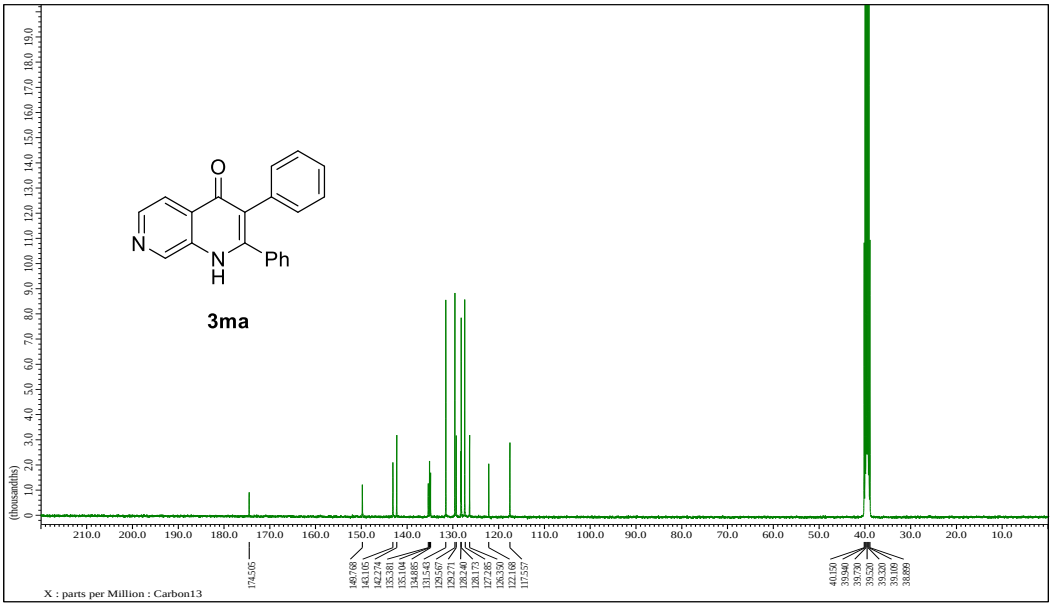
3la ^{13}C-NMR (100 MHz, DMSO)



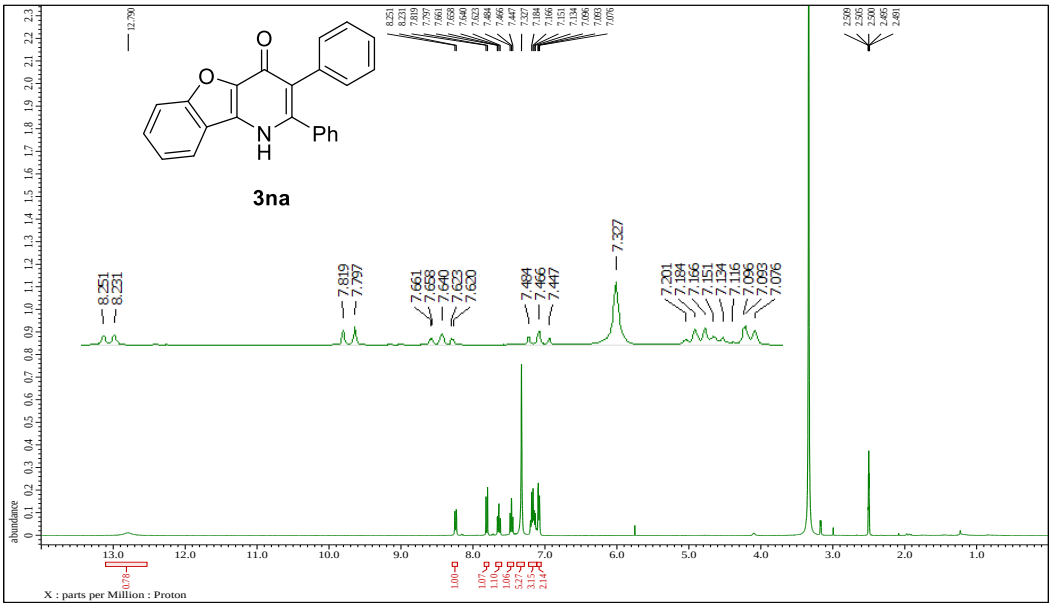
3ma ^{1}H-NMR (400 MHz, DMSO)



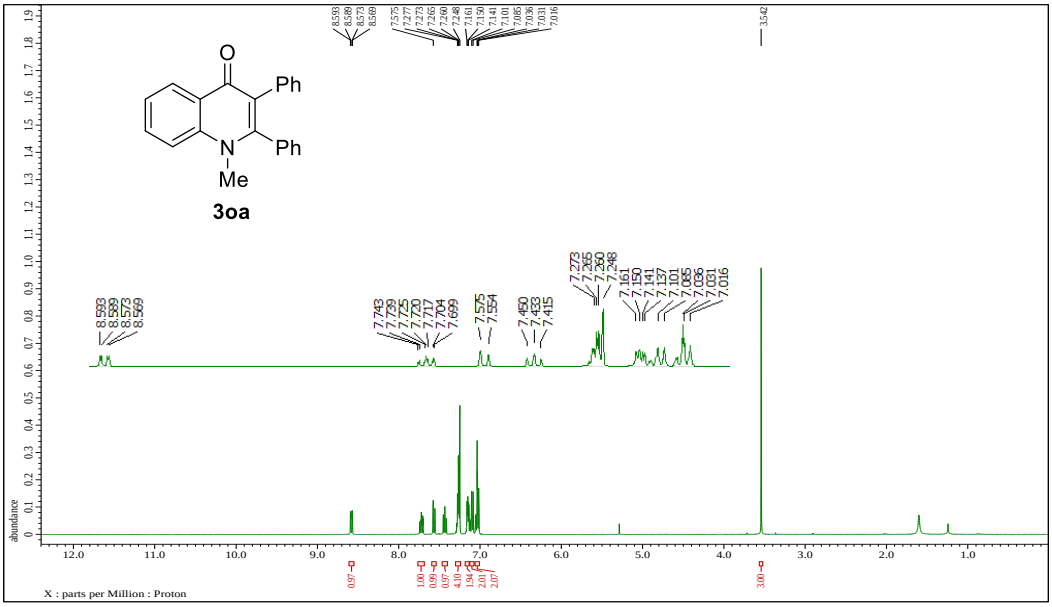
3ma ^{13}C-NMR (100 MHz, DMSO)



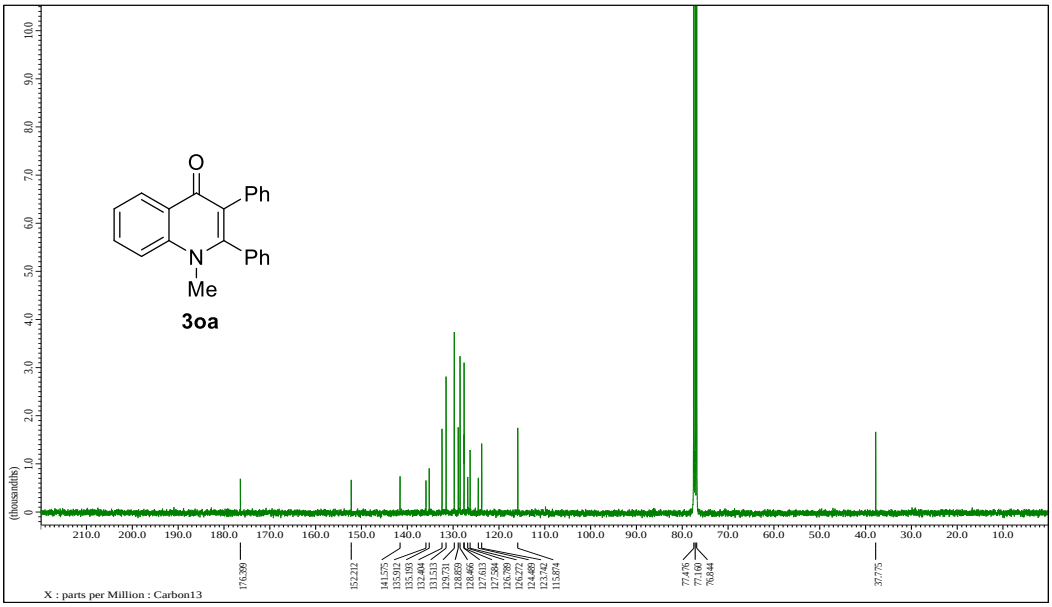
3na ^{1}H-NMR (400 MHz, DMSO)



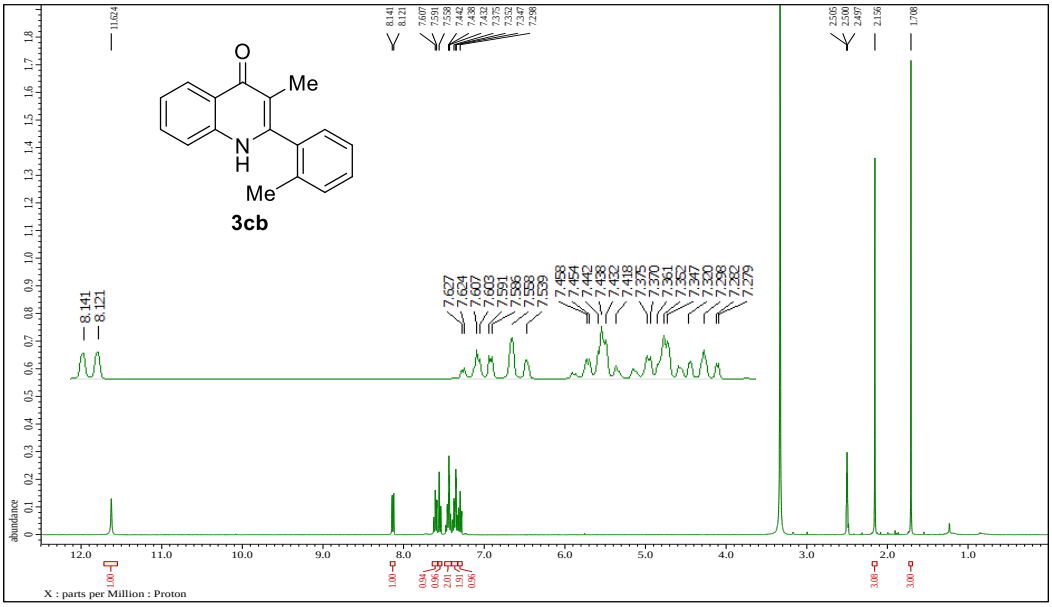
3oa ^{1}H-NMR (400 MHz, $CDCl_3$)



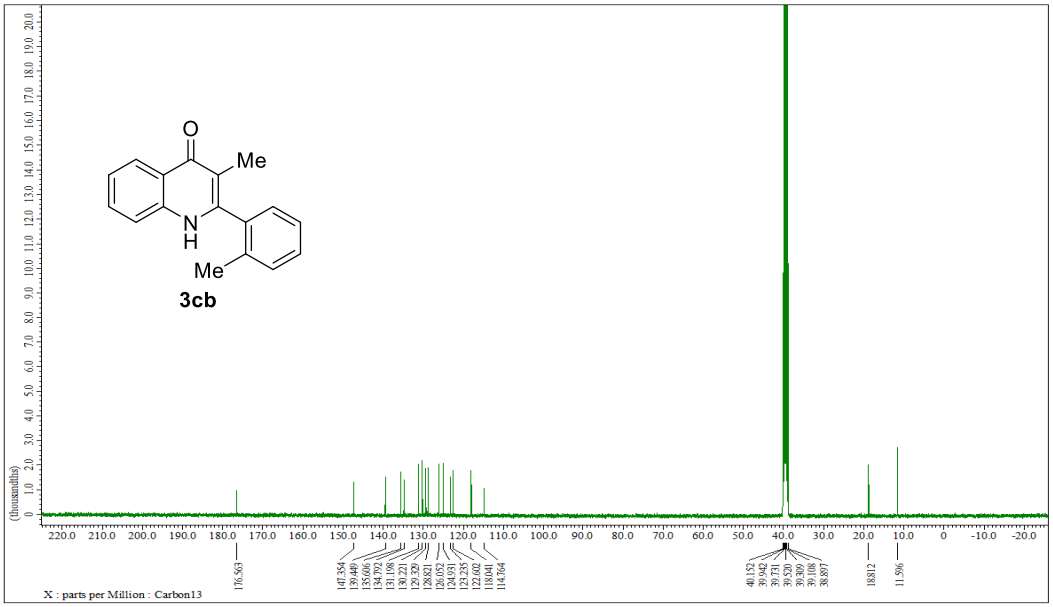
3oa ^{13}C-NMR (100 MHz, $CDCl_3$)



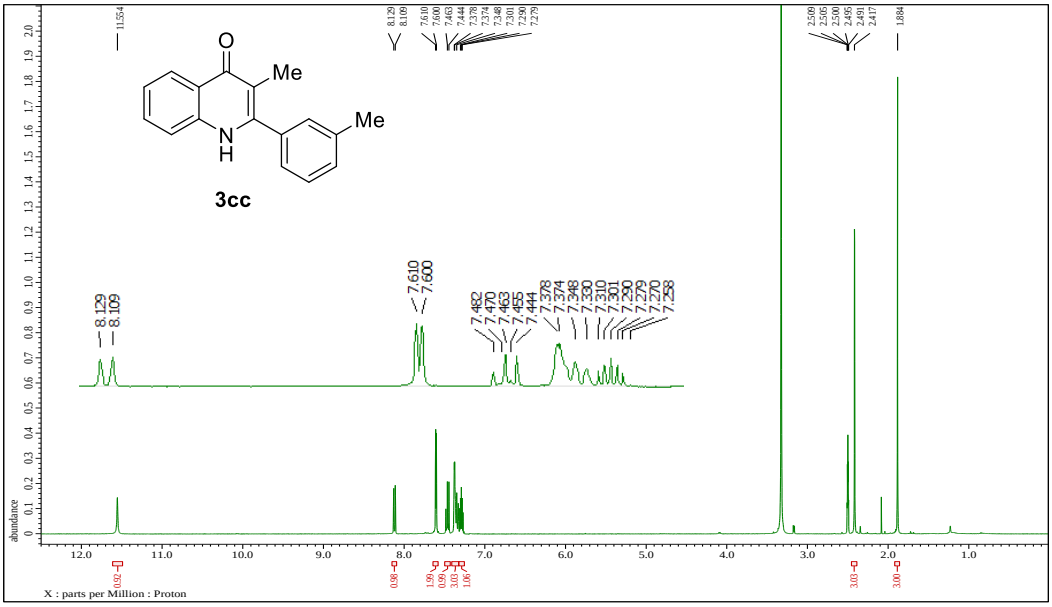
3cb ^{1}H-NMR (400 MHz, DMSO)



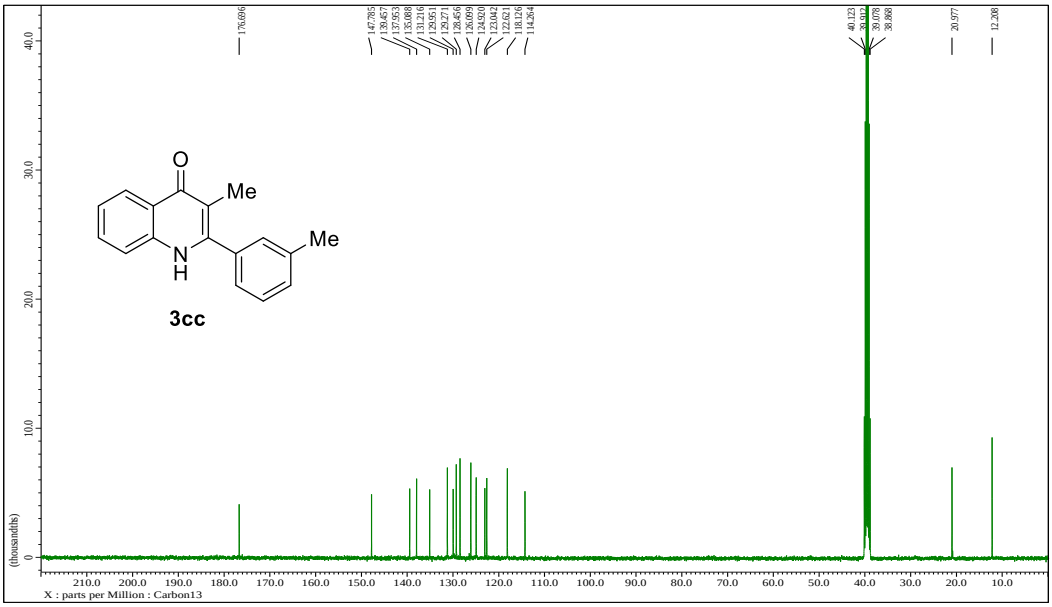
3cb ^{13}C-NMR (100 MHz, DMSO)



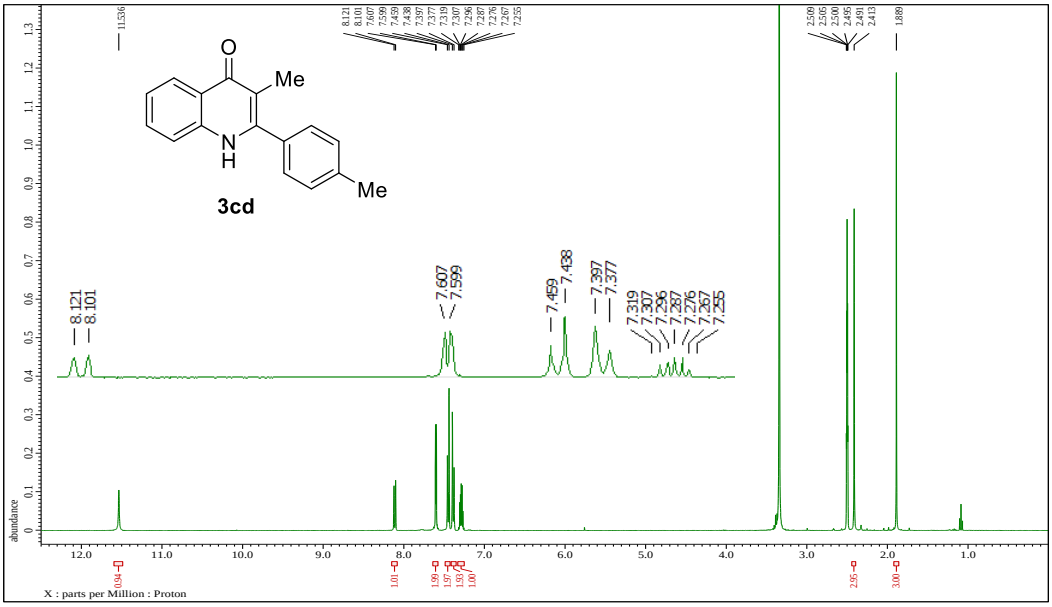
3cc ^{1}H-NMR (400 MHz, DMSO)



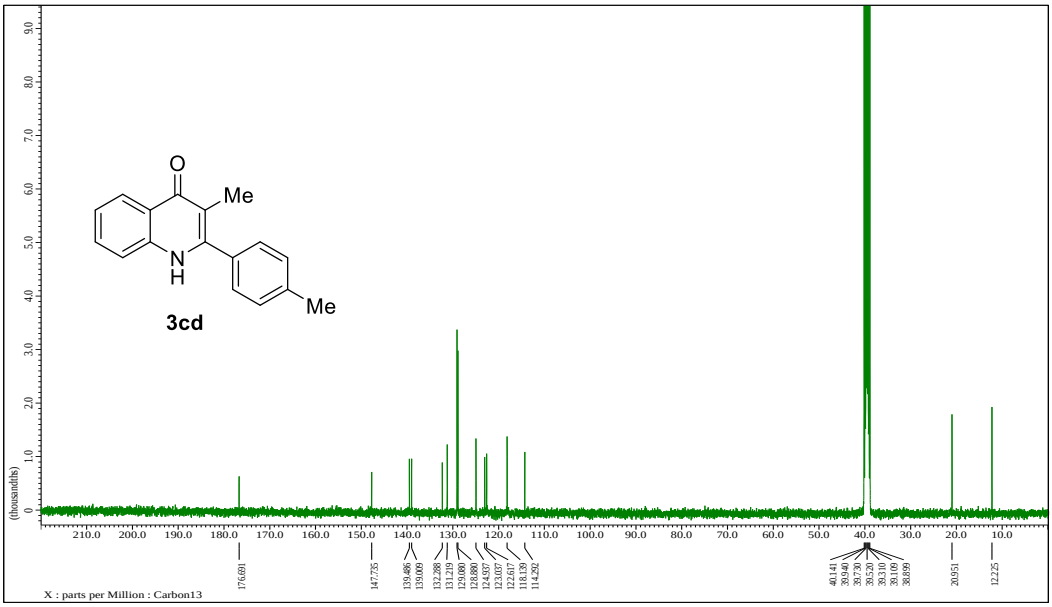
3cc ^{13}C-NMR (100 MHz, DMSO)



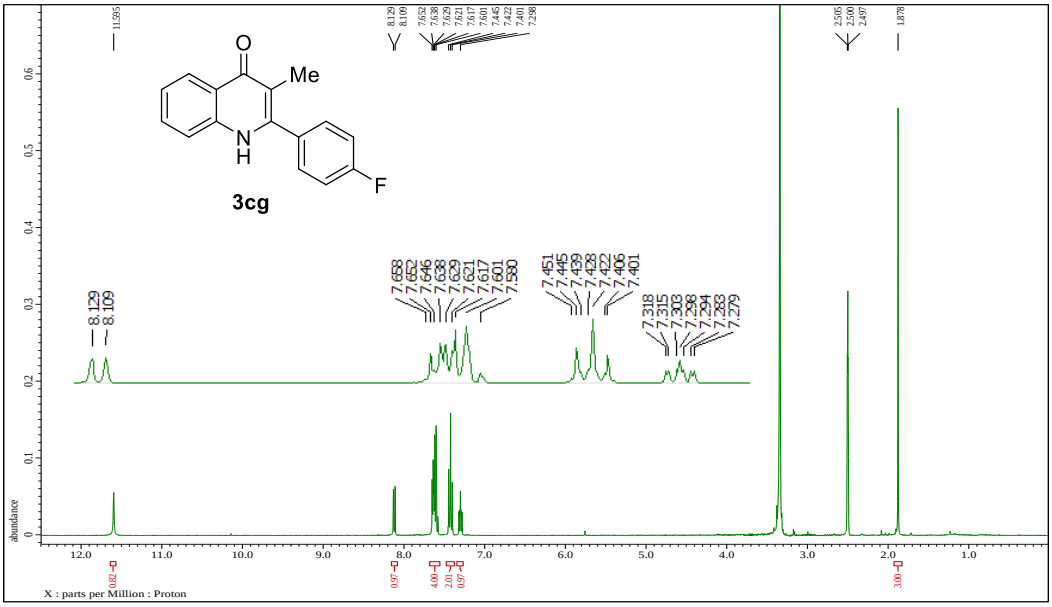
3cd ^{1}H-NMR (400 MHz, DMSO)



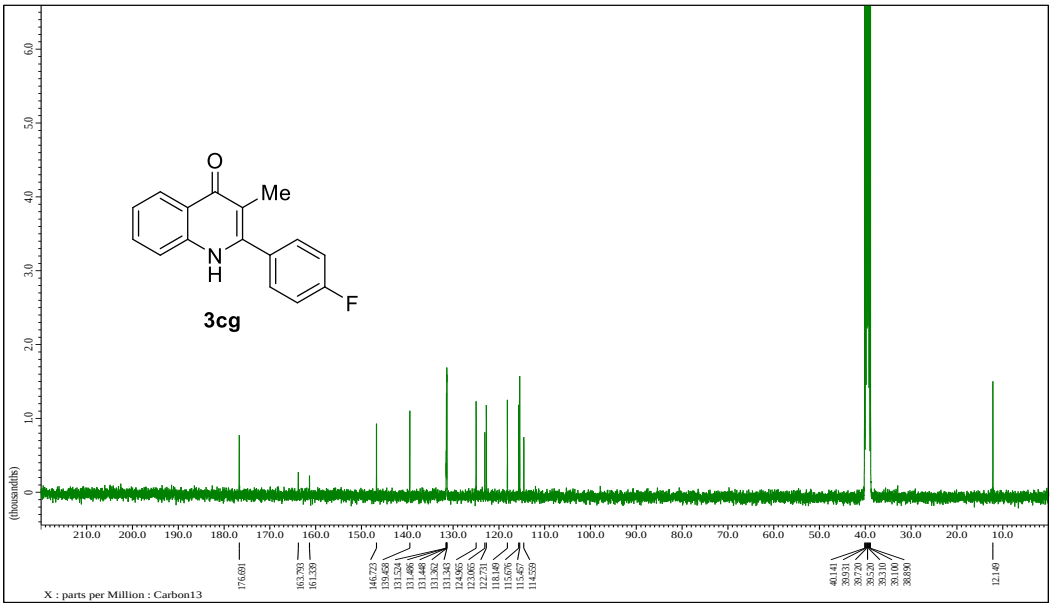
3cd ^{13}C-NMR (100 MHz, DMSO)



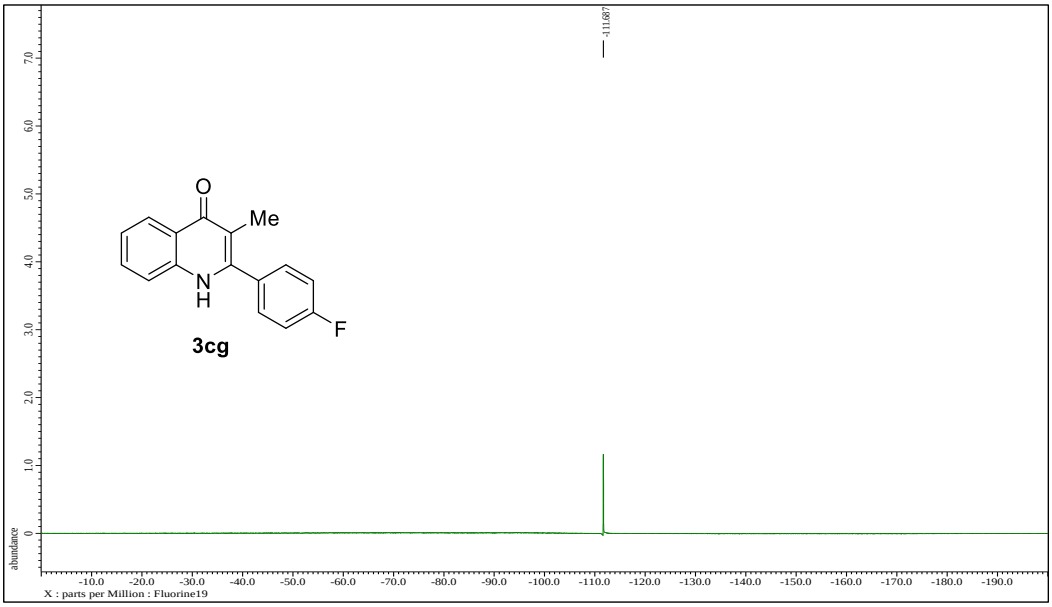
3cg ^{1}H-NMR (400 MHz, DMSO)



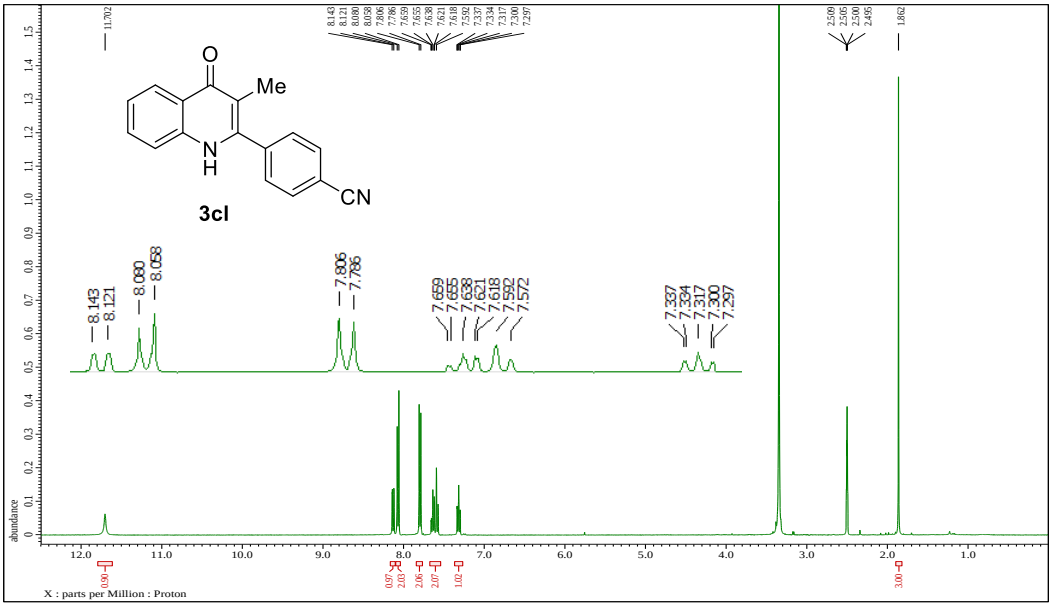
3cg ^{13}C-NMR (100 MHz, DMSO)



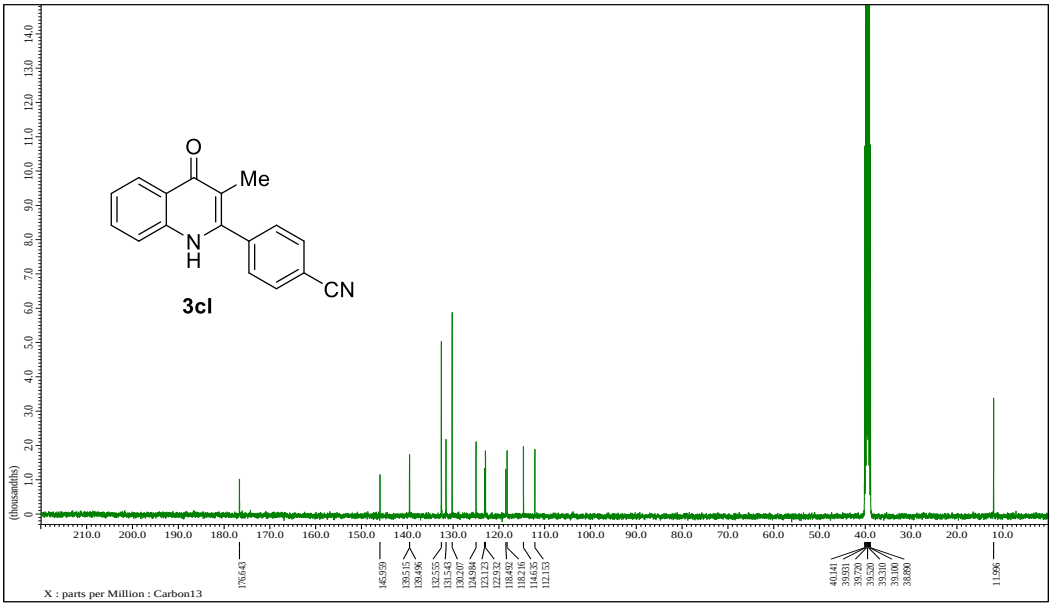
3cg ^{19}F-NMR (376 MHz, DMSO)



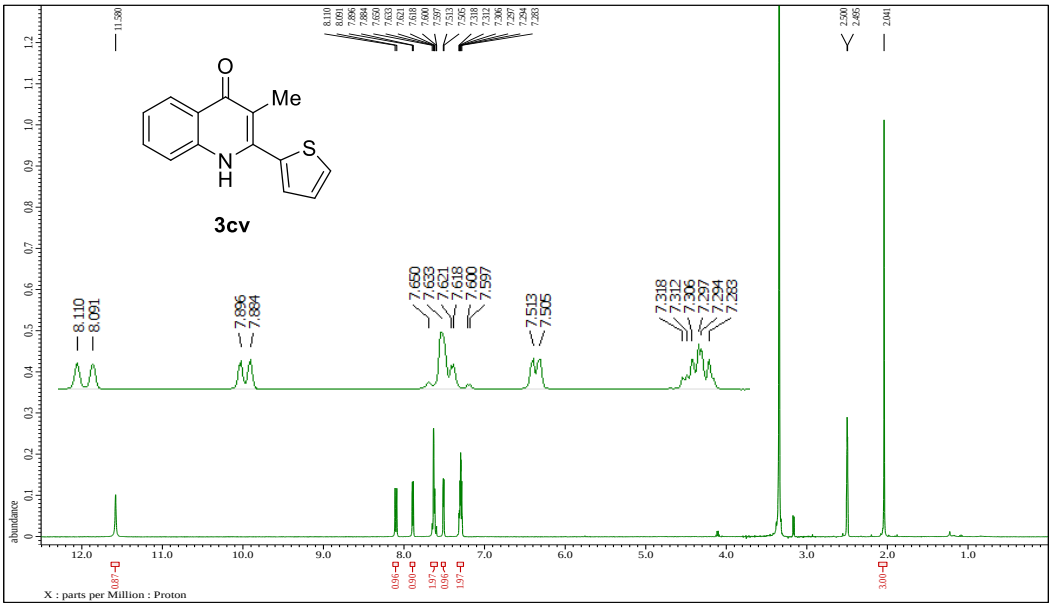
3cl ^{1}H-NMR (400 MHz, DMSO)



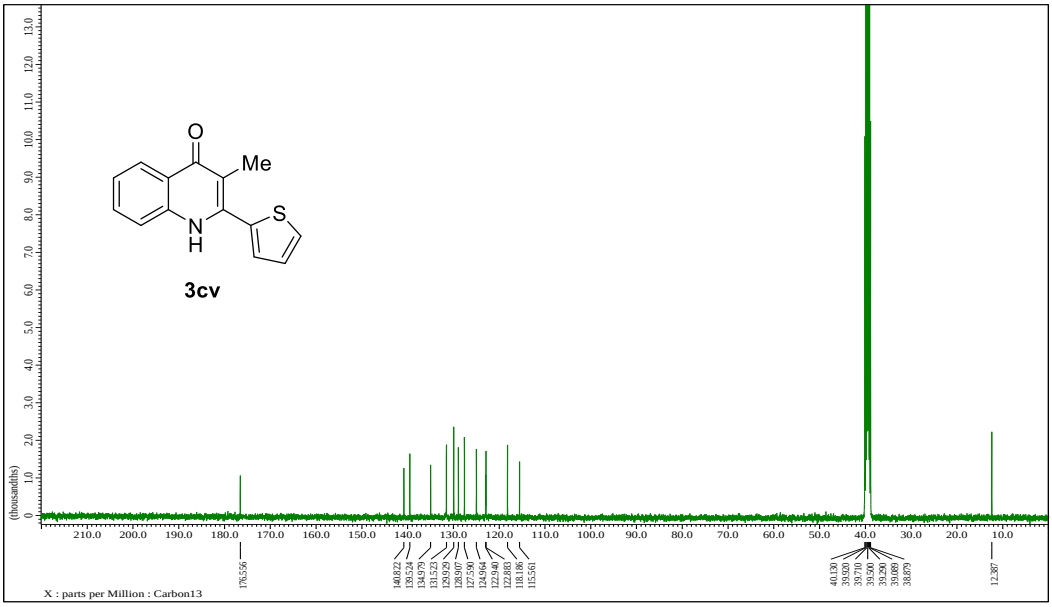
3cl ^{13}C-NMR (100 MHz, DMSO)



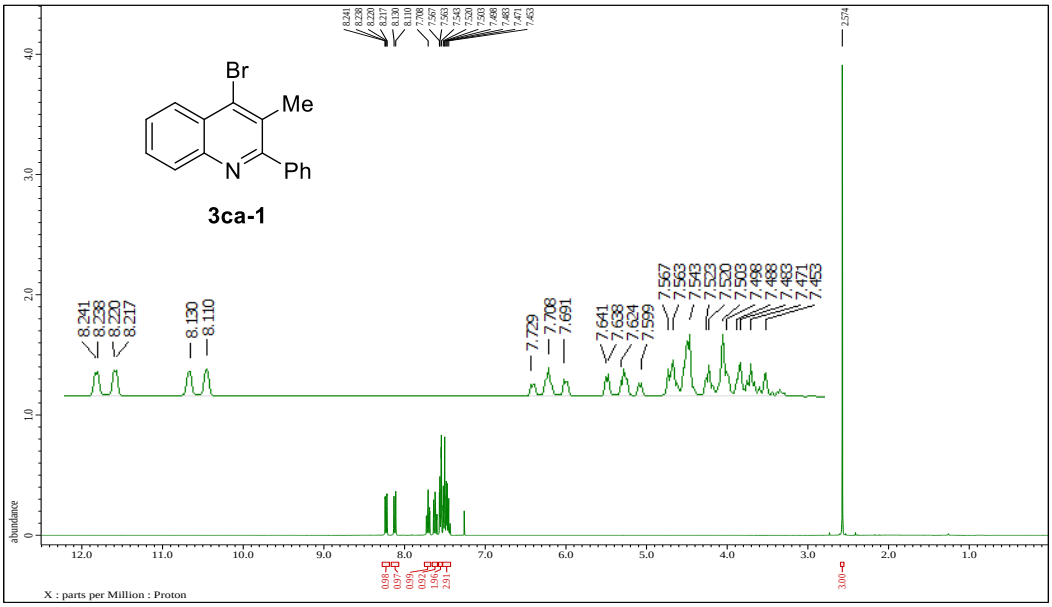
3cv ^{1}H-NMR (400 MHz, DMSO)



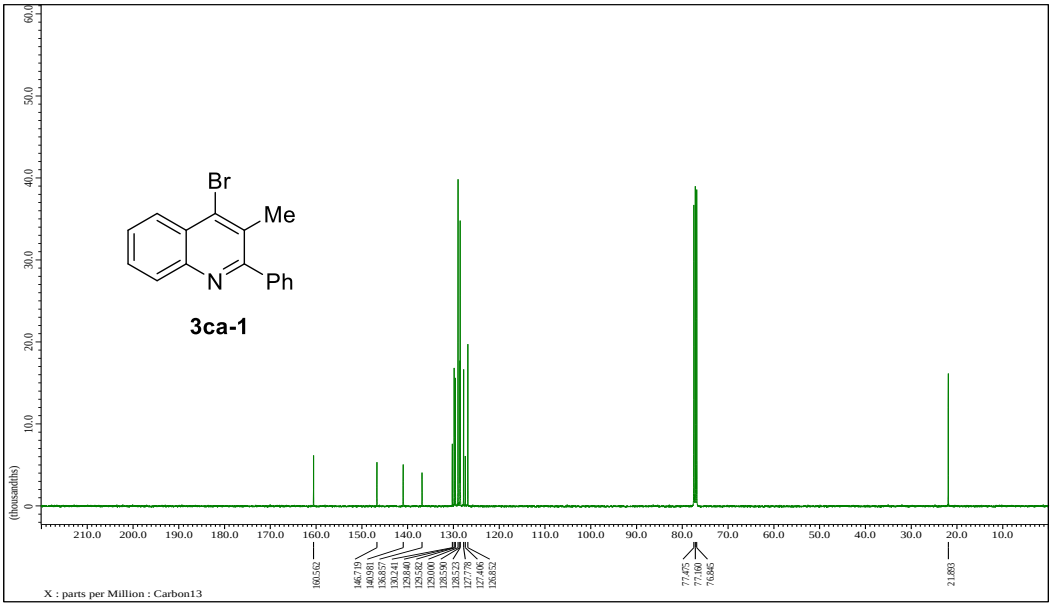
3cv ^{13}C-NMR (100 MHz, DMSO)



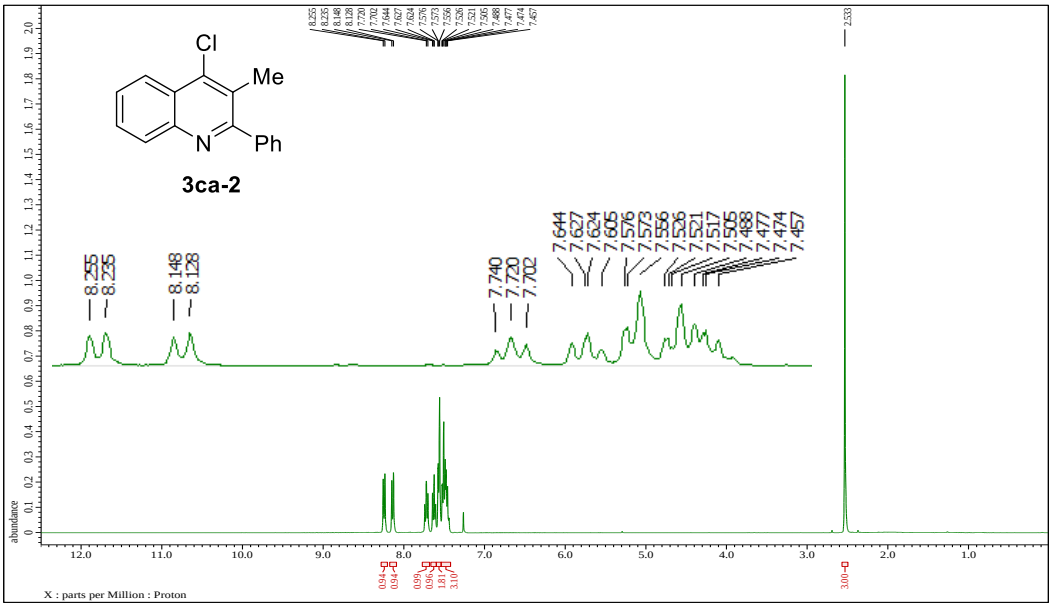
3ca-1 ^{1}H-NMR (400 MHz, $CDCl_3$)



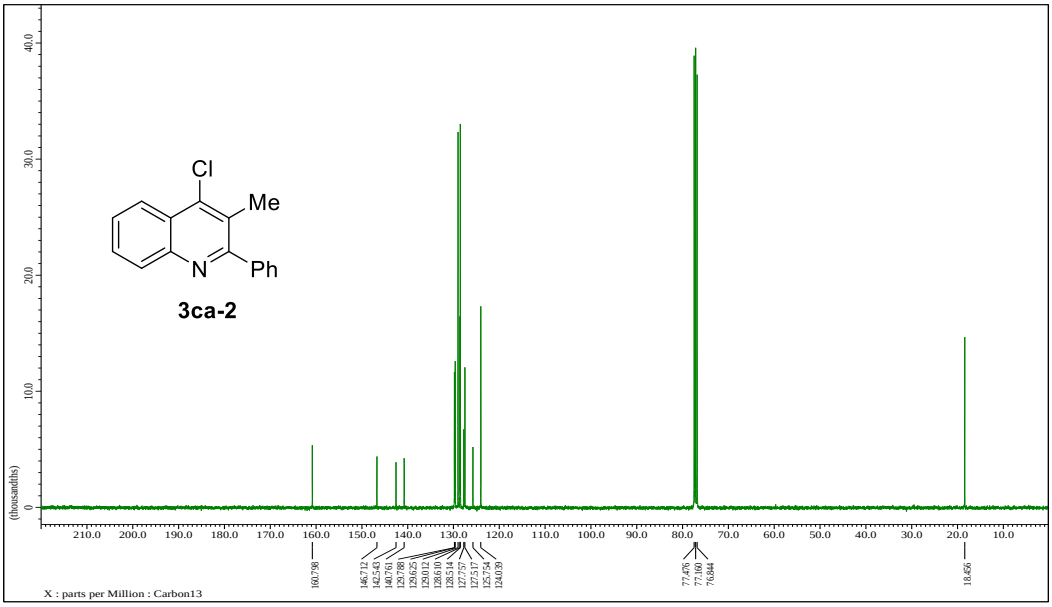
3ca-1 ^{13}C-NMR (100 MHz, $CDCl_3$)



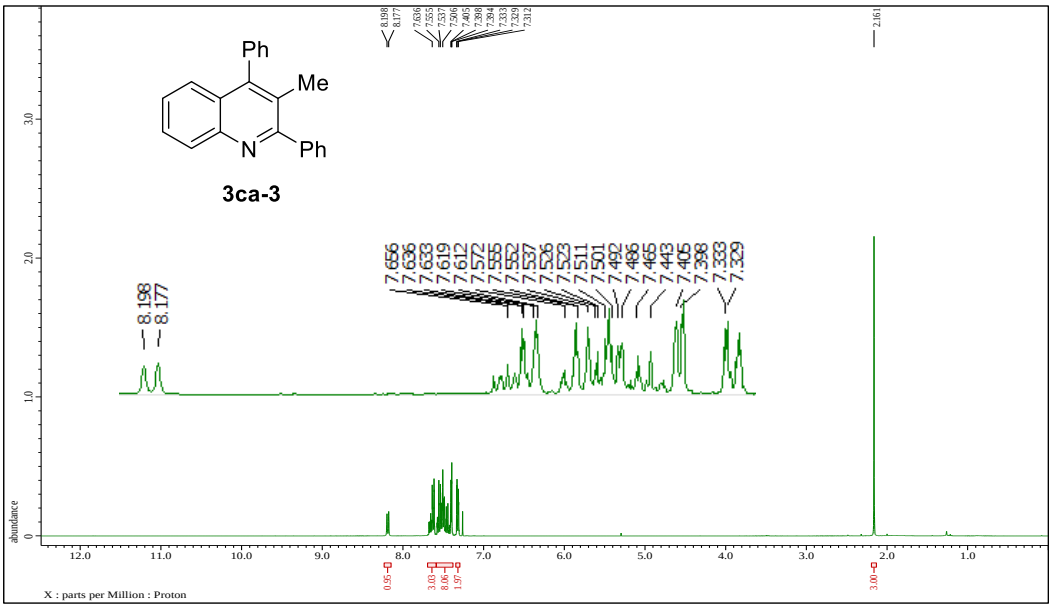
3ca-2 ^{1}H-NMR (400 MHz, $CDCl_3$)



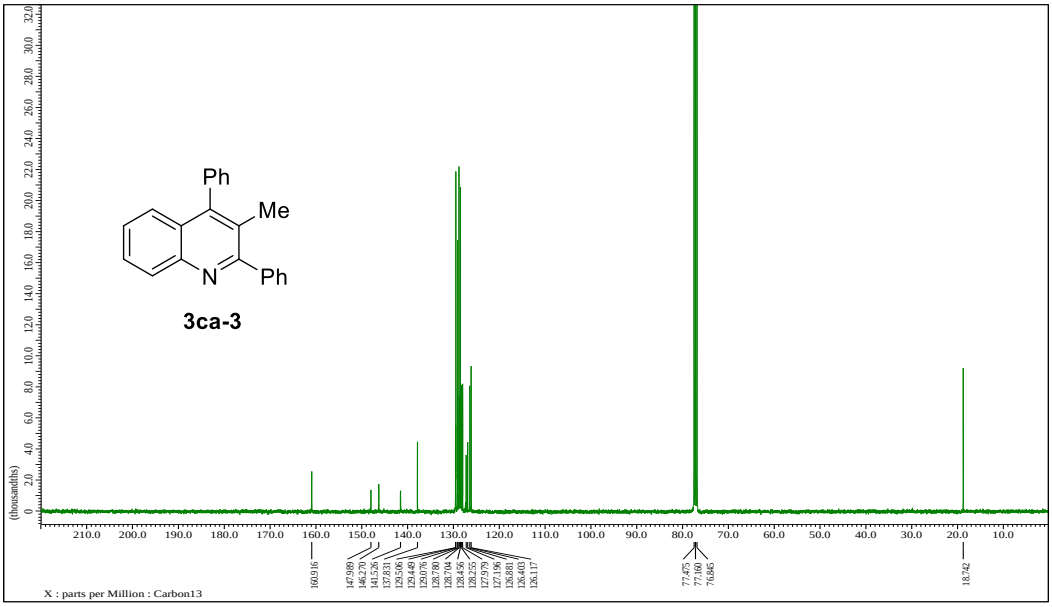
3ca-2 ^{13}C-NMR (100 MHz, $CDCl_3$)



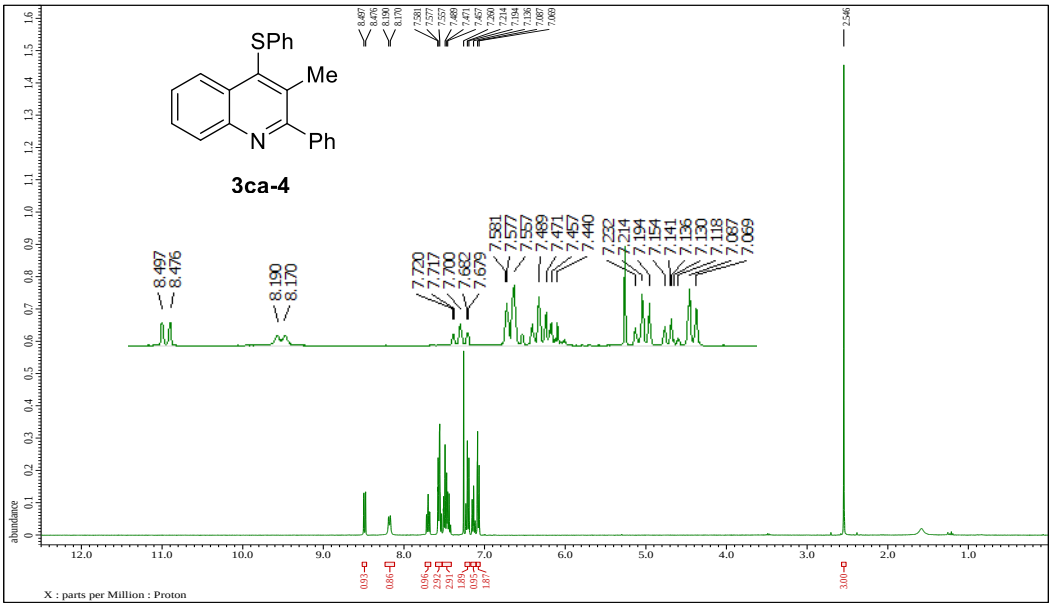
3ca-3 ^{1}H-NMR (400 MHz, $CDCl_3$)



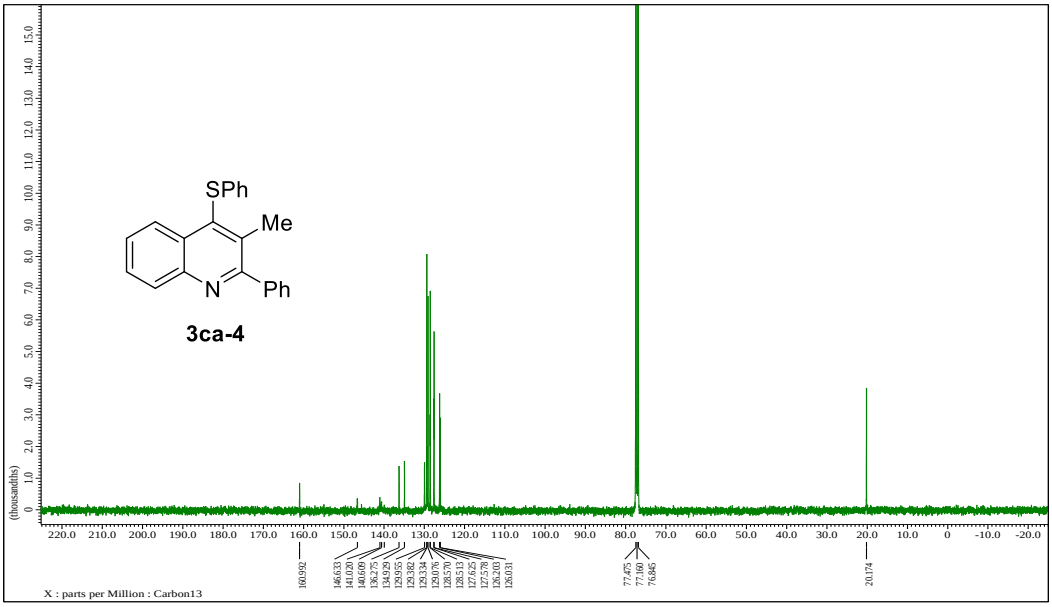
3ca-3 ^{13}C-NMR (100 MHz, $CDCl_3$)



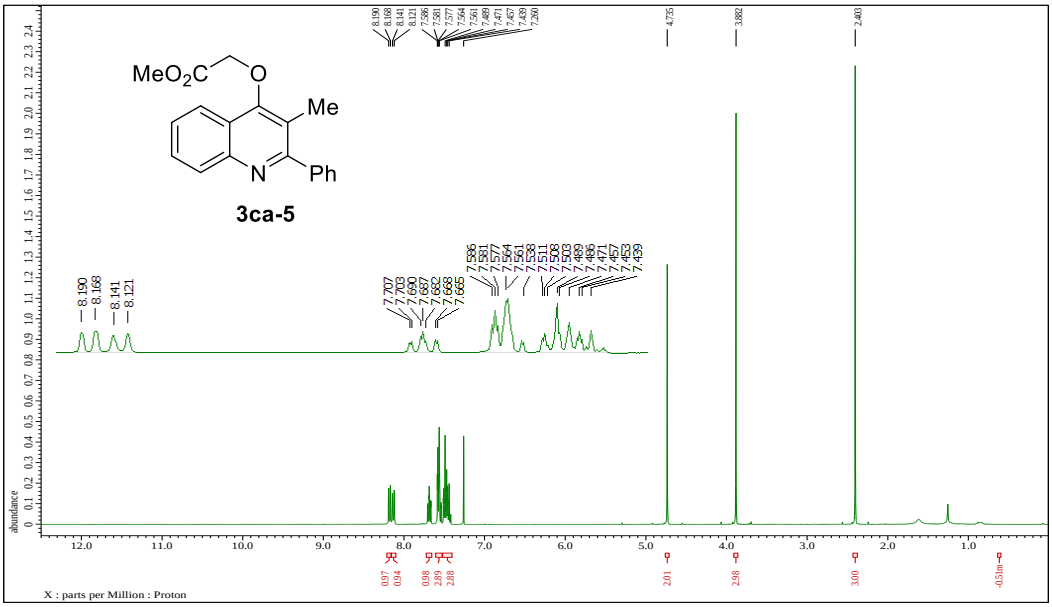
3ca-4 ^{1}H-NMR (400 MHz, $CDCl_3$)



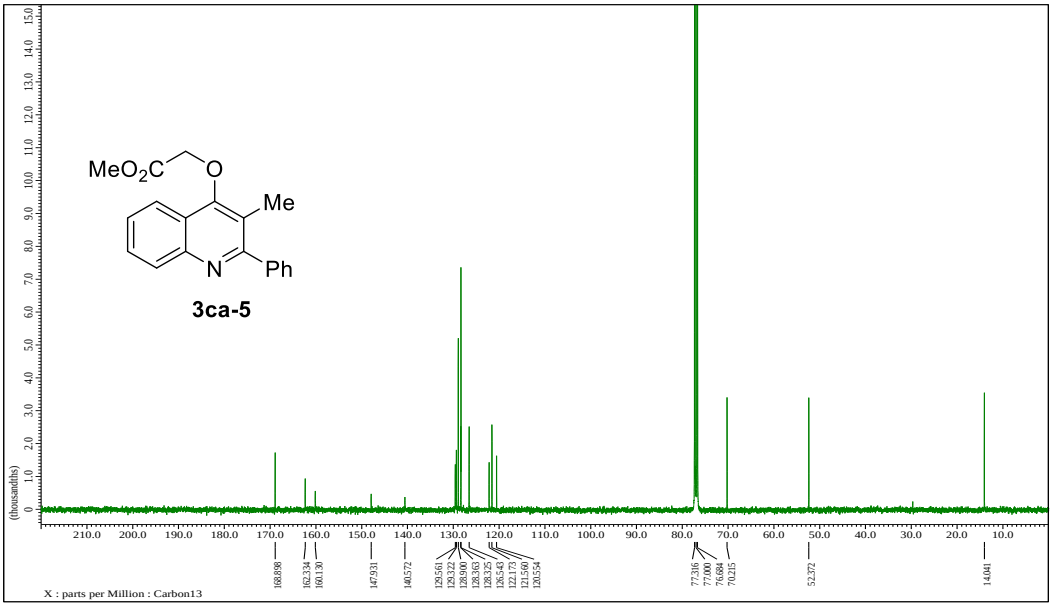
3ca-4 ^{13}C-NMR (100 MHz, $CDCl_3$)



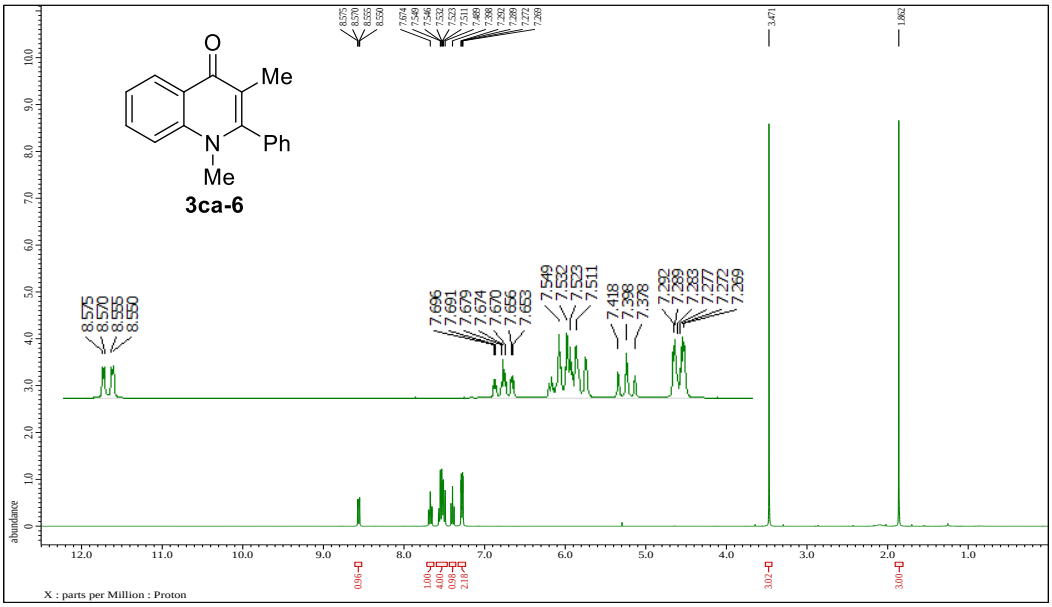
3ca-5 ^{1}H-NMR (400 MHz, $CDCl_3$)



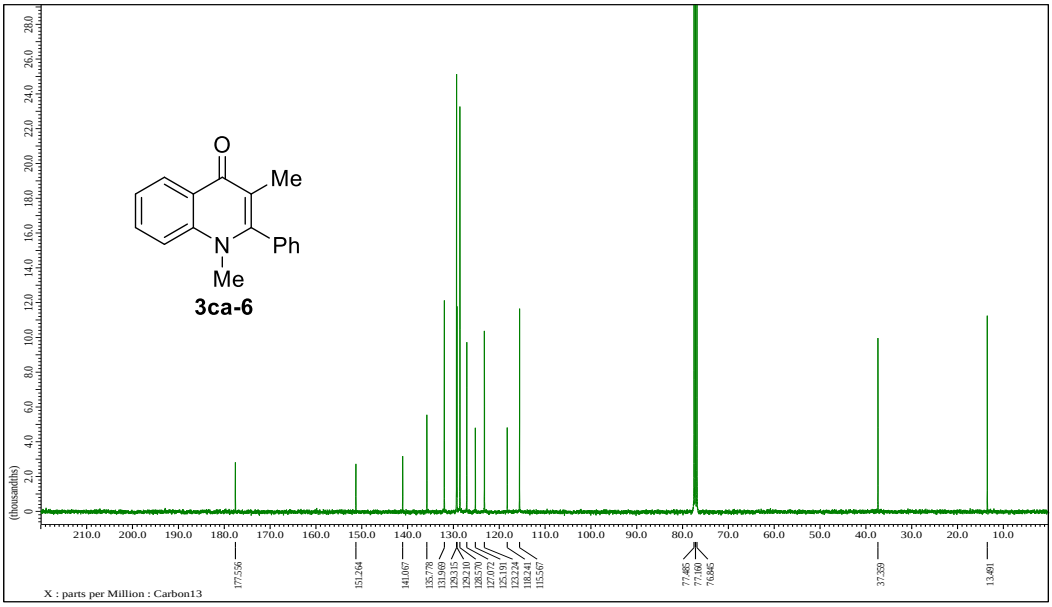
3ca-5 ^{13}C-NMR (100 MHz, $CDCl_3$)



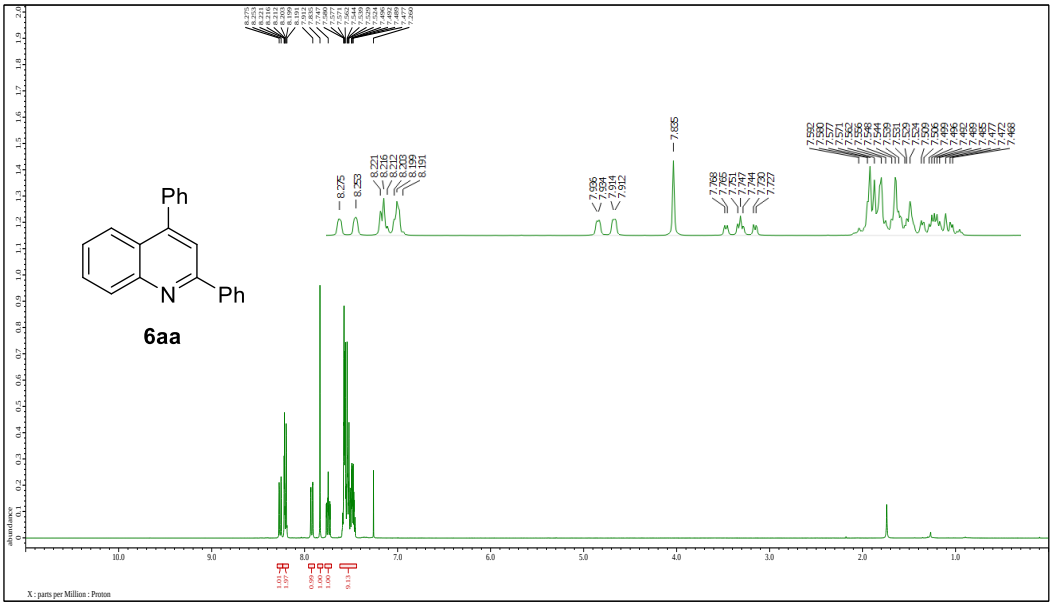
3ca-6 ^{1}H-NMR (400 MHz, $CDCl_3$)



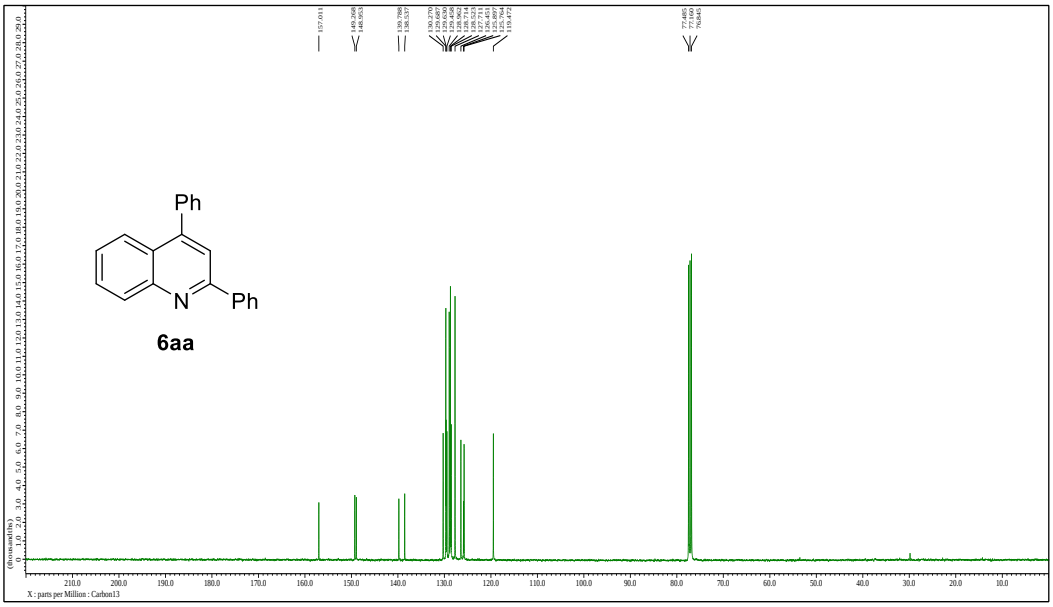
3ca-6 ^{13}C-NMR (100 MHz, $CDCl_3$)



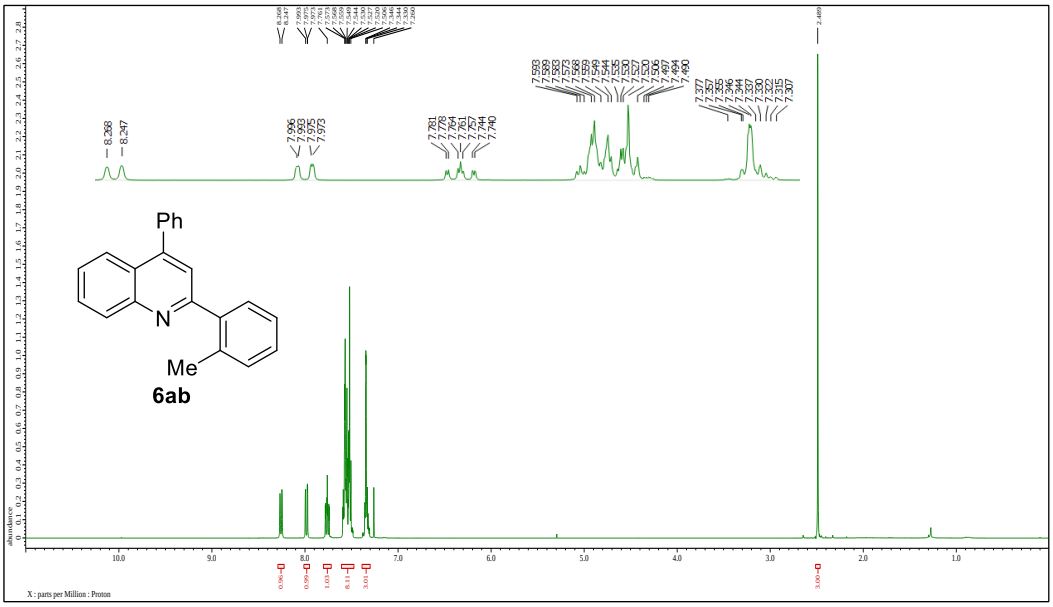
6aa ^{1}H-NMR (400 MHz, $CDCl_3$)



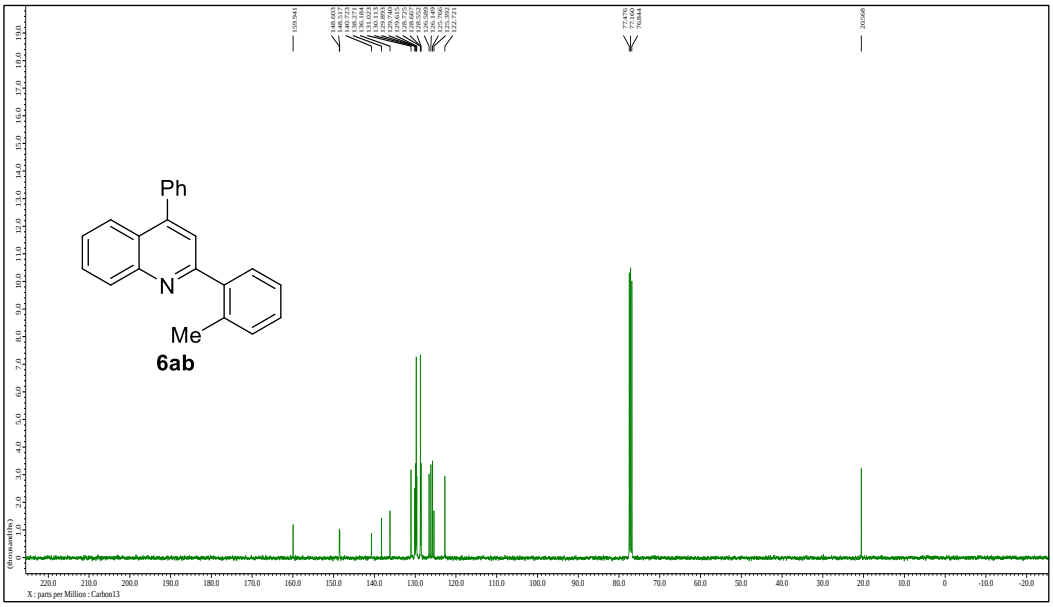
6aa ^{13}C-NMR (100 MHz, $CDCl_3$)



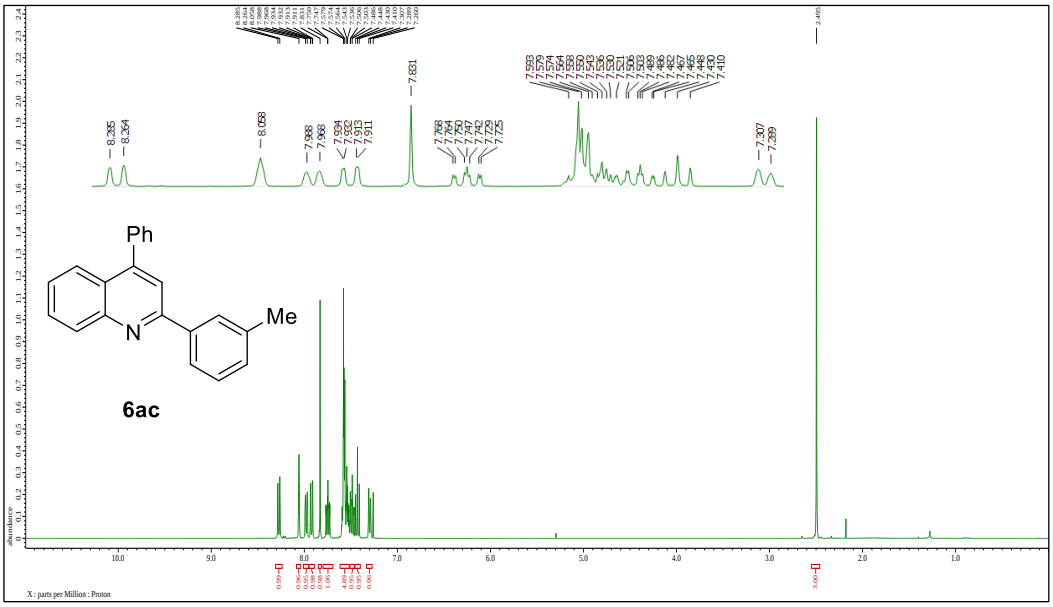
6ab ^{1}H-NMR (400 MHz, $CDCl_3$)



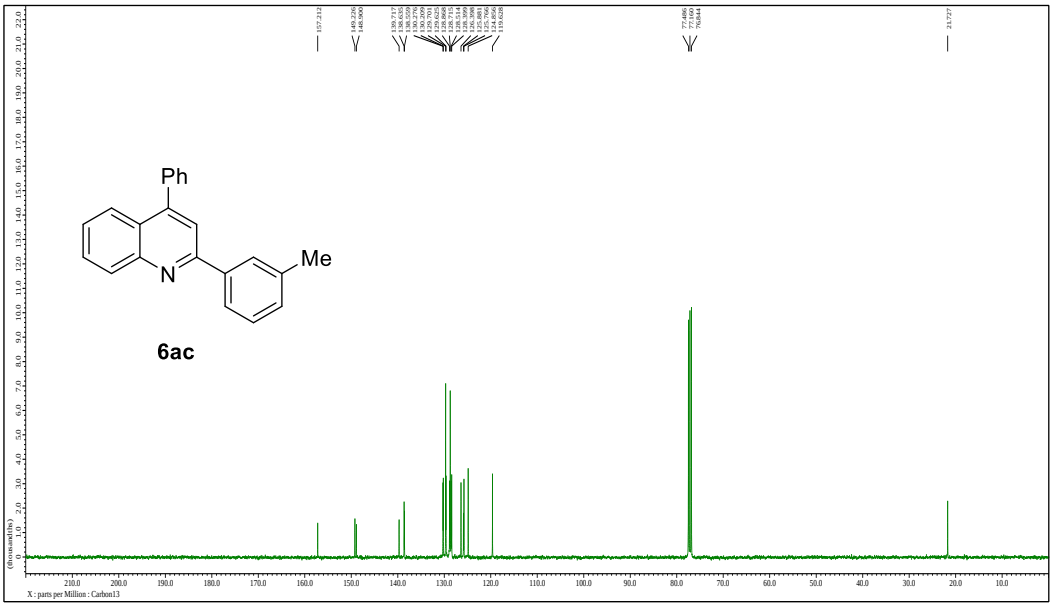
6ab ^{13}C-NMR (100 MHz, $CDCl_3$)



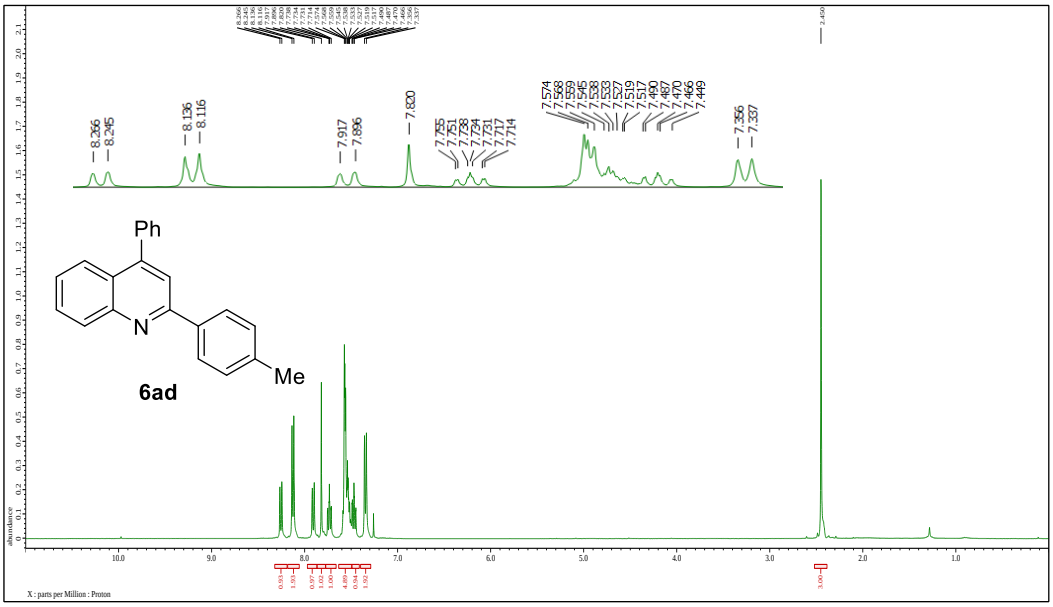
6ac ^{1}H-NMR (400 MHz, $CDCl_3$)



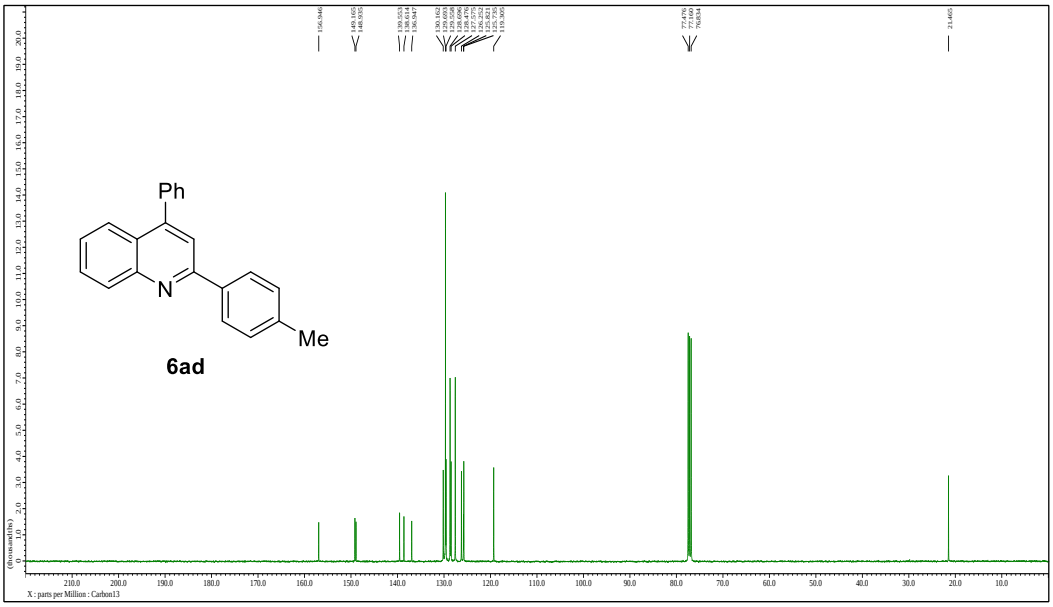
6ac ^{13}C-NMR (100 MHz, $CDCl_3$)



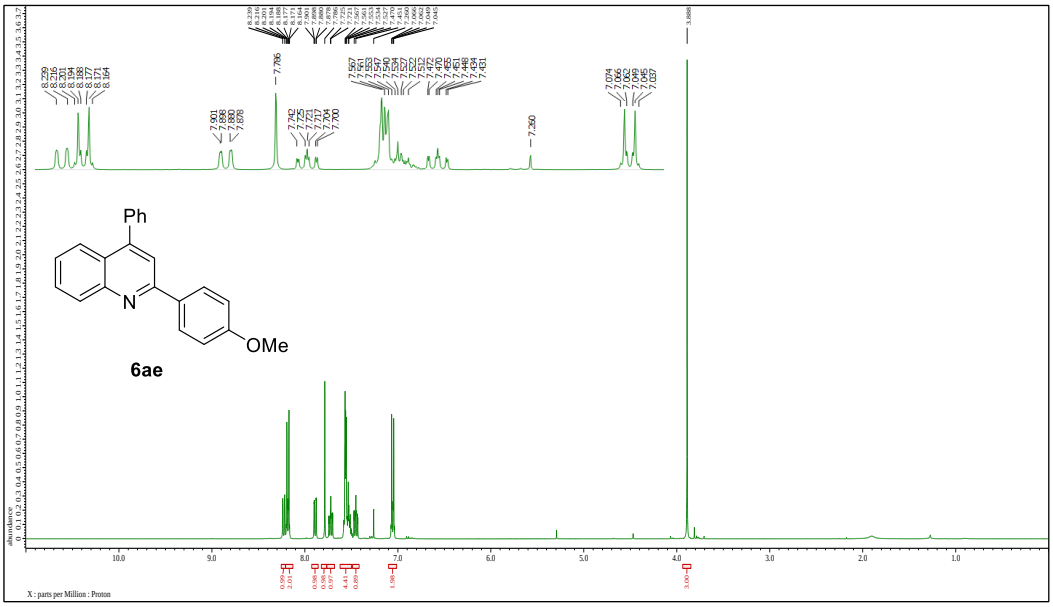
6ad ^{1}H-NMR (400 MHz, $CDCl_3$)



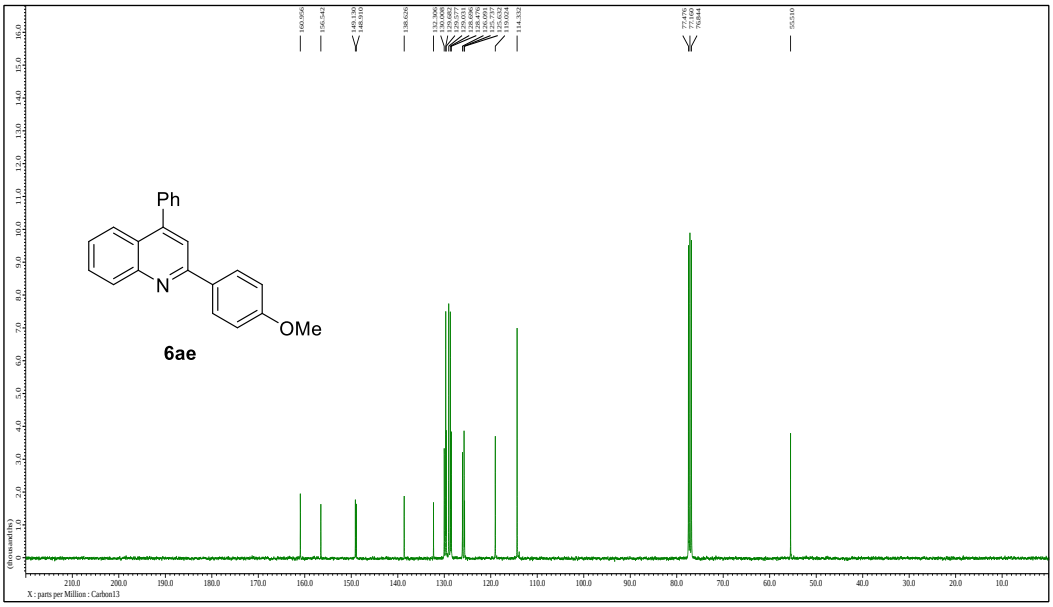
6ad ^{13}C-NMR (100 MHz, $CDCl_3$)



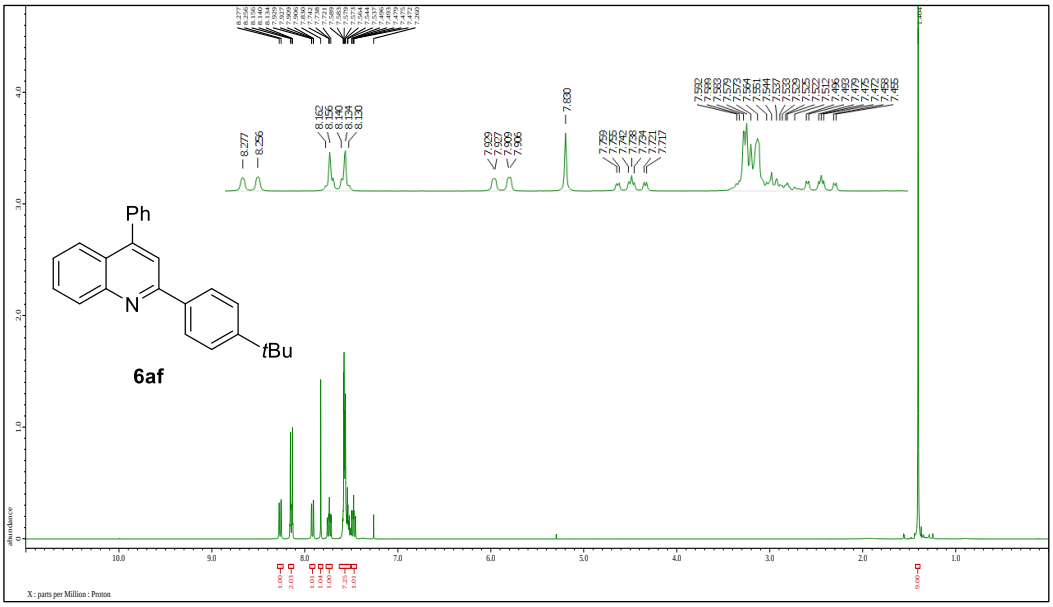
6ae ^{1}H-NMR (400 MHz, $CDCl_3$)



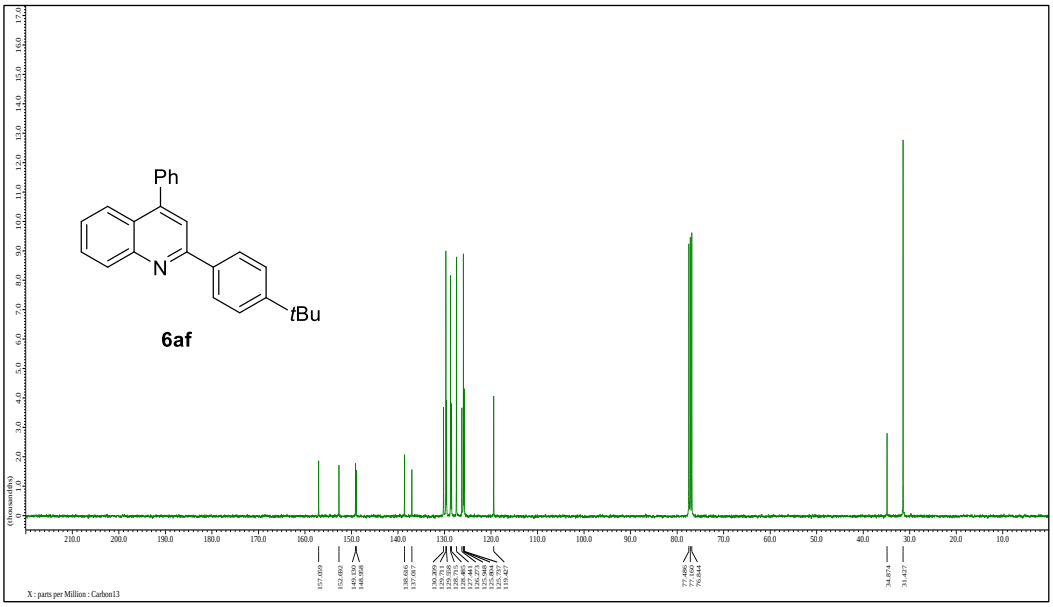
6ae ^{13}C-NMR (100 MHz, $CDCl_3$)



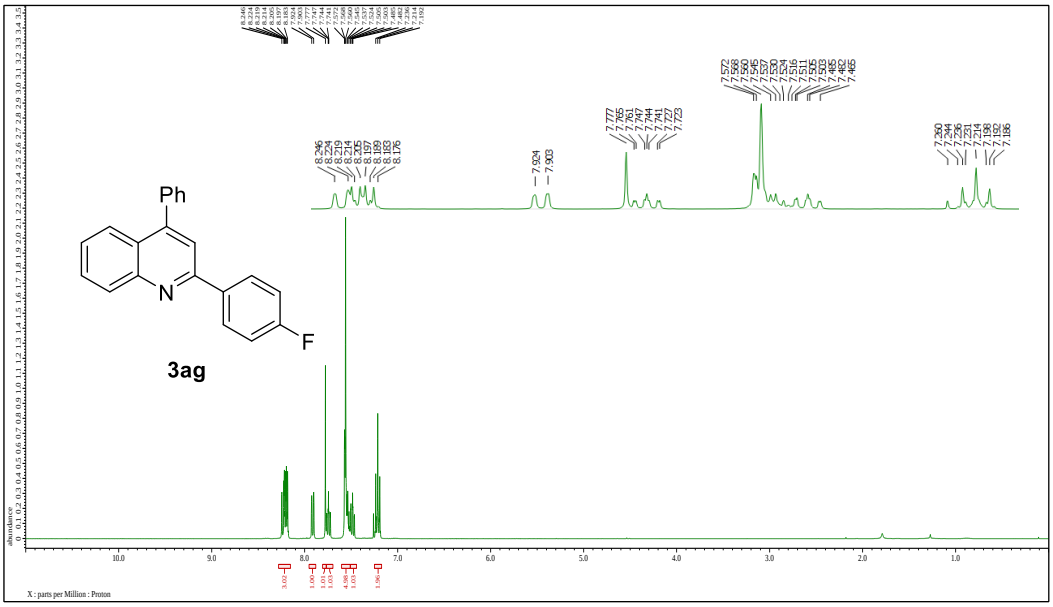
6af ^{1}H-NMR (400 MHz, $CDCl_3$)



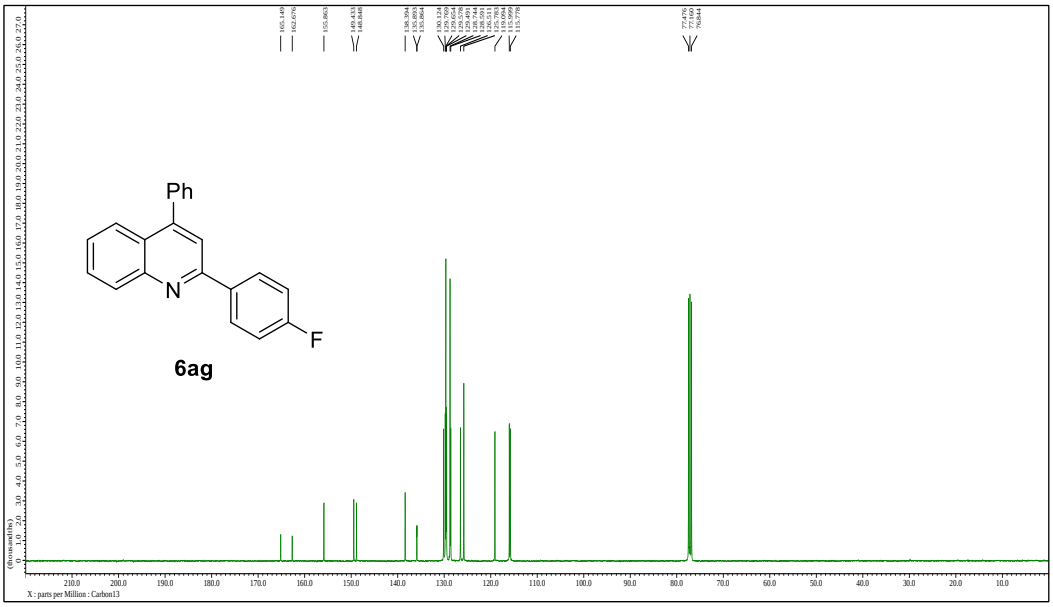
6af ^{13}C-NMR (100 MHz, $CDCl_3$)



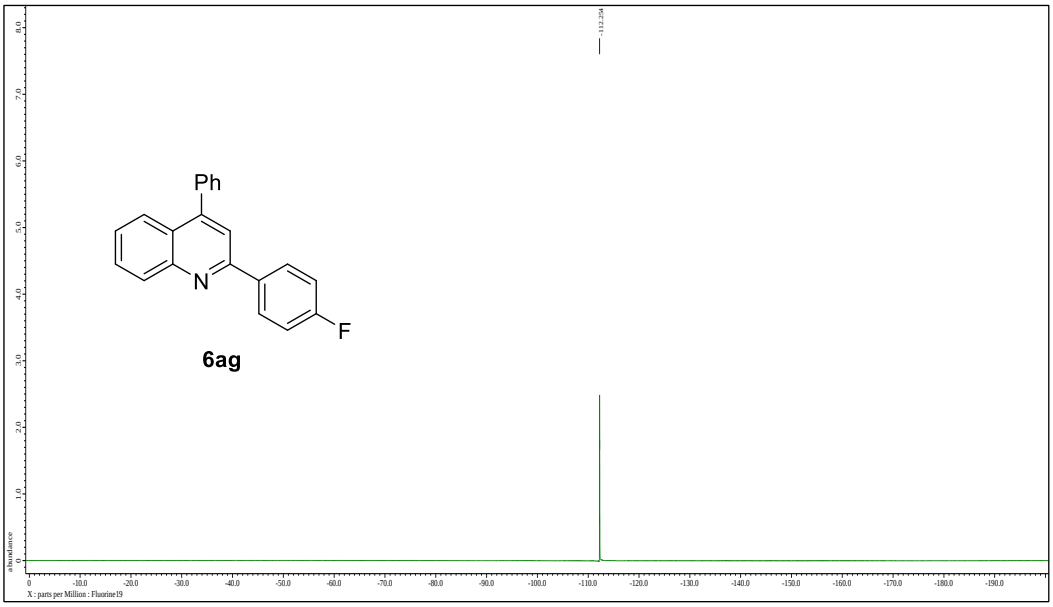
6ag ^{1}H-NMR (400 MHz, $CDCl_3$)



6ag ^{13}C-NMR (100 MHz, $CDCl_3$)

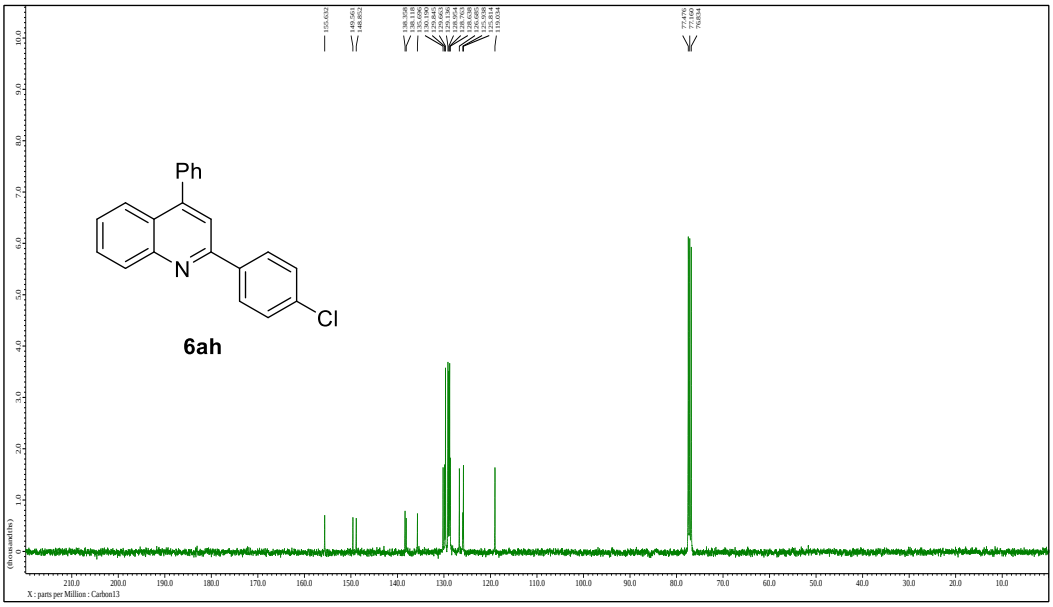


6ag ^{19}F-NMR (376 MHz, $CDCl_3$)

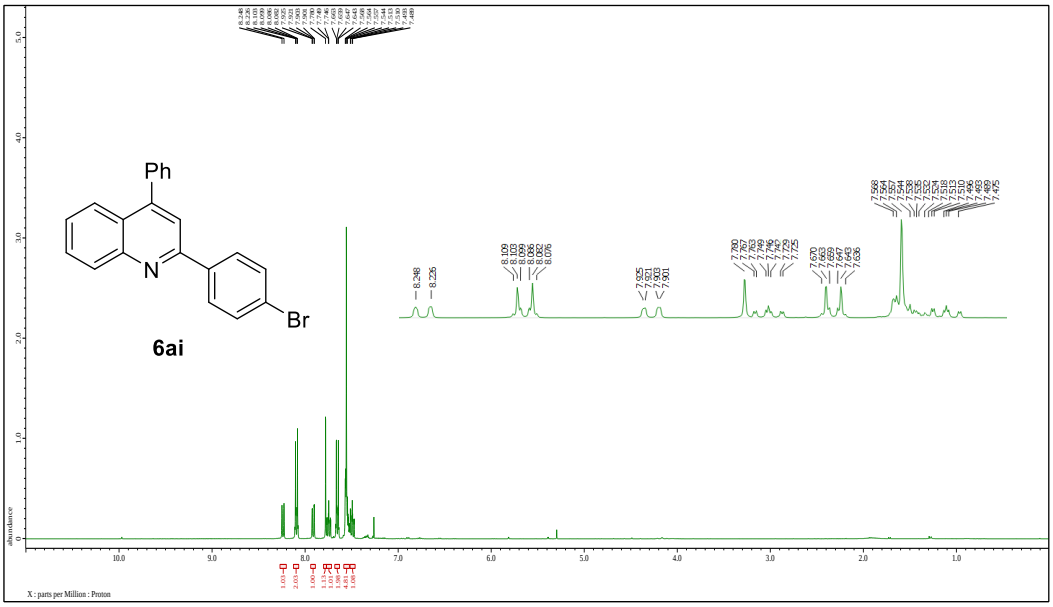


6ah ^{1}H-NMR (400 MHz, $CDCl_3$)

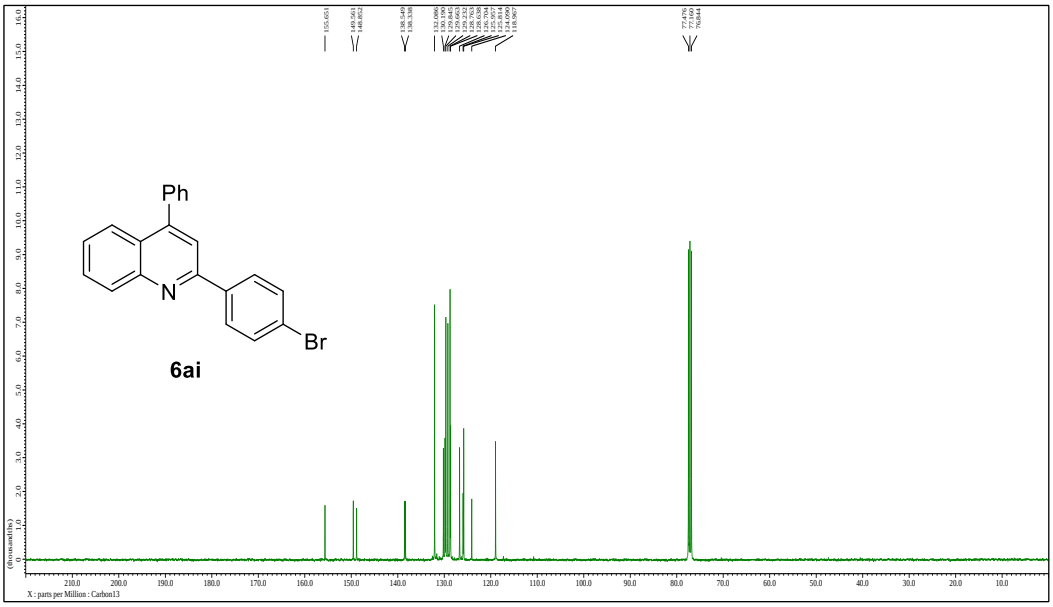
6ah ^{13}C-NMR (100 MHz, $CDCl_3$)



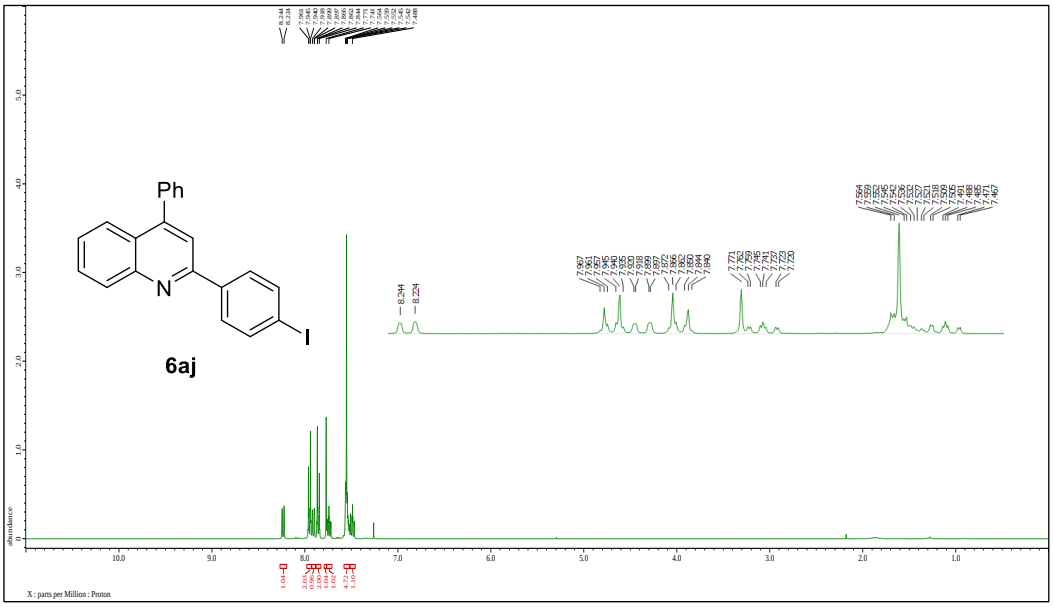
6ai ^{1}H-NMR (400 MHz, $CDCl_3$)



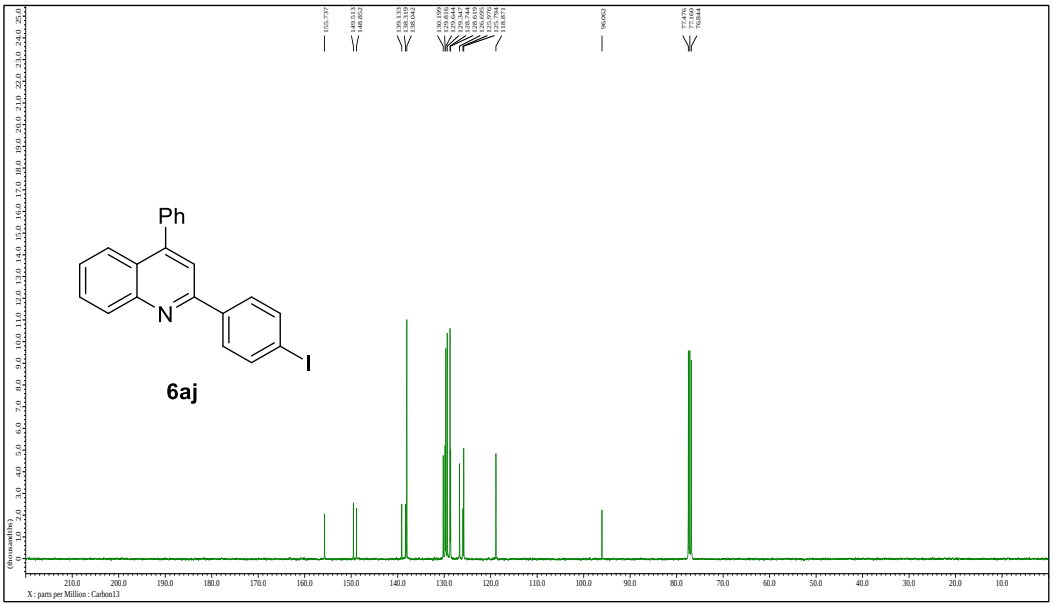
6ai ^{13}C-NMR (100 MHz, $CDCl_3$)



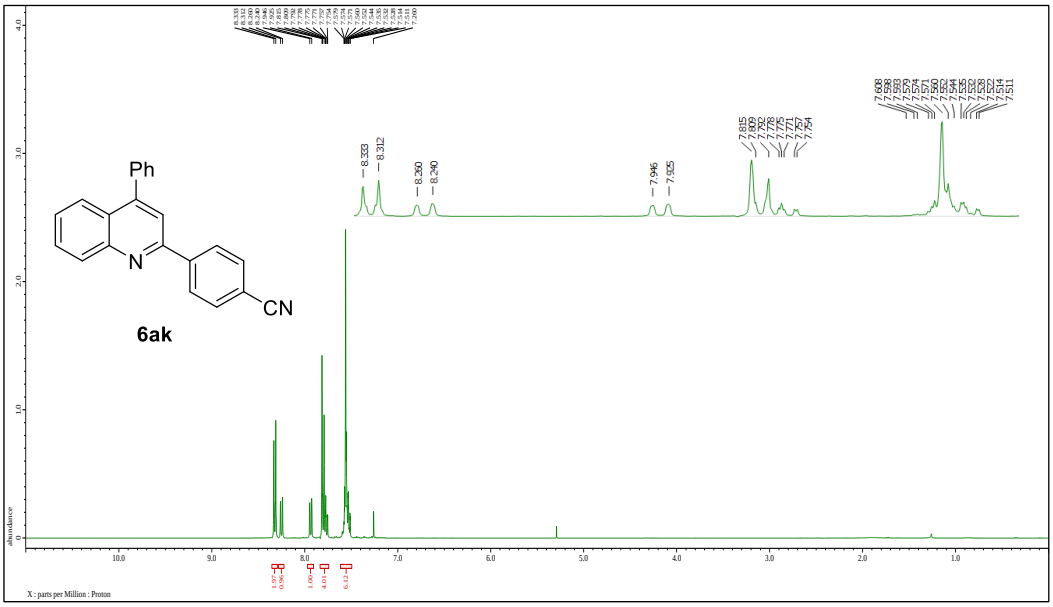
6aj ^{1}H-NMR (400 MHz, $CDCl_3$)



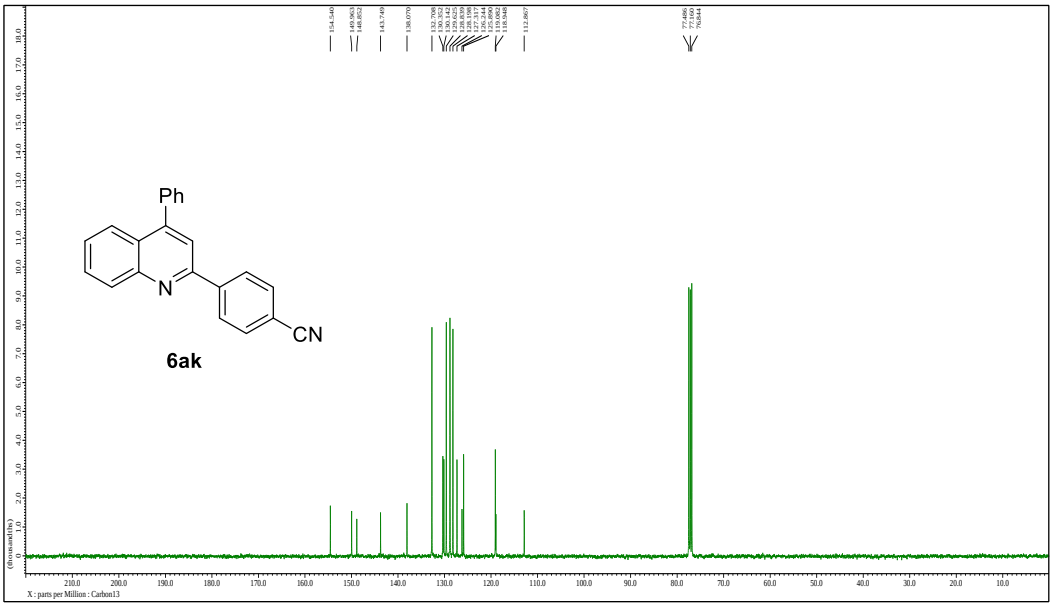
6aj ^{13}C-NMR (100 MHz, $CDCl_3$)



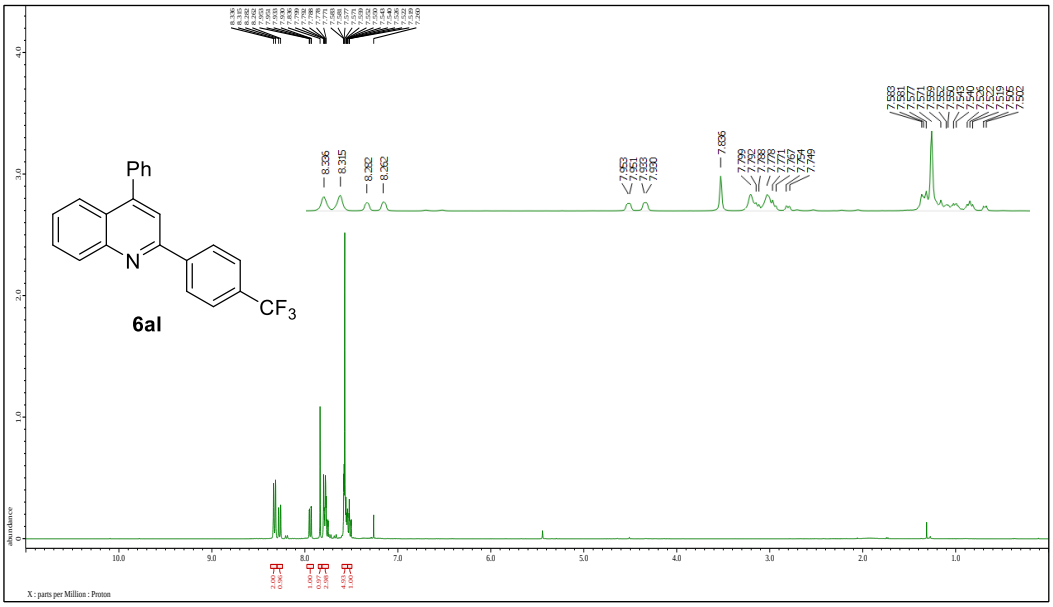
6ak ^{1}H-NMR (400 MHz, $CDCl_3$)



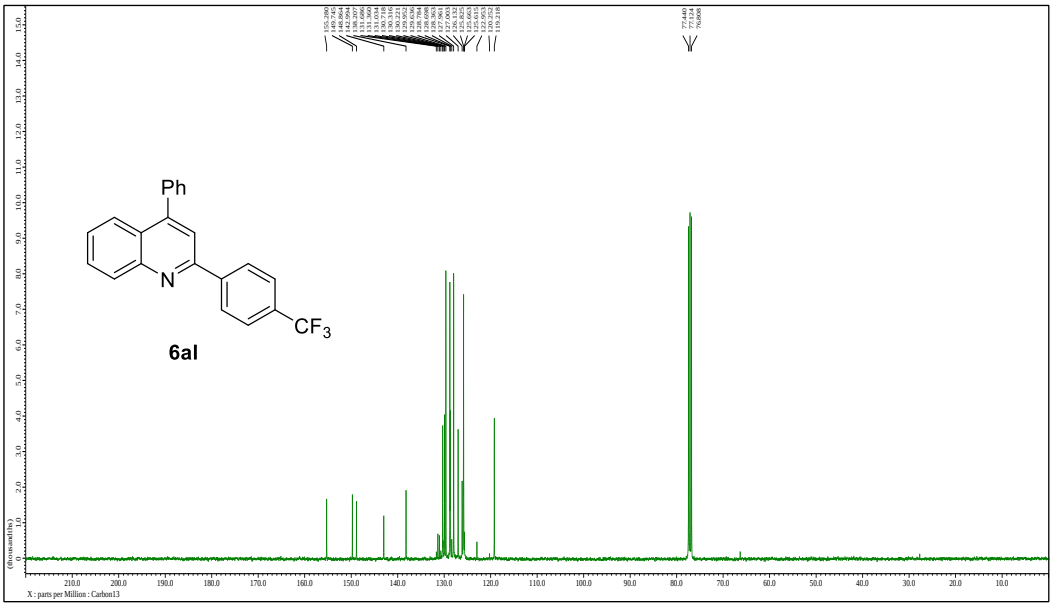
6ak ^{13}C-NMR (100 MHz, $CDCl_3$)



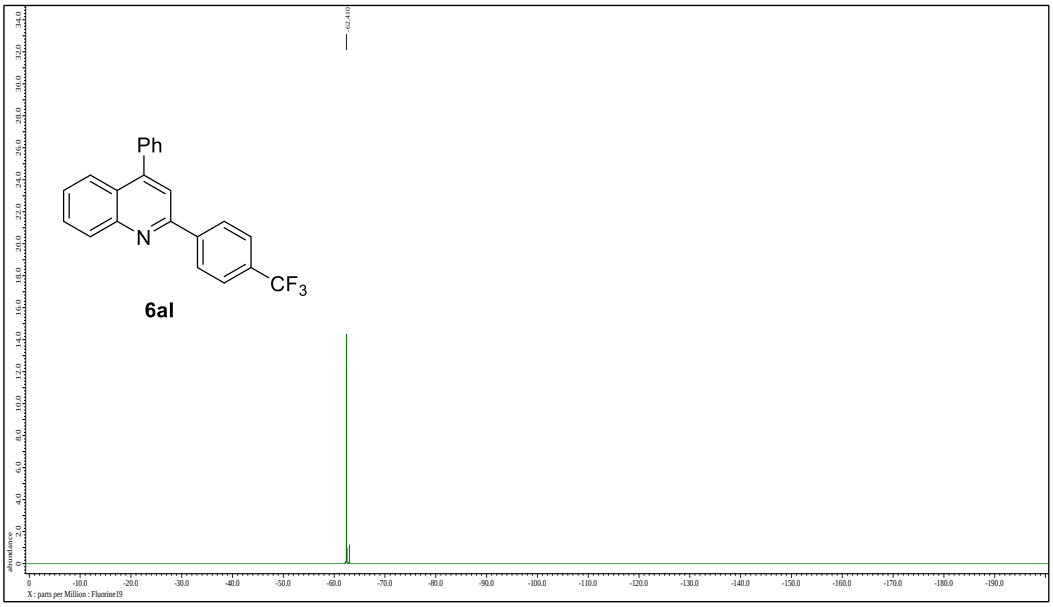
6al ^{1}H-NMR (400 MHz, $CDCl_3$)



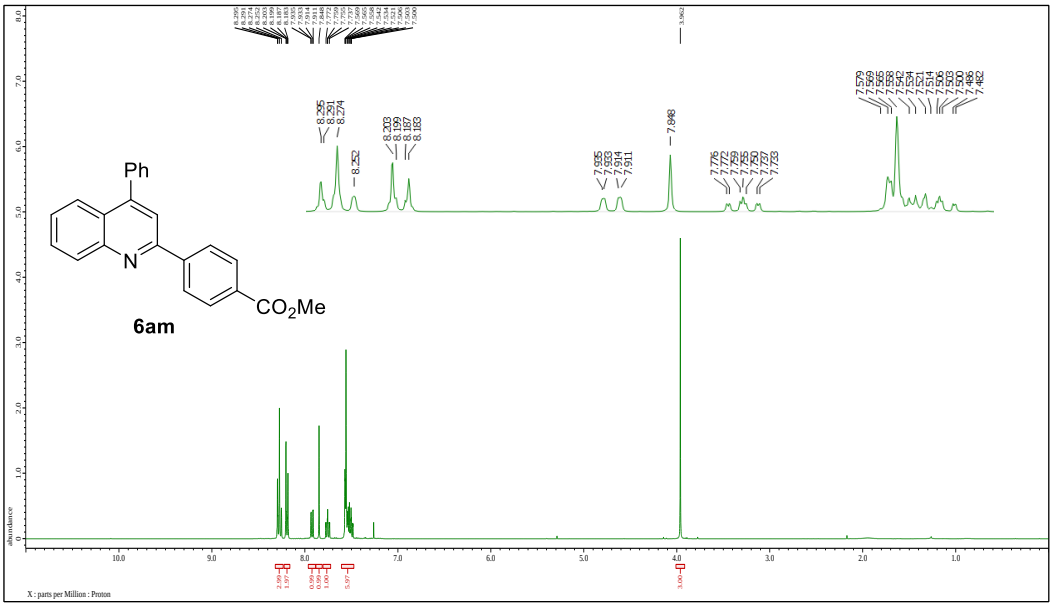
6al ^{13}C-NMR (100 MHz, $CDCl_3$)



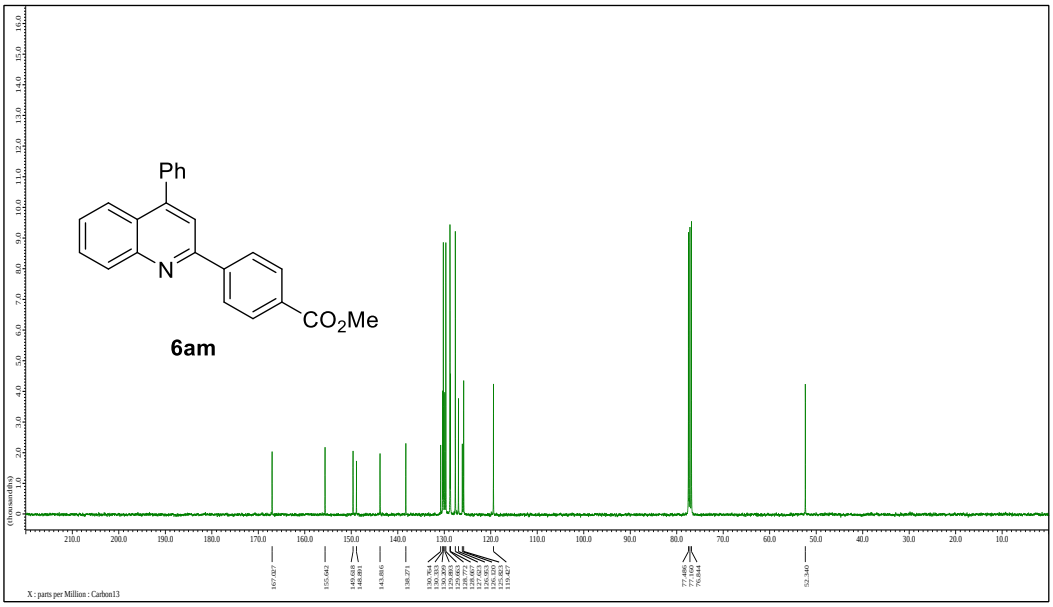
6al ^{19}F-NMR (376 MHz, $CDCl_3$)



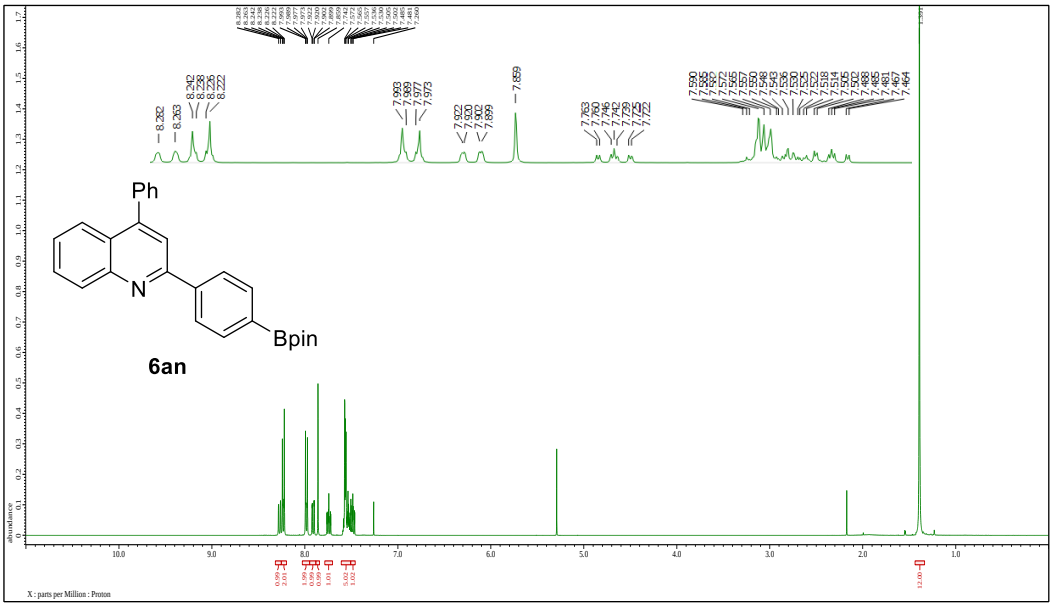
6am ^{1}H-NMR (400 MHz, $CDCl_3$)



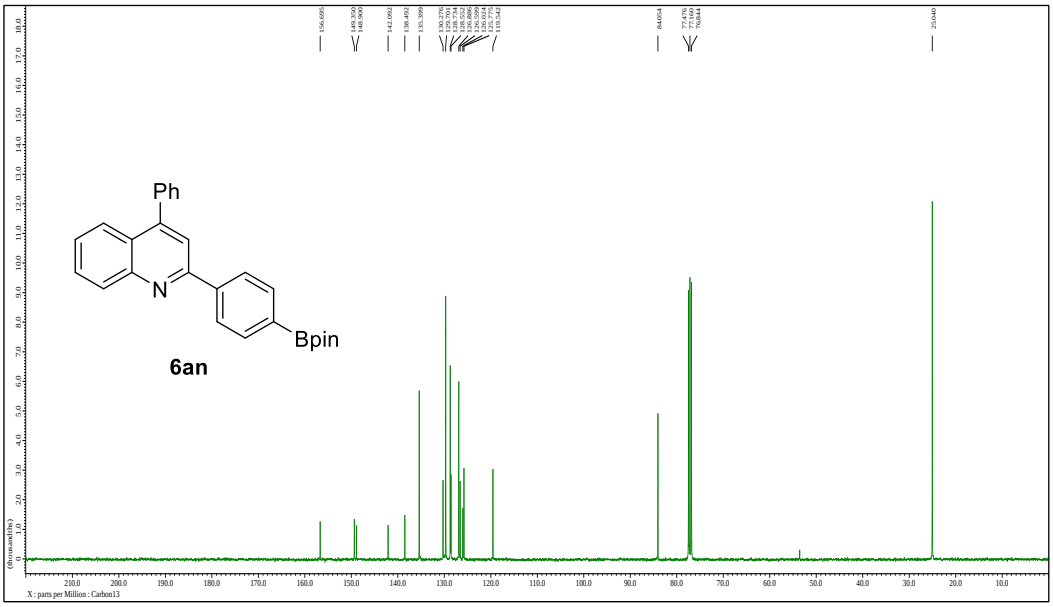
6am ^{13}C-NMR (100 MHz, $CDCl_3$)



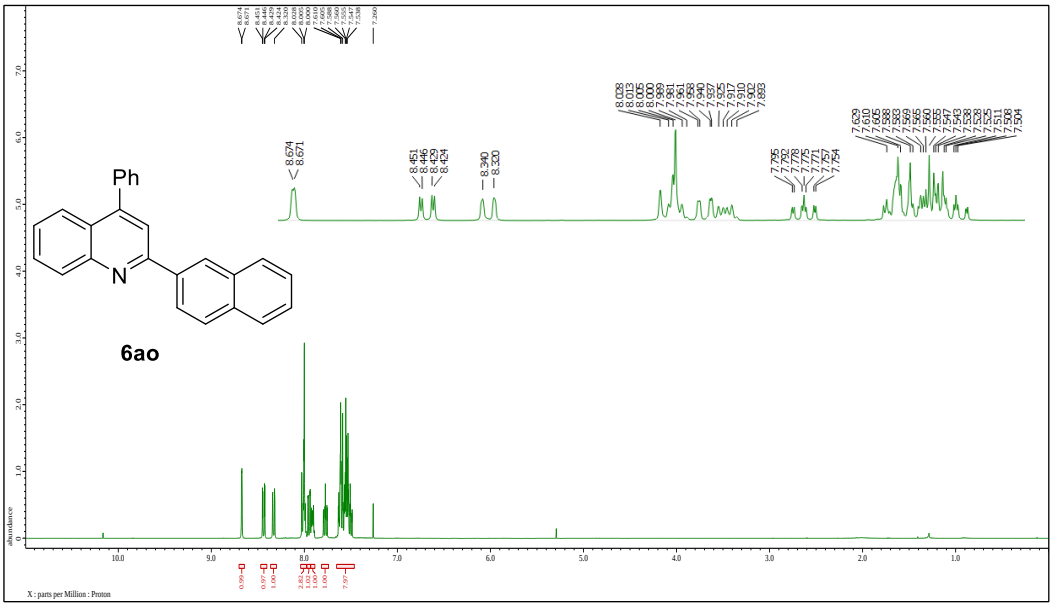
6an ^{1}H-NMR (400 MHz, $CDCl_3$)



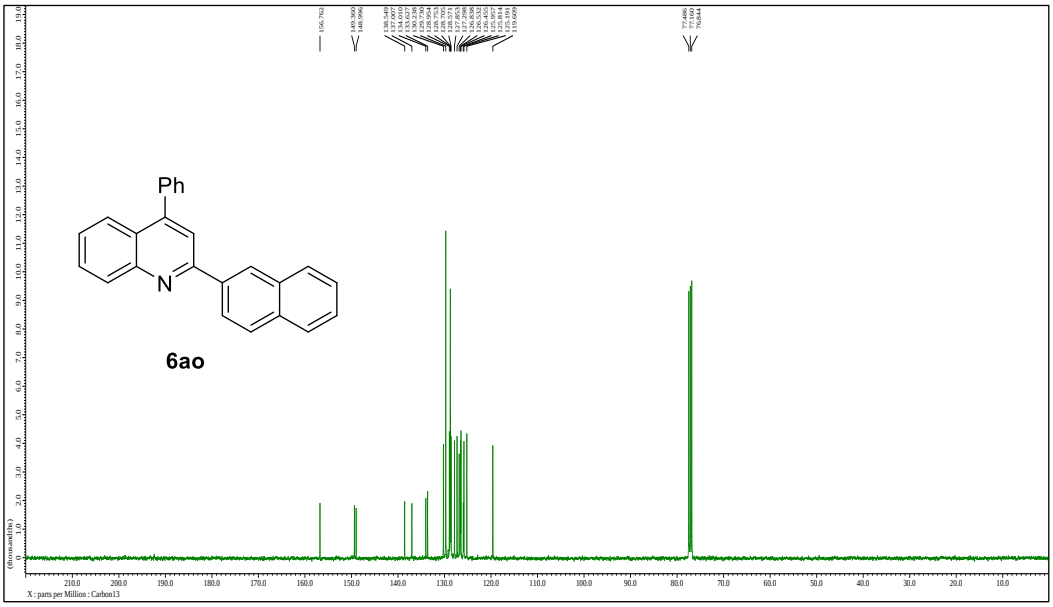
6an ^{13}C-NM (100 MHz, $CDCl_3$)



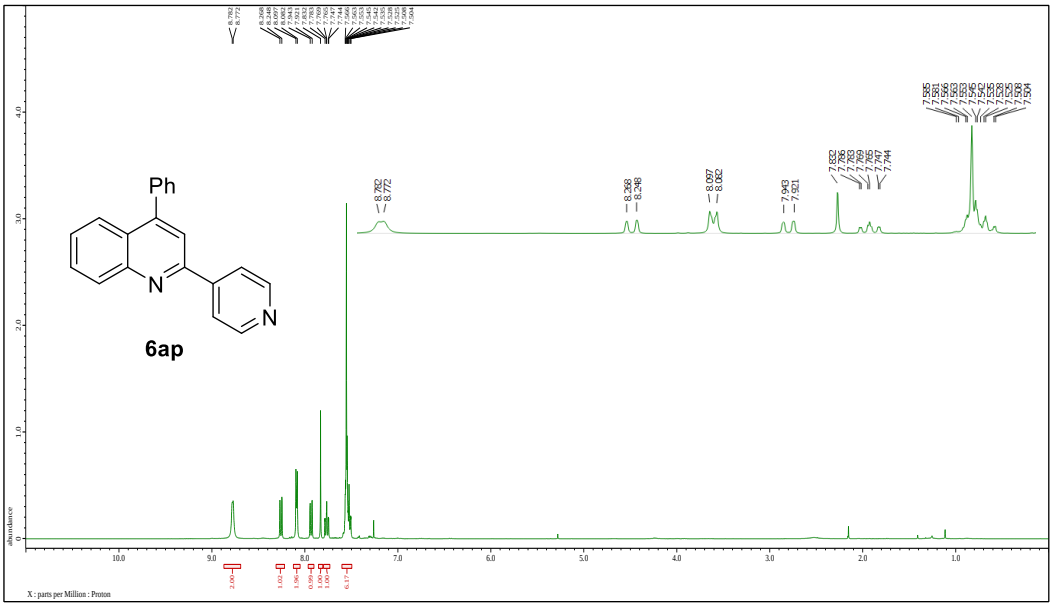
6ao ^{1}H-NMR (400 MHz, $CDCl_3$)



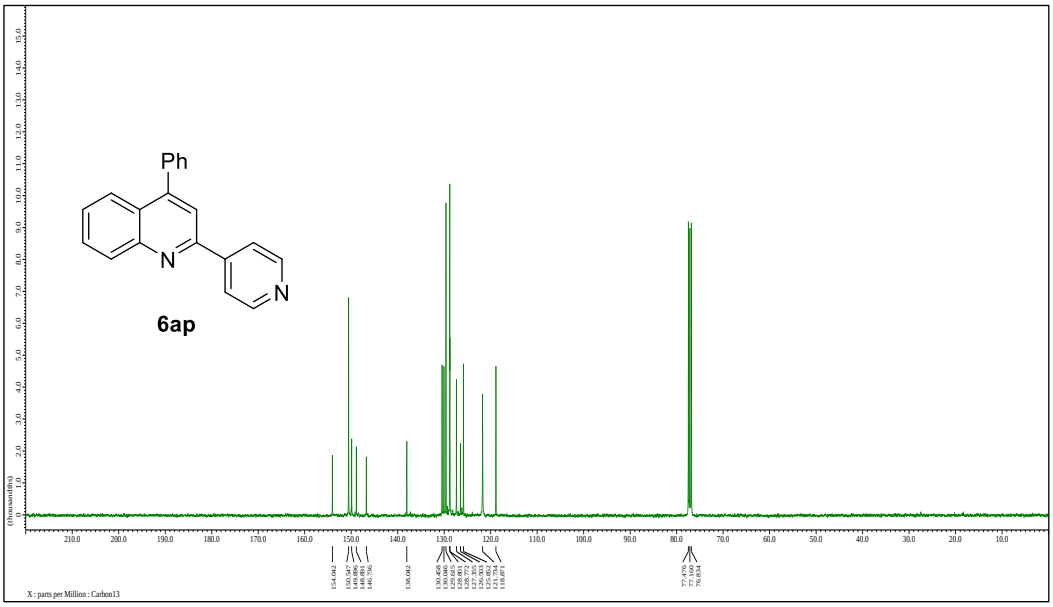
6ao ^{13}C-NMR (100 MHz, $CDCl_3$)



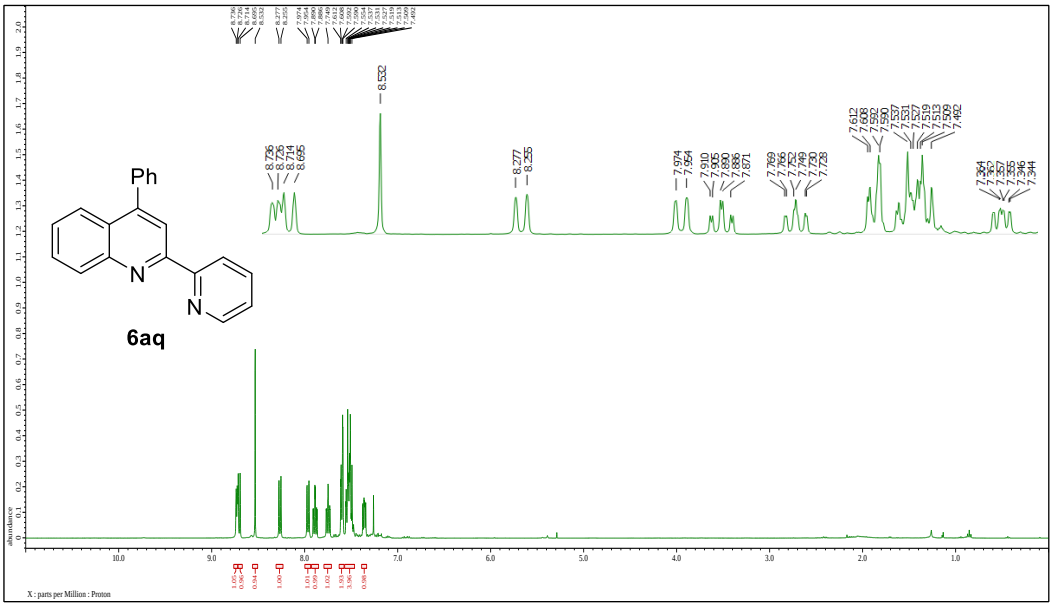
6ap ^{1}H-NMR (400 MHz, $CDCl_3$)



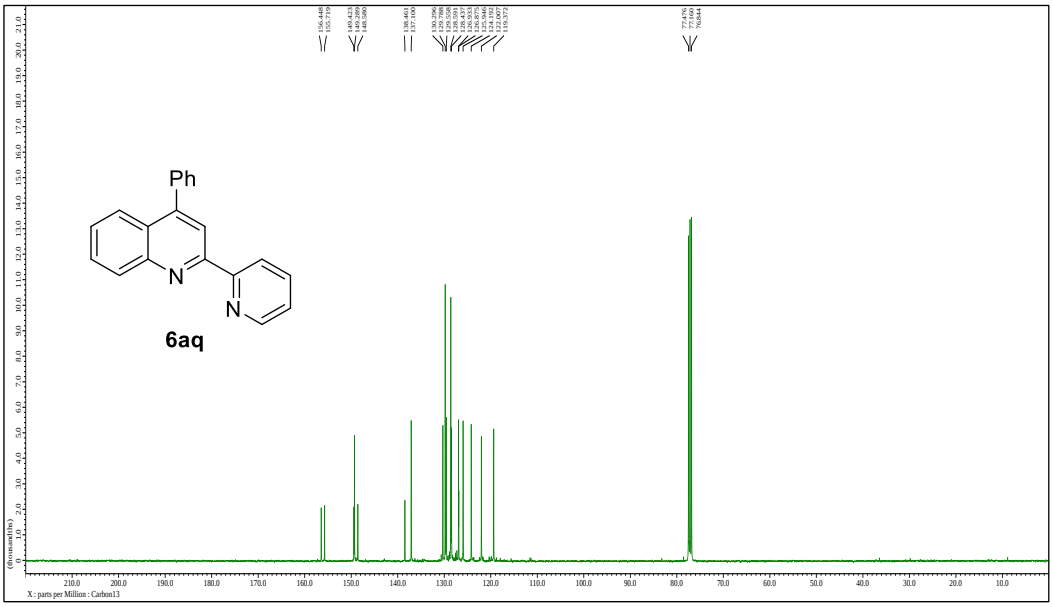
6ap ^{13}C-NMR (100 MHz, $CDCl_3$)



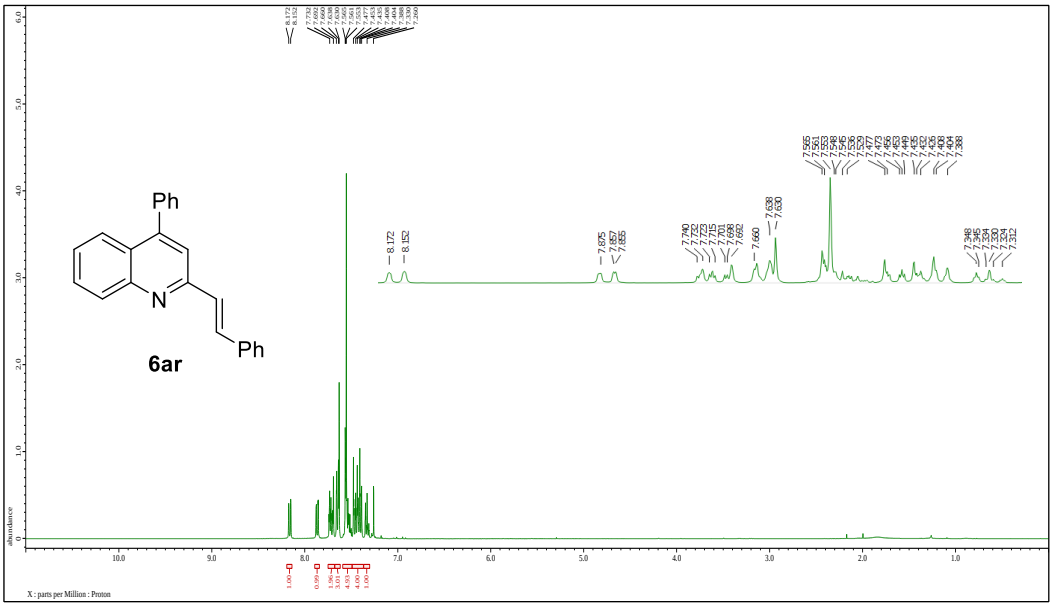
6aq ^{1}H-NMR (400 MHz, $CDCl_3$)



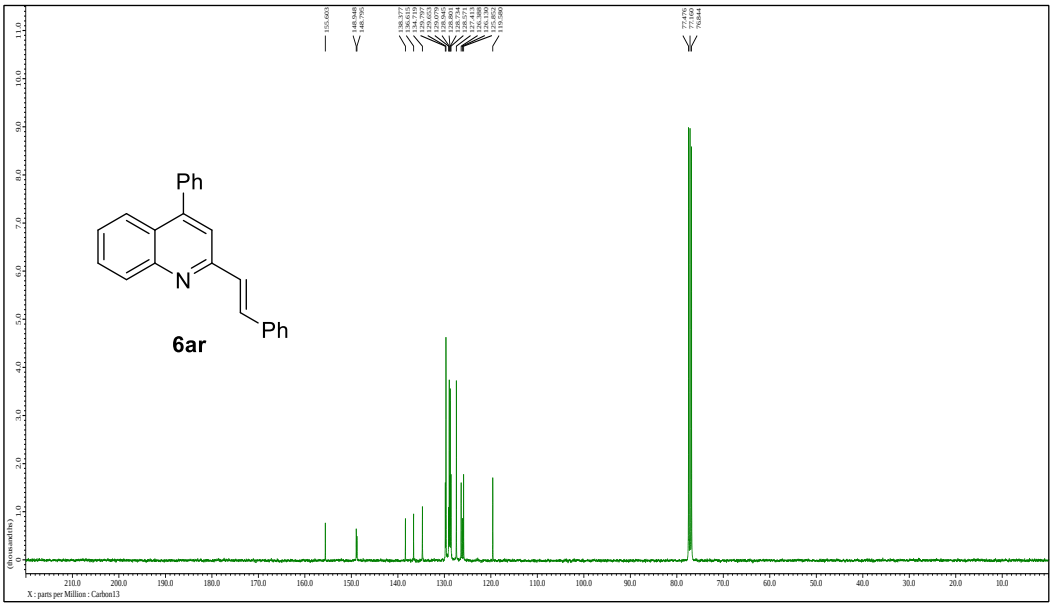
6aq ^{13}C-NMR (100 MHz, $CDCl_3$)



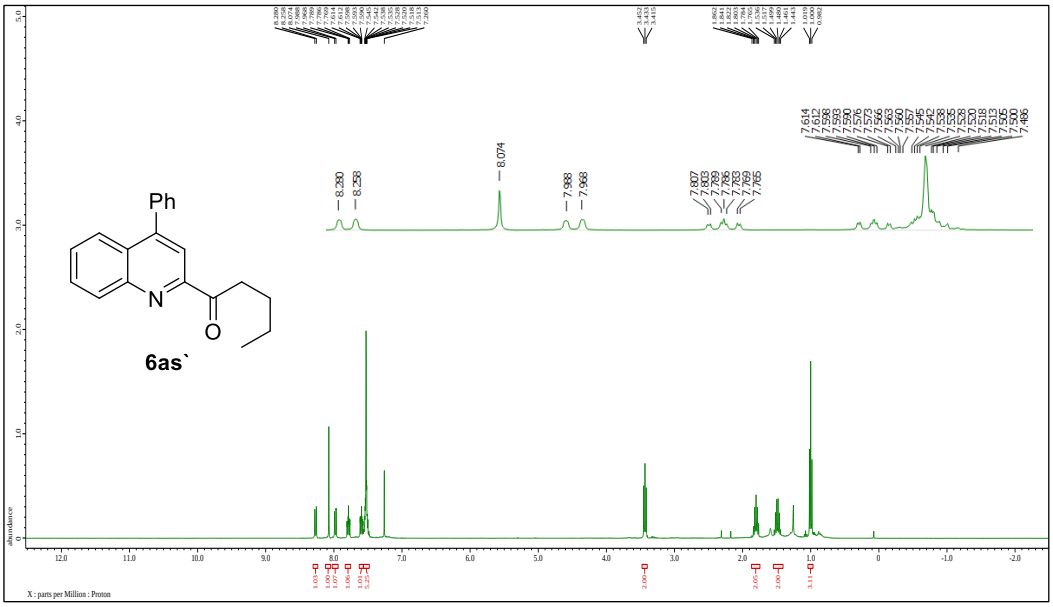
6ar ^{1}H-NMR (400 MHz, $CDCl_3$)



6ar ^{13}C-NMR (100 MHz, $CDCl_3$)

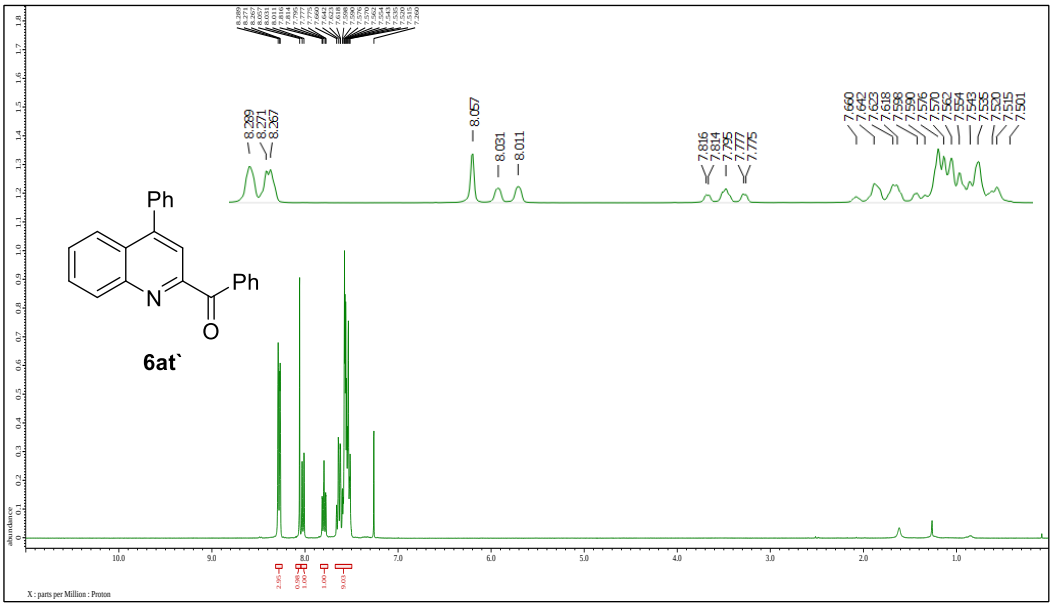


6as′ ^{1}H-NMR (400 MHz, $CDCl_3$)

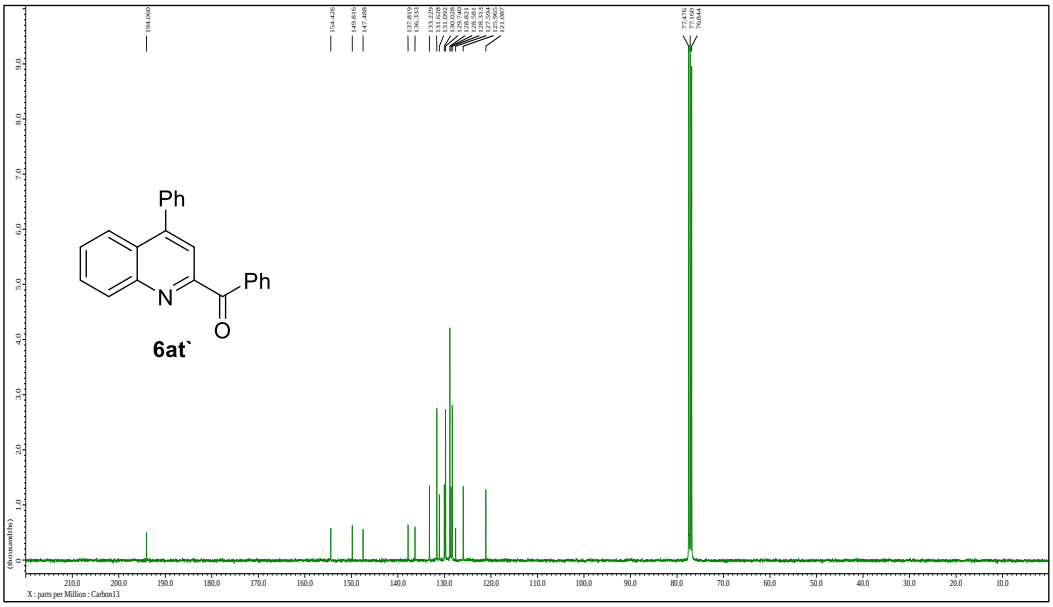


6as′ ^{13}C-NMR (100 MHz, $CDCl_3$)

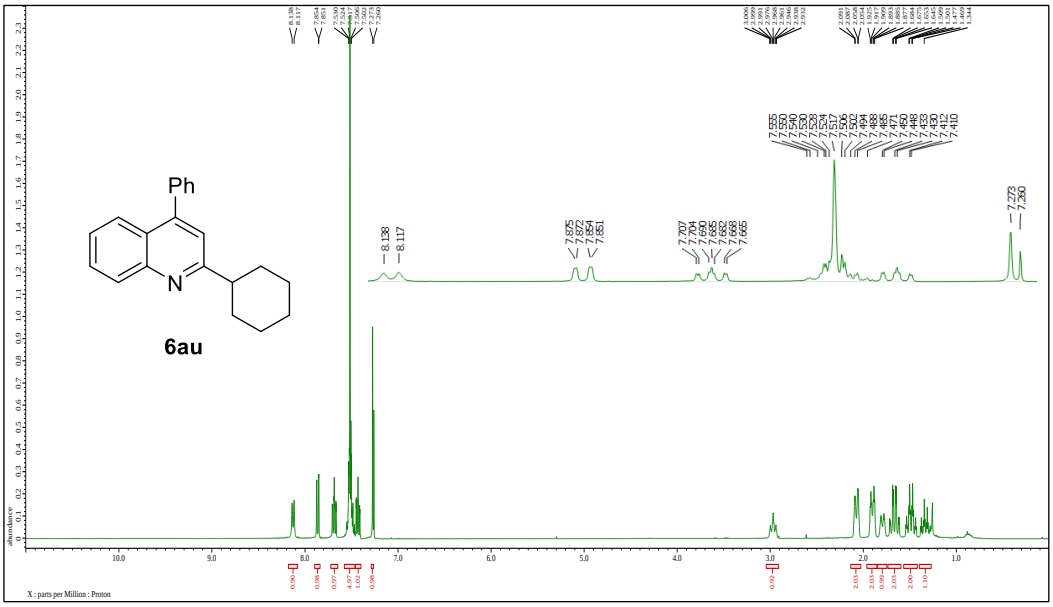
6at′ ^{1}H-NMR (400 MHz, $CDCl_3$)



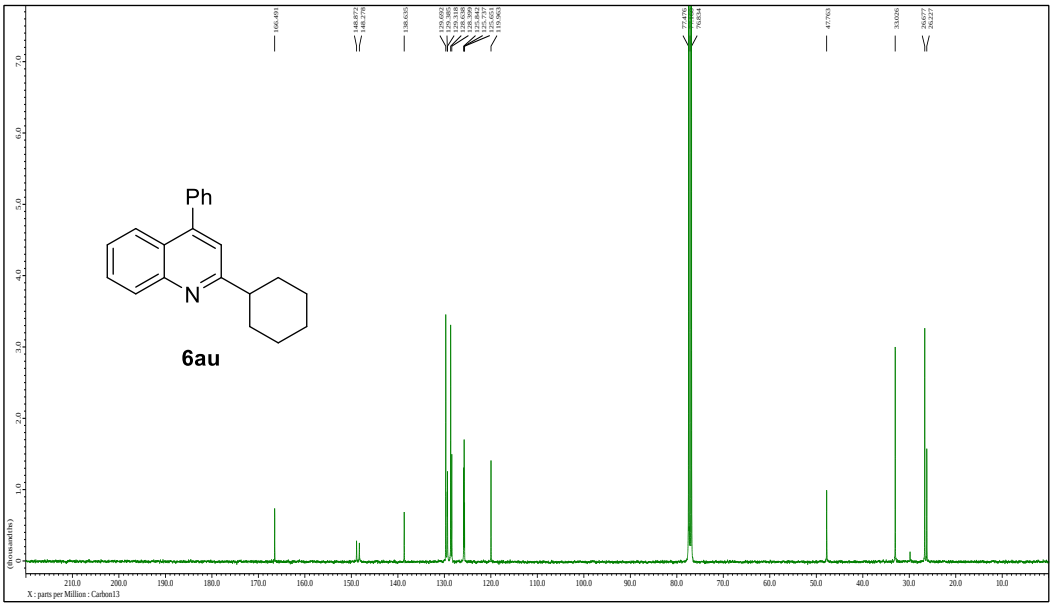
6at′ ^{13}C-NMR (100 MHz, $CDCl_3$)



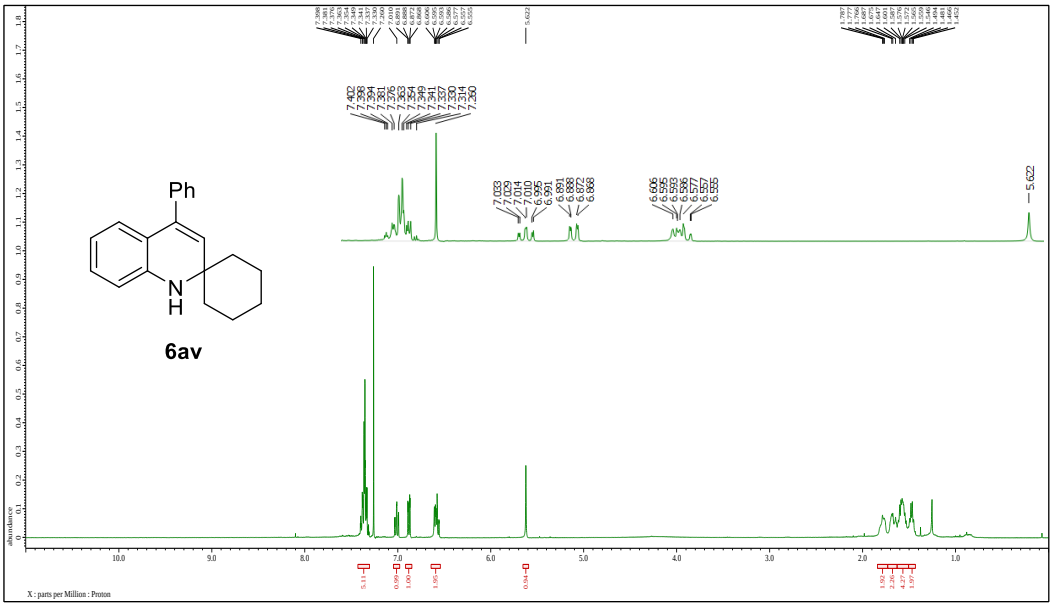
6au ^{1}H-NMR (400 MHz, $CDCl_3$)



6au ^{13}C-NMR (100 MHz, $CDCl_3$)



6av ^{1}H-NMR (400 MHz, $CDCl_3$)



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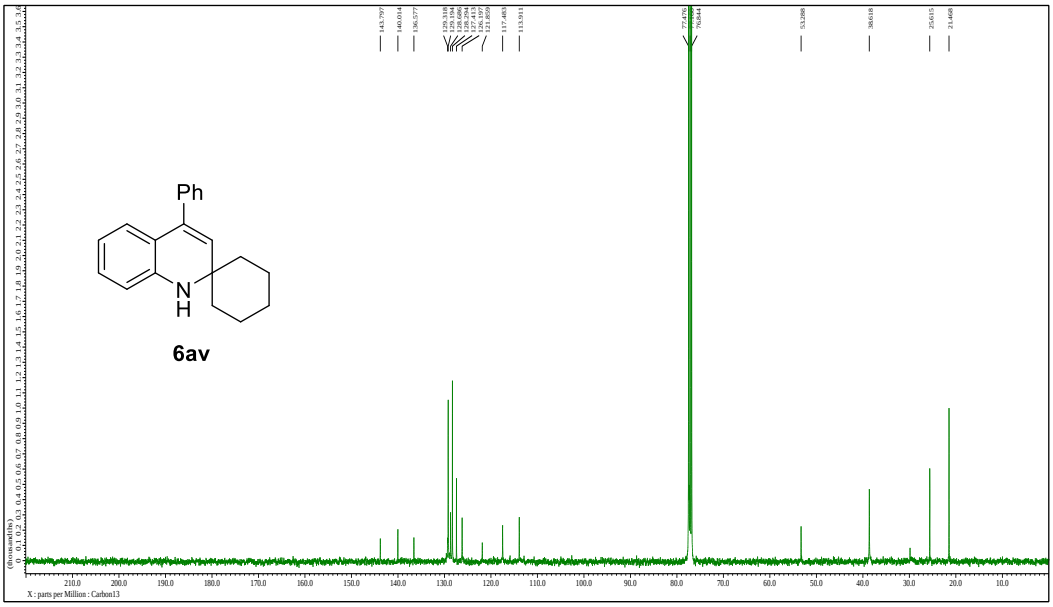
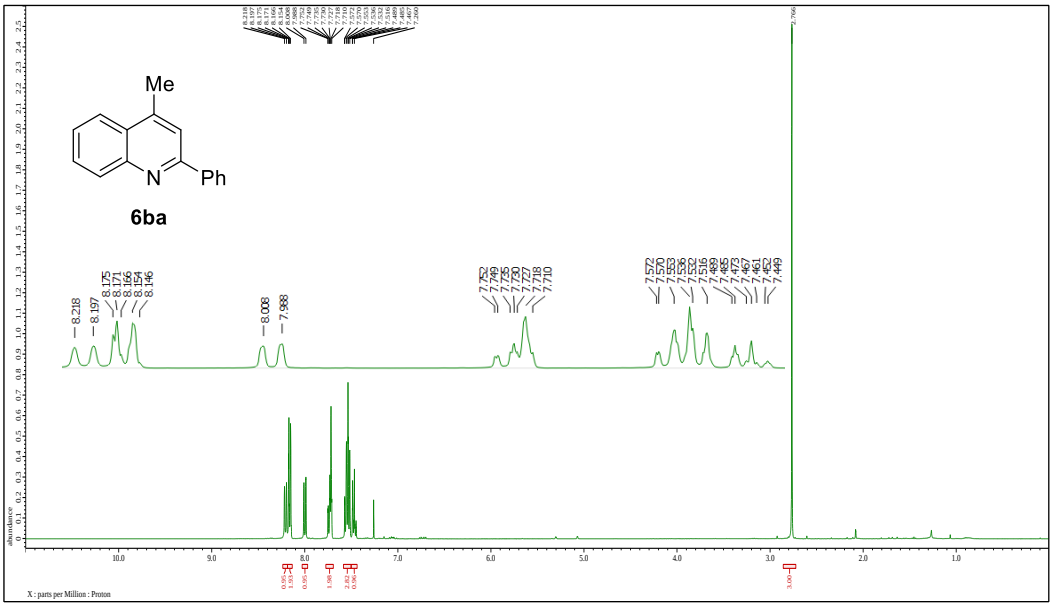
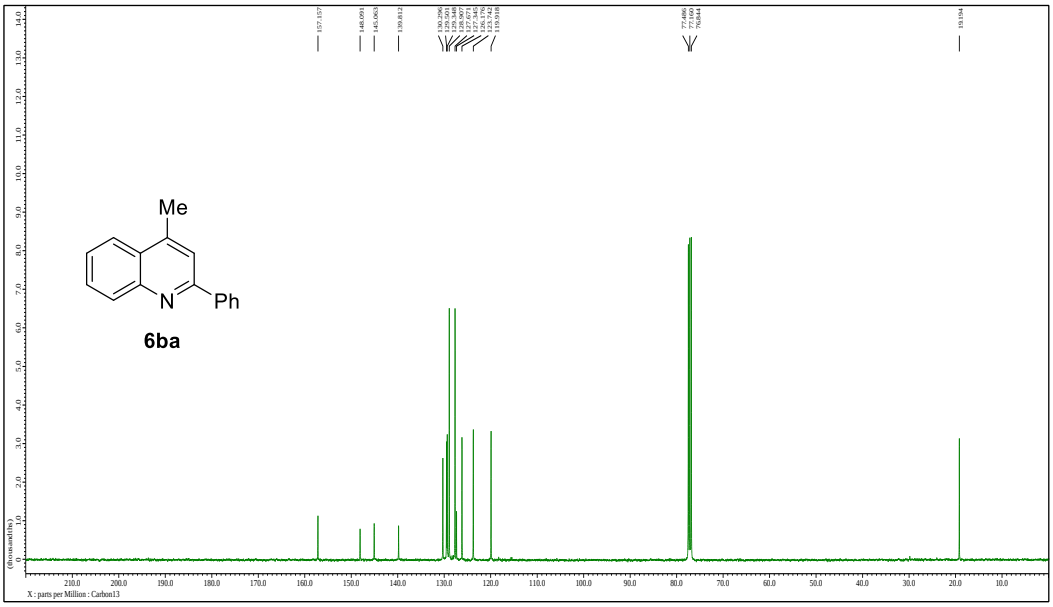


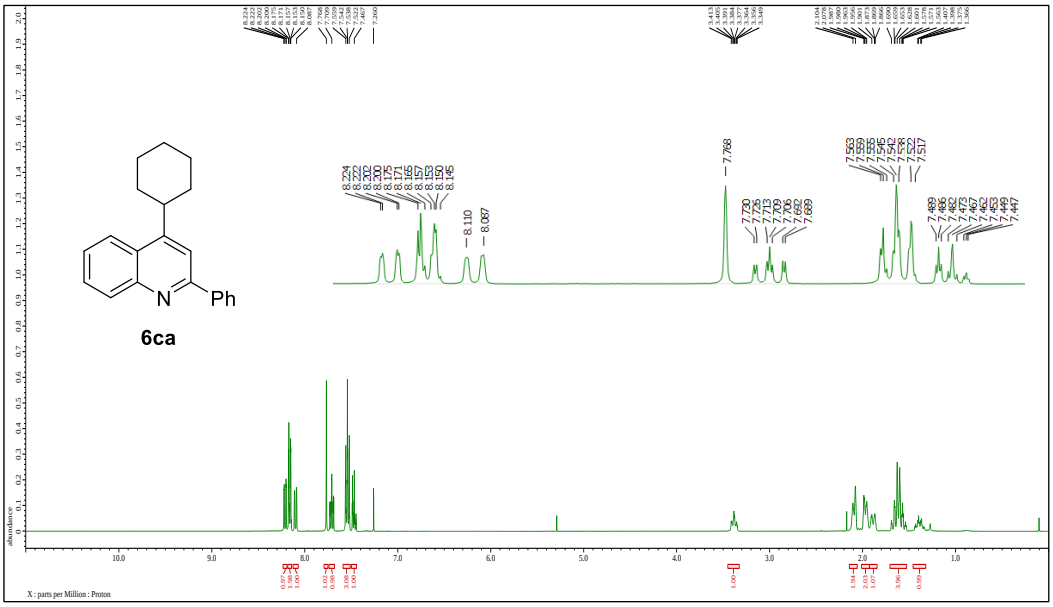
6ba ^{1}H-NMR (400 MHz, $CDCl_3$)



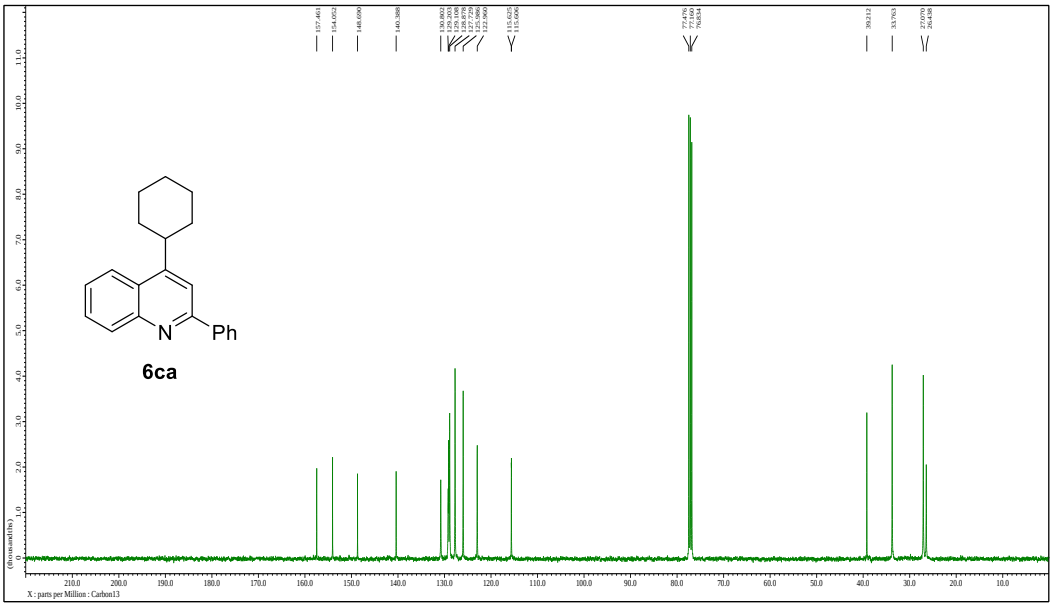
6ba ^{13}C-NMR (100 MHz, $CDCl_3$)



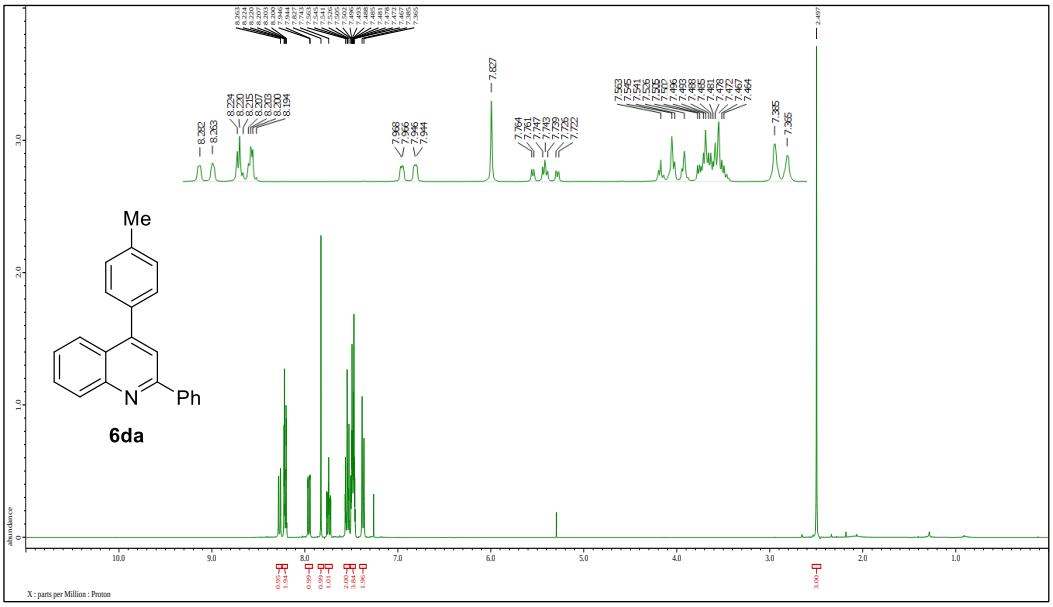
6ca ^{1}H-NMR (400 MHz, $CDCl_3$)



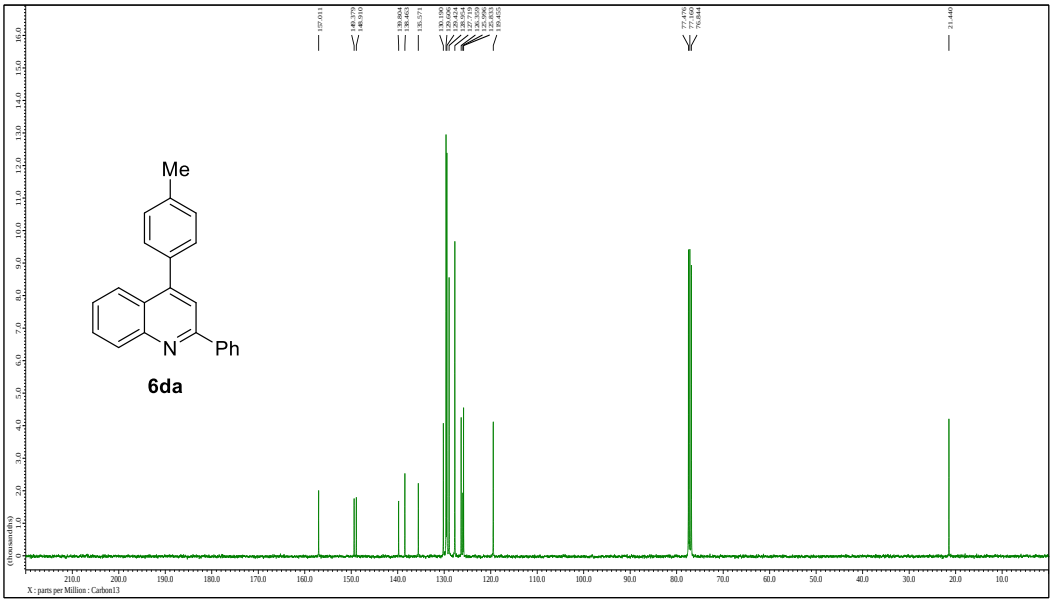
6ca ^{13}C-NMR (100 MHz, $CDCl_3$)



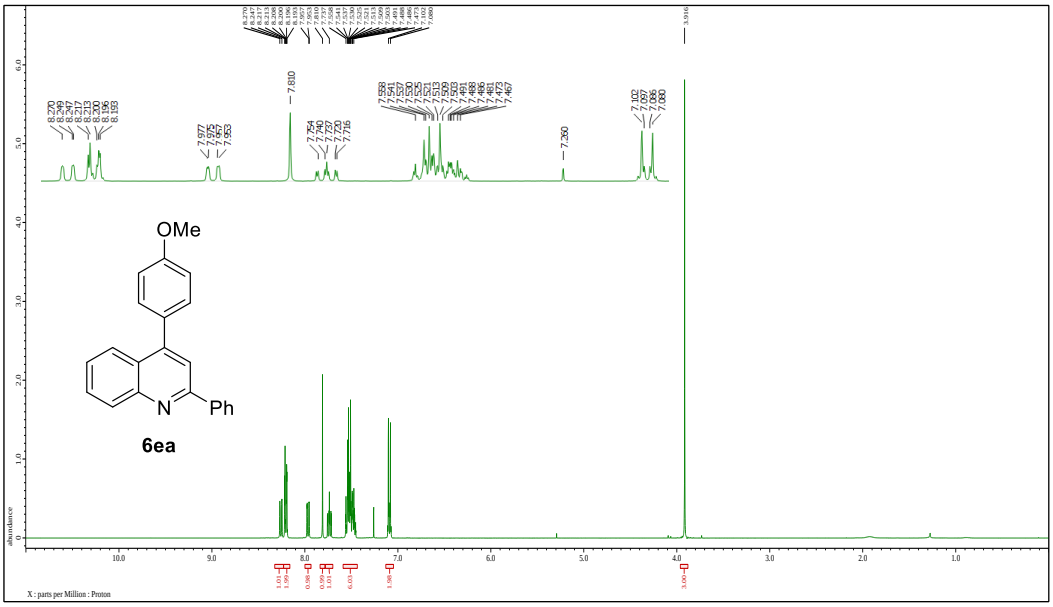
6da ^{1}H-NMR (400 MHz, $CDCl_3$)



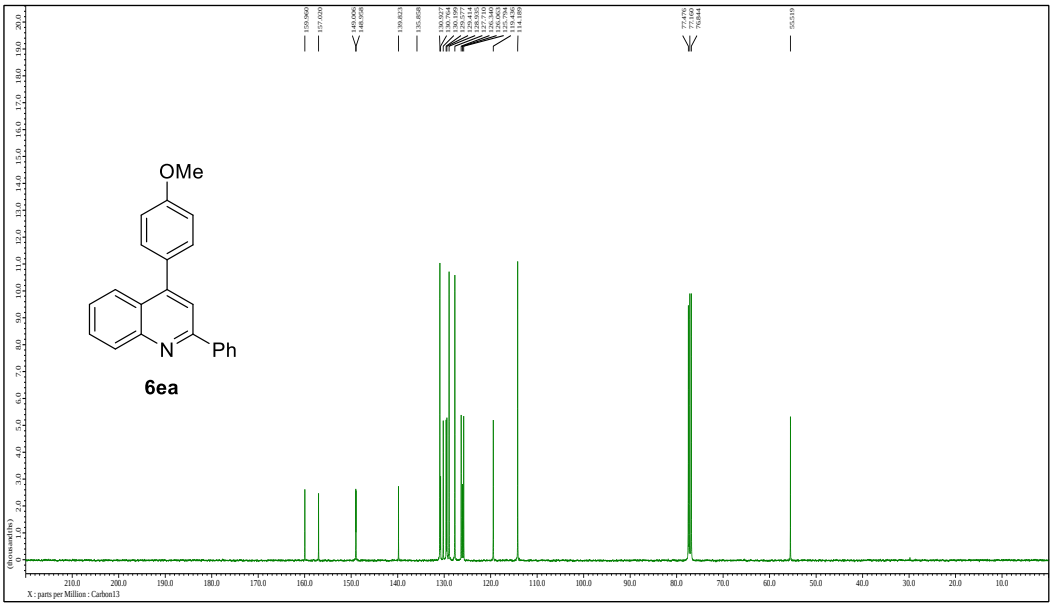
6da ^{13}C-NMR (100 MHz, $CDCl_3$)



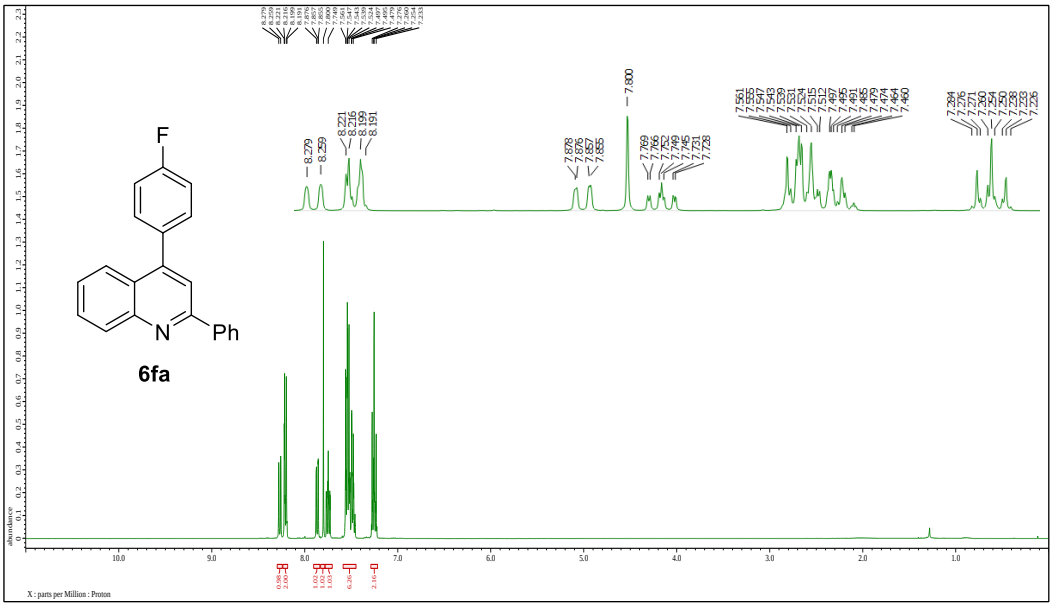
6ea ^{1}H-NMR (400 MHz, $CDCl_3$)



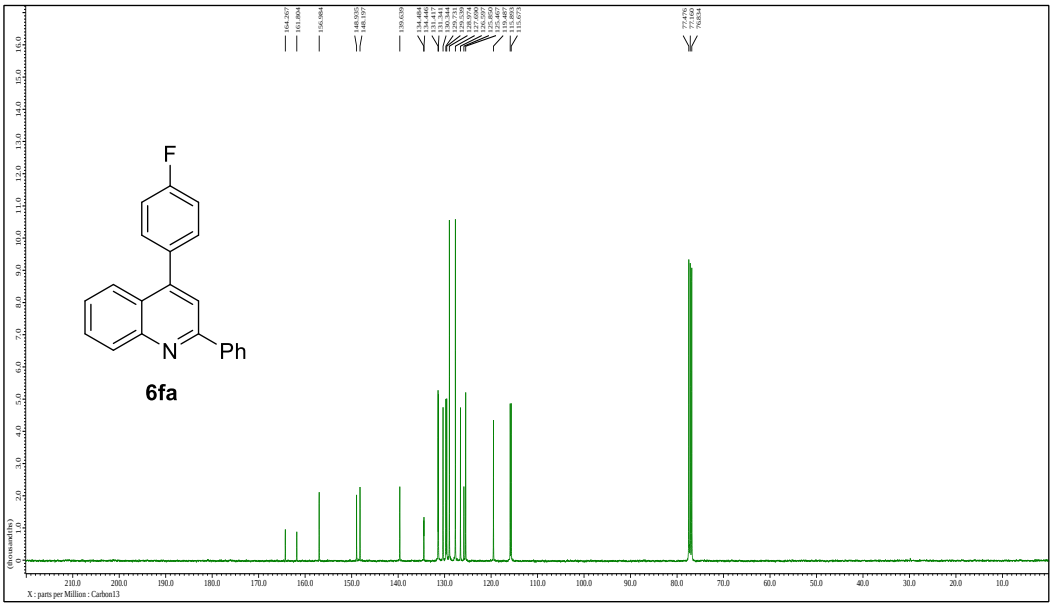
6ea ^{13}C-NMR (100 MHz, $CDCl_3$)



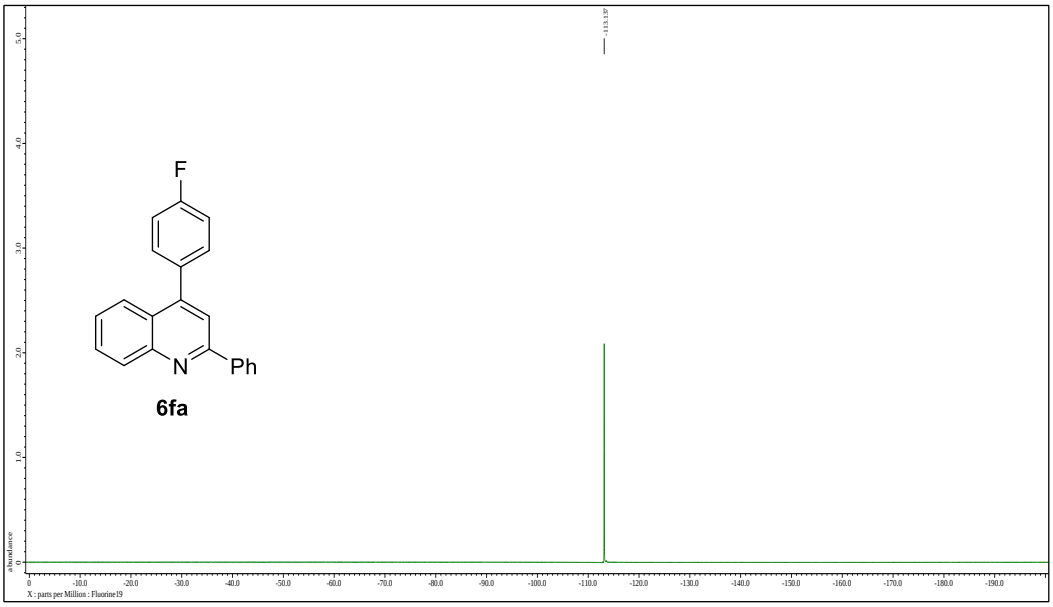
6fa ^{1}H-NMR (400 MHz, $CDCl_3$)



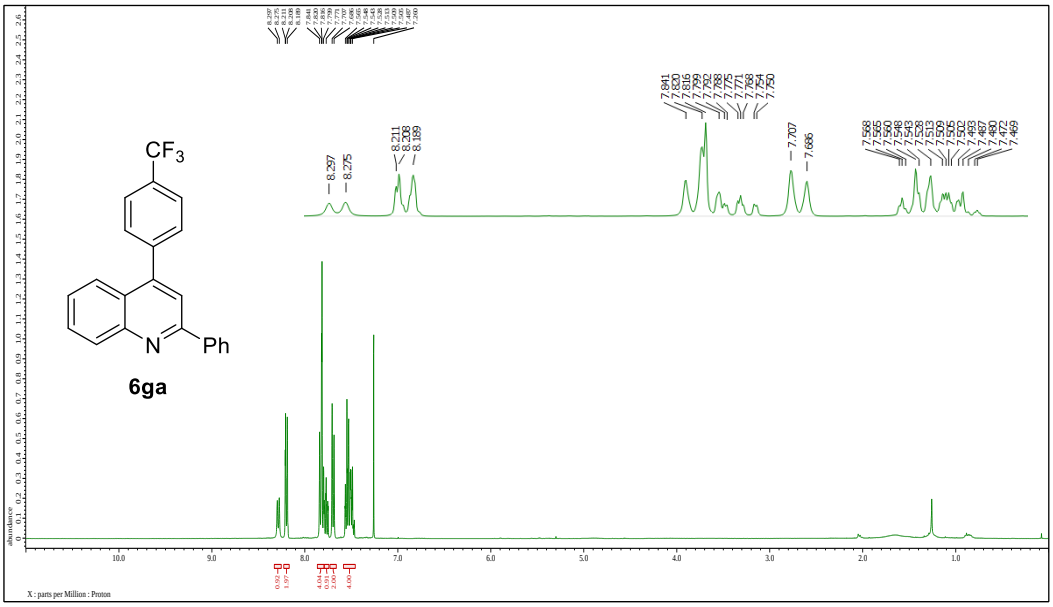
6fa ^{13}C-NMR (100 MHz, $CDCl_3$)



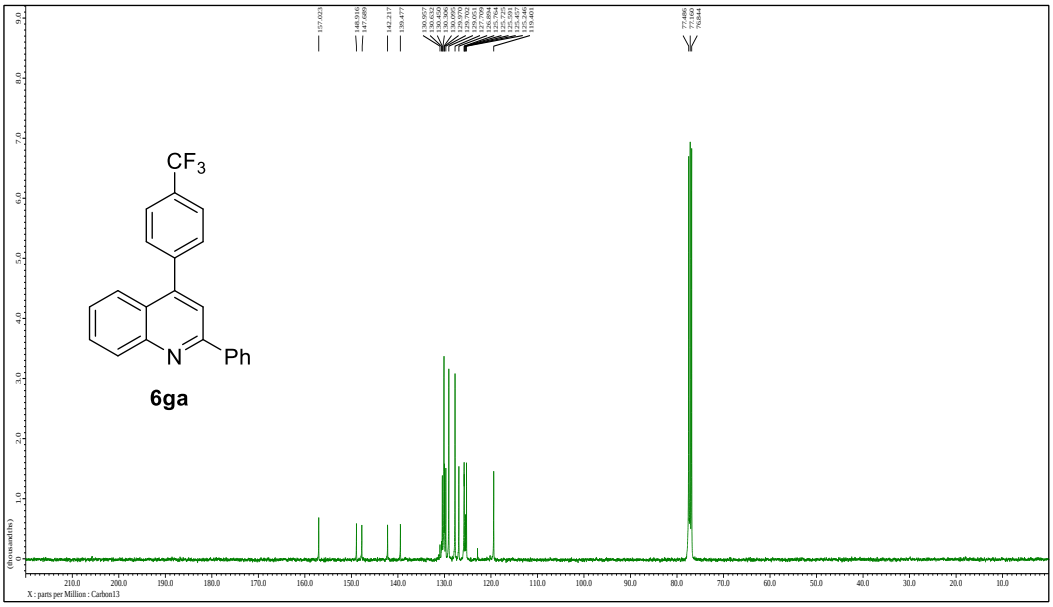
6fa ^{19}F-NMR (376 MHz, $CDCl_3$)



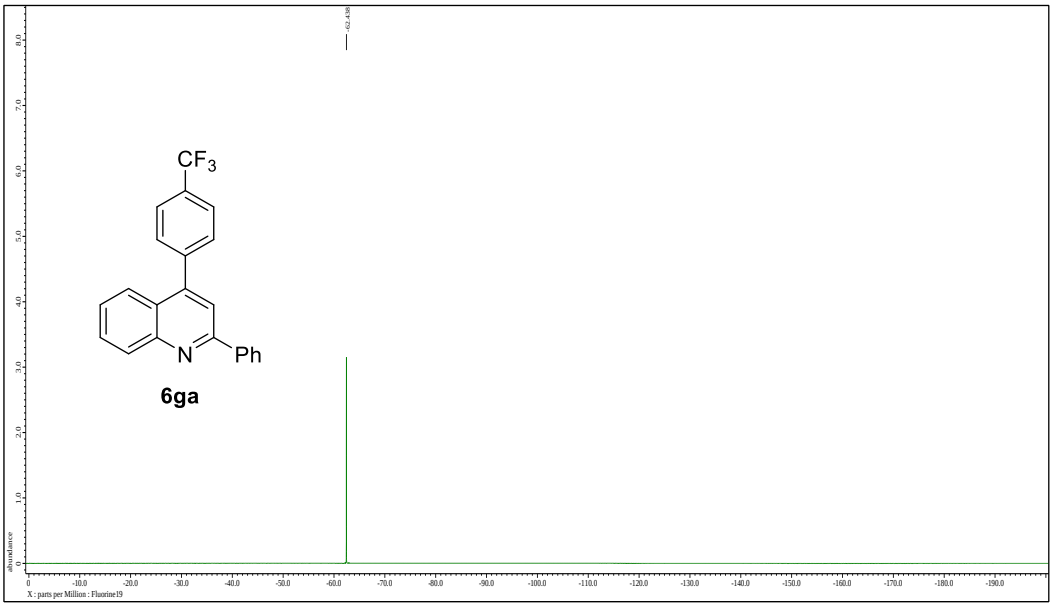
6ga ^{1}H-NMR (400 MHz, $CDCl_3$)



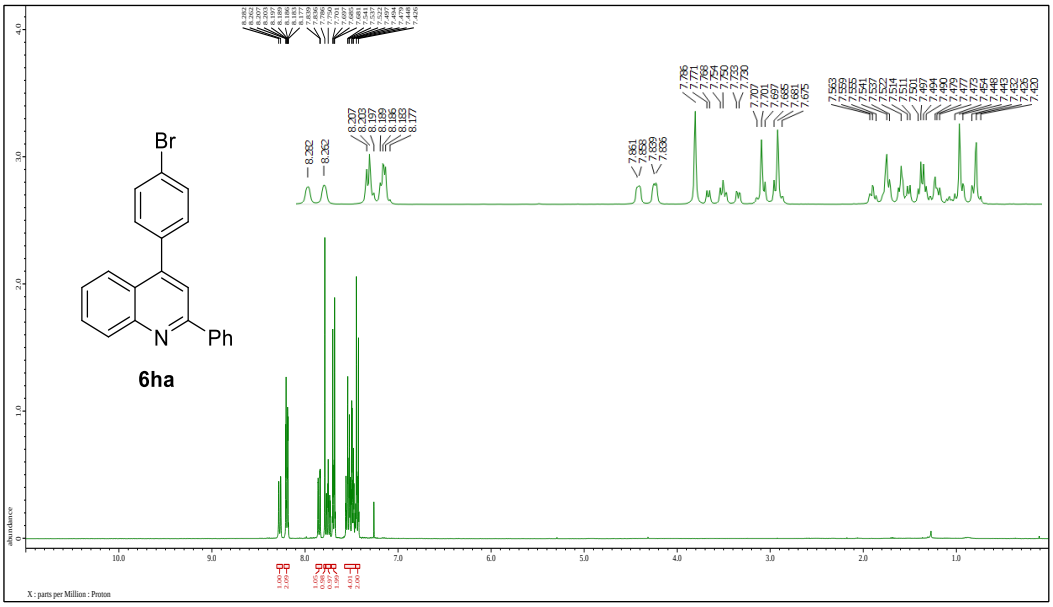
6ga ^{13}C-NMR (100 MHz, $CDCl_3$)



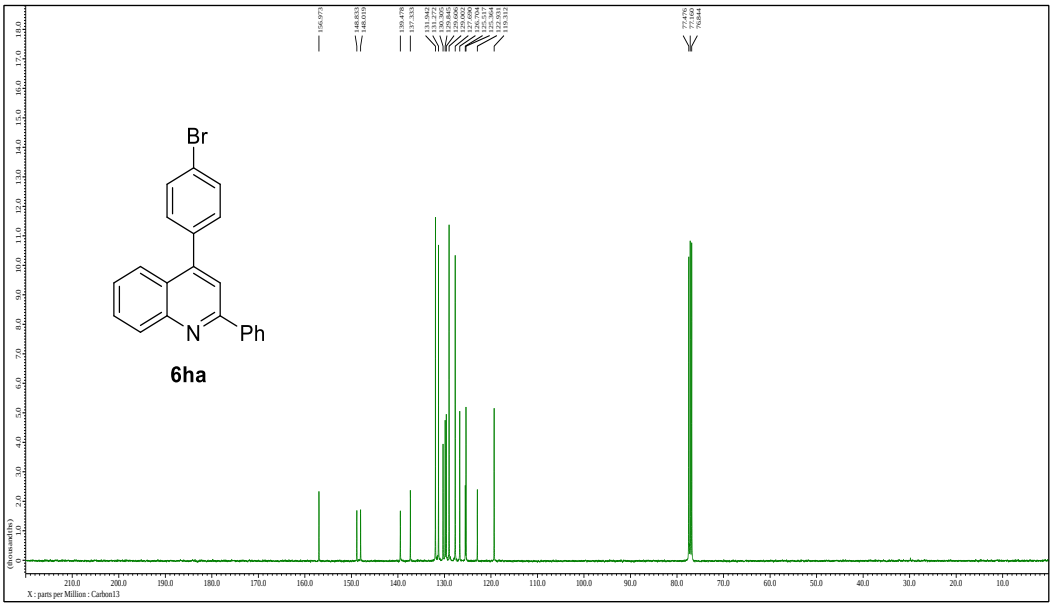
6ga ^{19}F-NMR (376 MHz, $CDCl_3$)



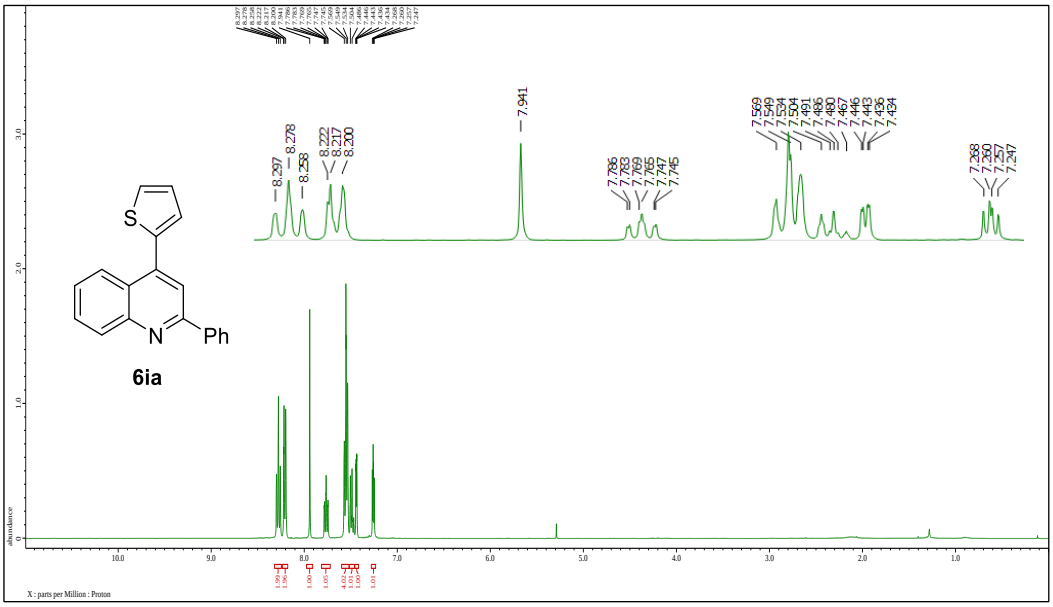
6ha ^{1}H-NMR (400 MHz, $CDCl_3$)



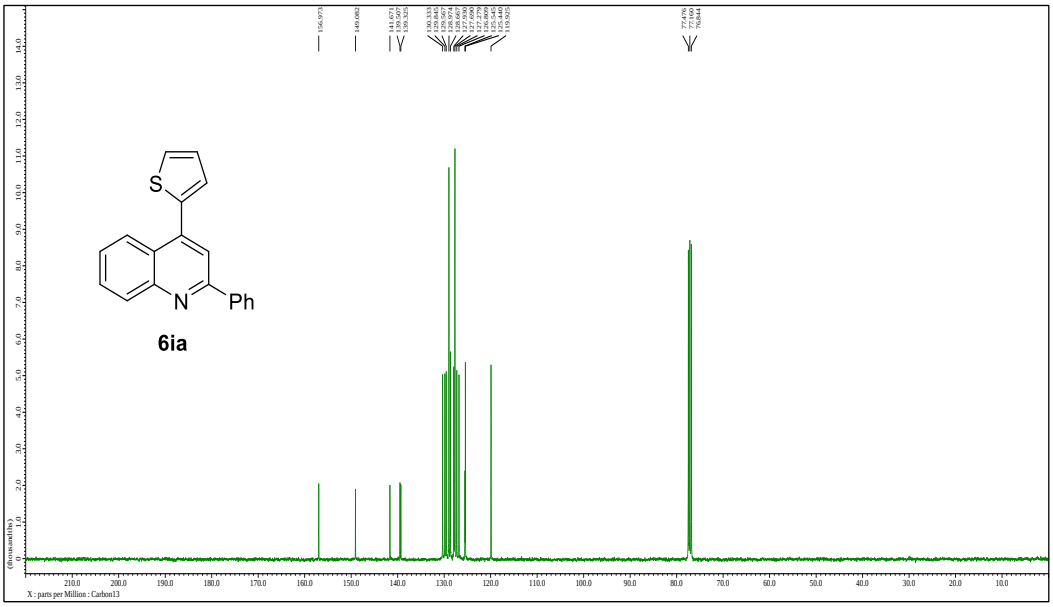
6ha ^{13}C-NMR (100 MHz, $CDCl_3$)



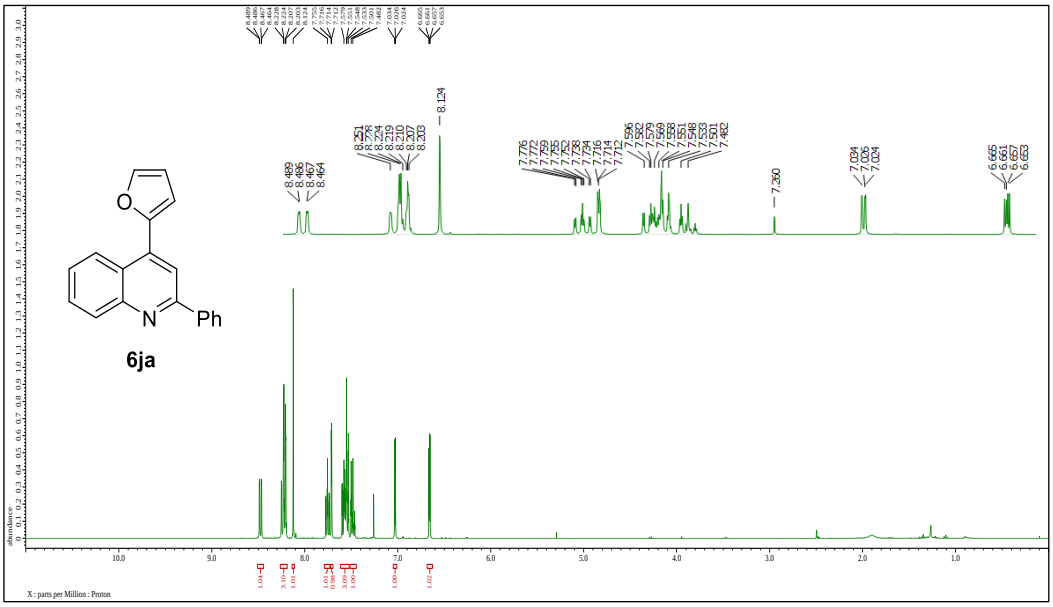
6ia ^{1}H-NMR (400 MHz, $CDCl_3$)



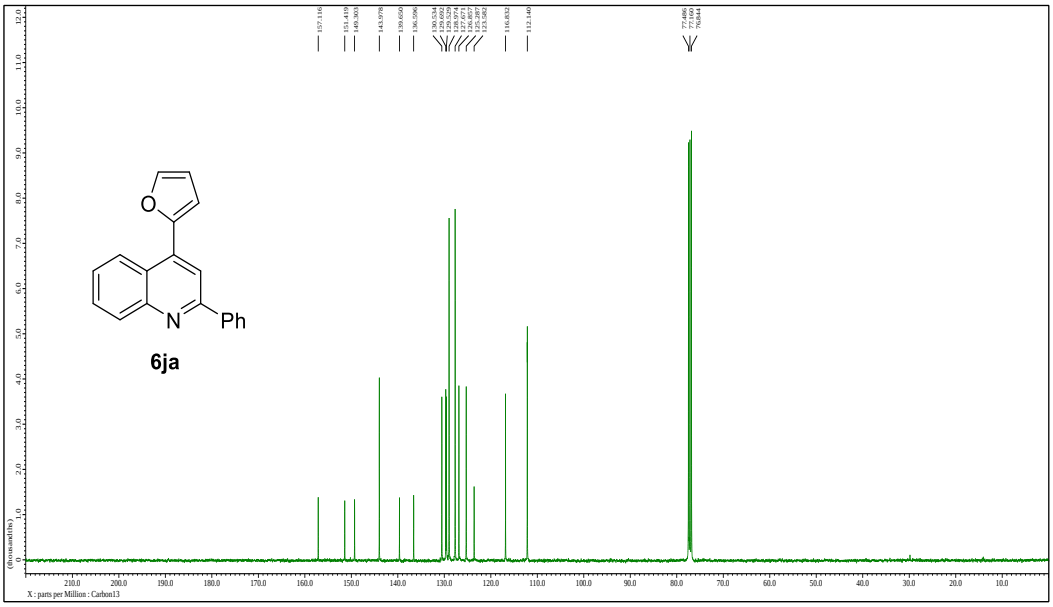
6ia ^{13}C-NMR (100 MHz, $CDCl_3$)



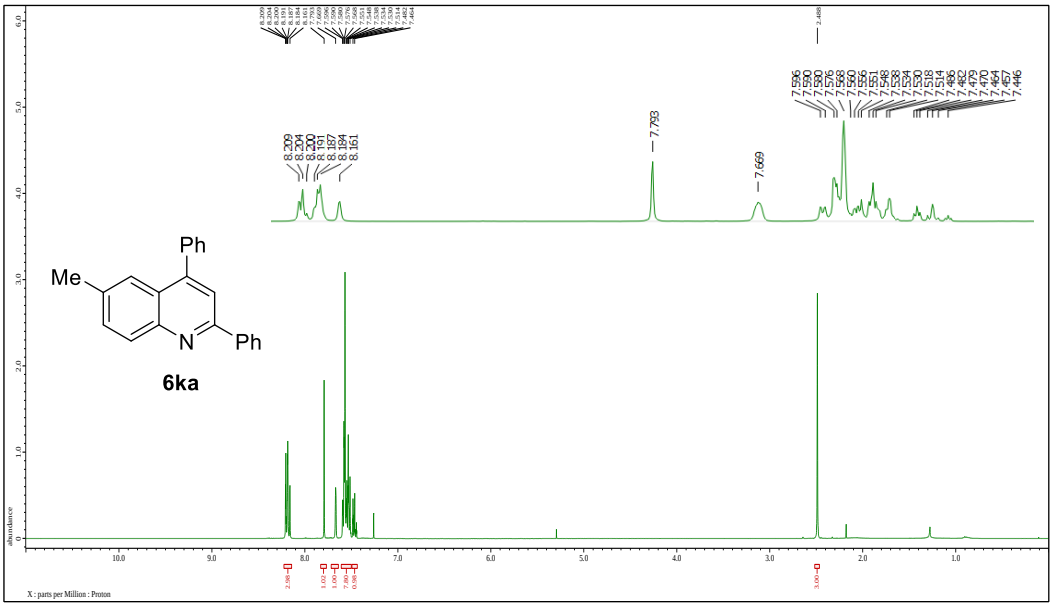
6ja ^{1}H-NMR (400 MHz, $CDCl_3$)



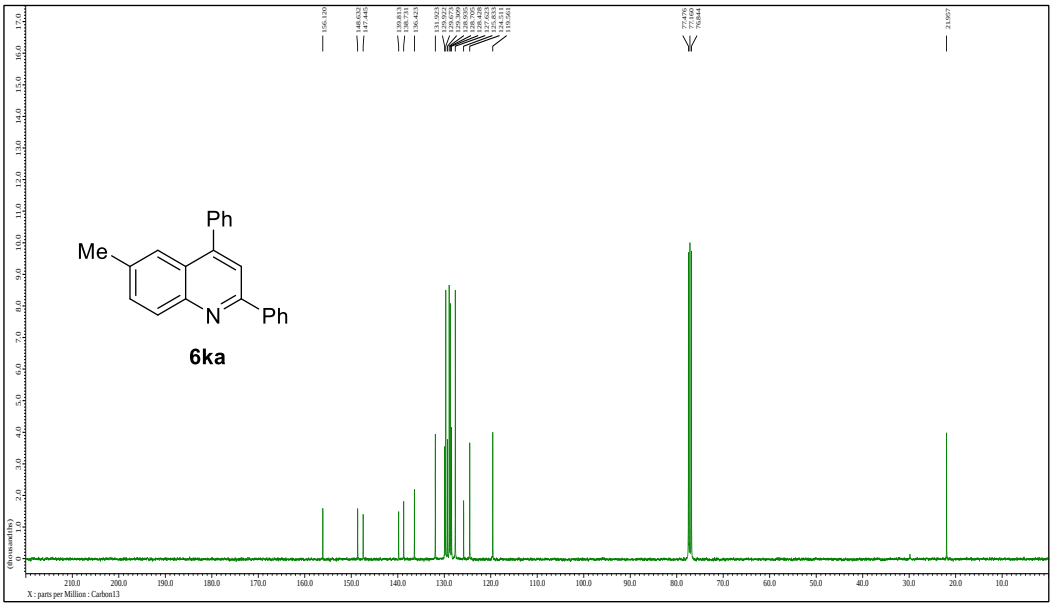
6ja ^{13}C-NMR (100 MHz, $CDCl_3$)



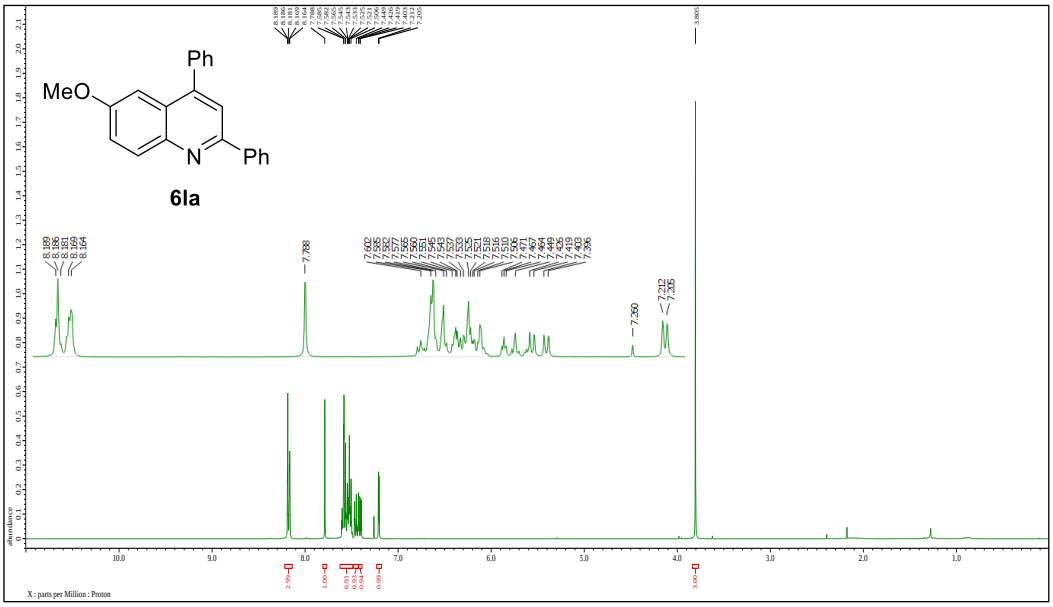
6ka ^{1}H-NMR (400 MHz, $CDCl_3$)



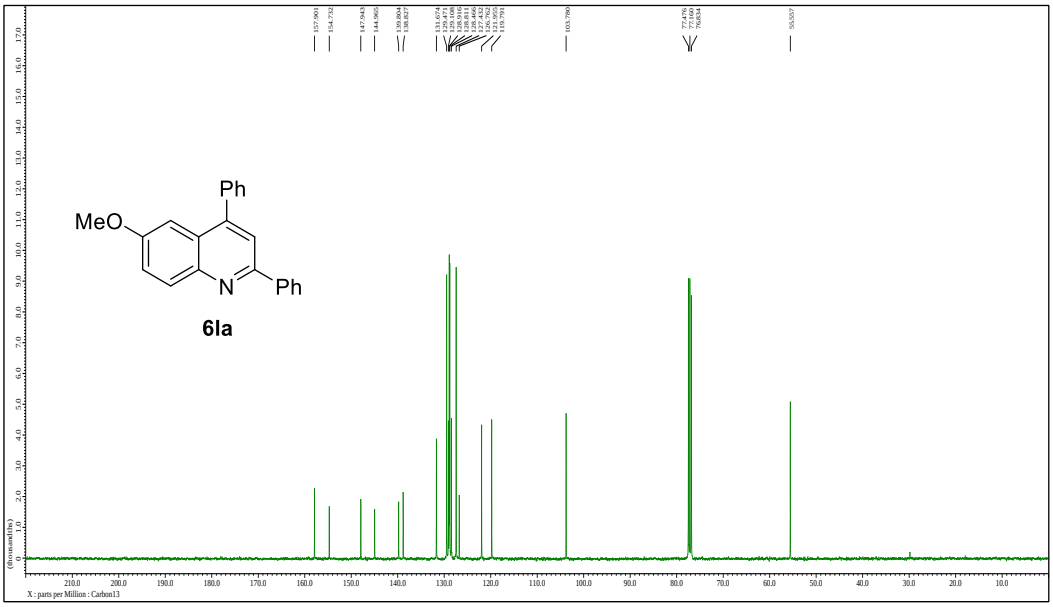
6ka ^{13}C-NMR (100 MHz, $CDCl_3$)



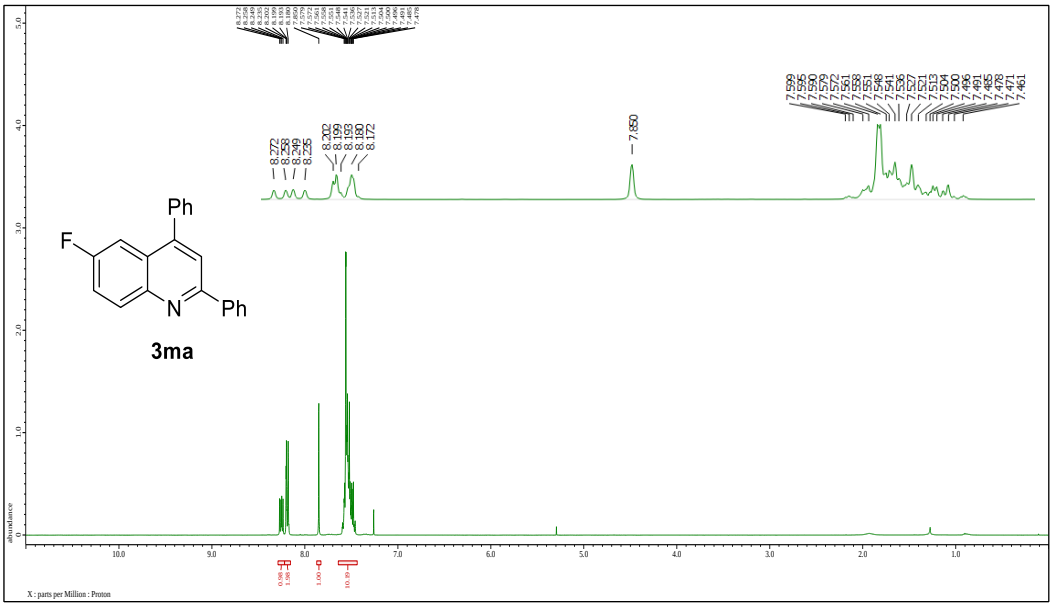
6la ^{1}H-NMR (400 MHz, $CDCl_3$)



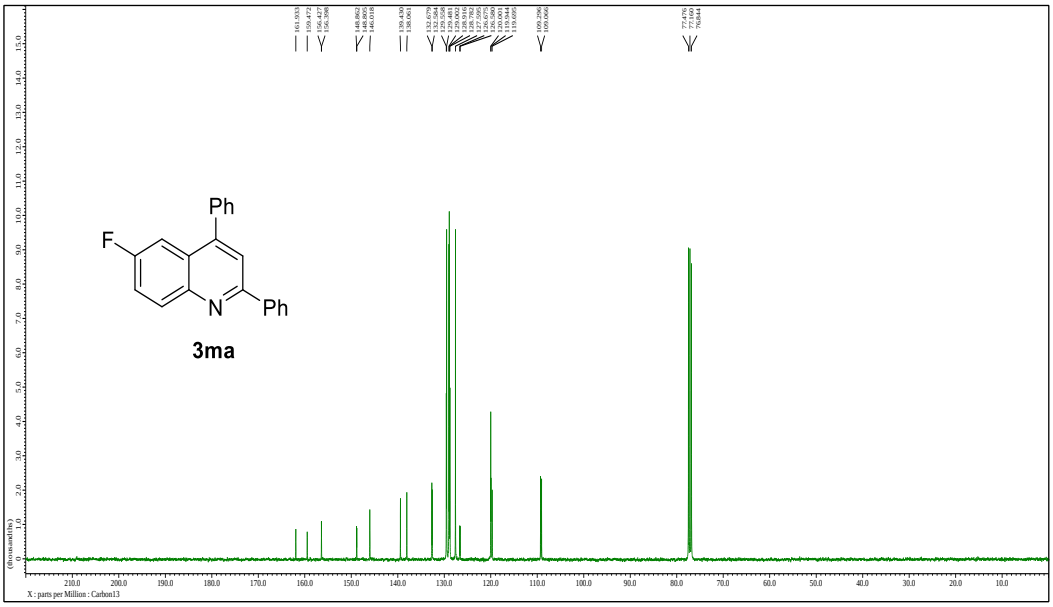
6la ^{13}C-NMR (100 MHz, $CDCl_3$)



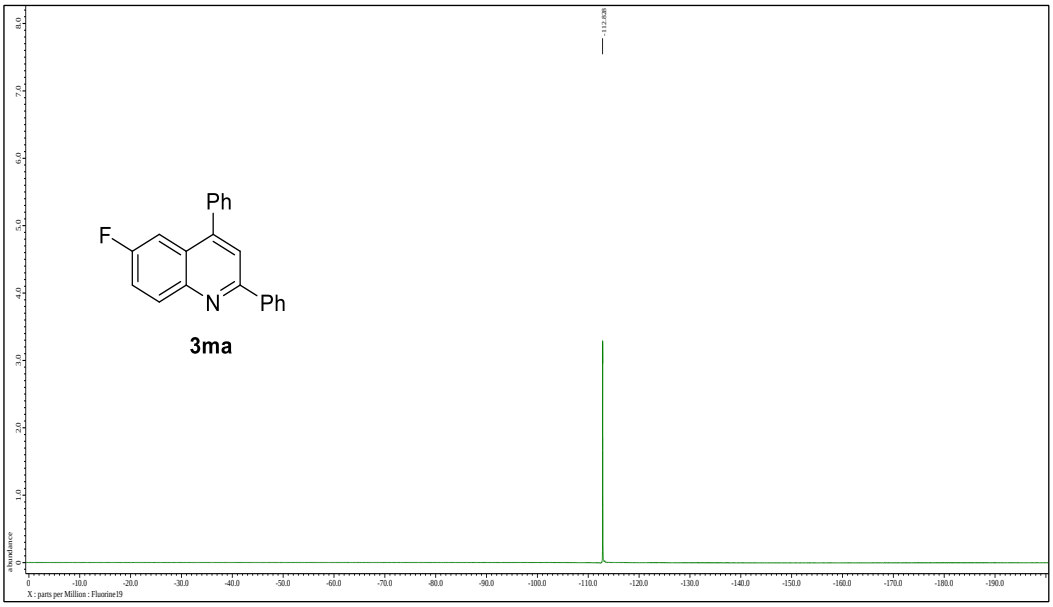
6ma ^{1}H-NMR (400 MHz, $CDCl_3$)



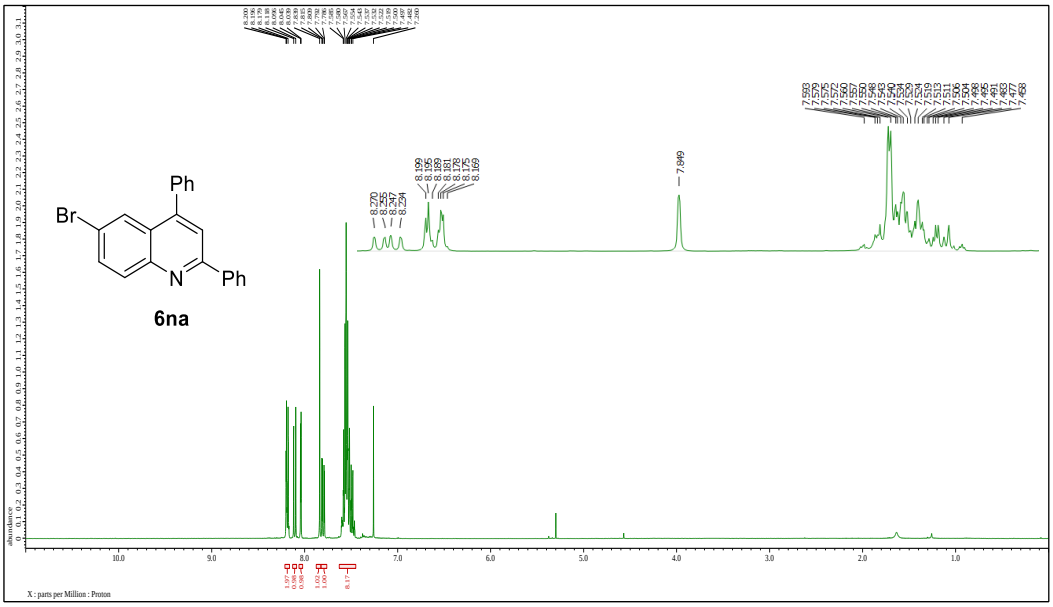
6ma ^{13}C-NMR (100 MHz, $CDCl_3$)



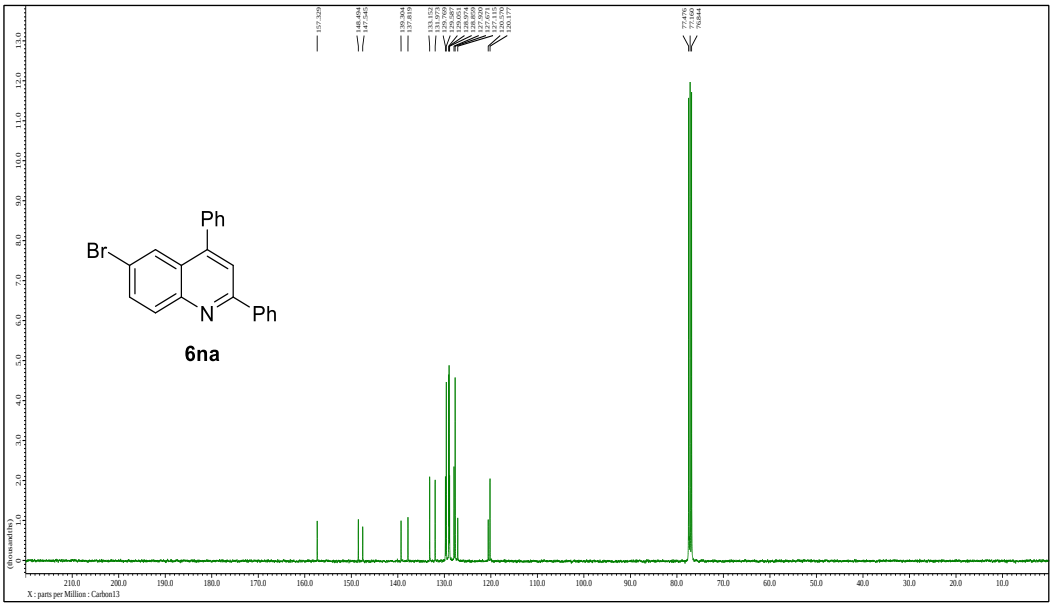
6ma ^{19}F-NMR (376 MHz, $CDCl_3$)



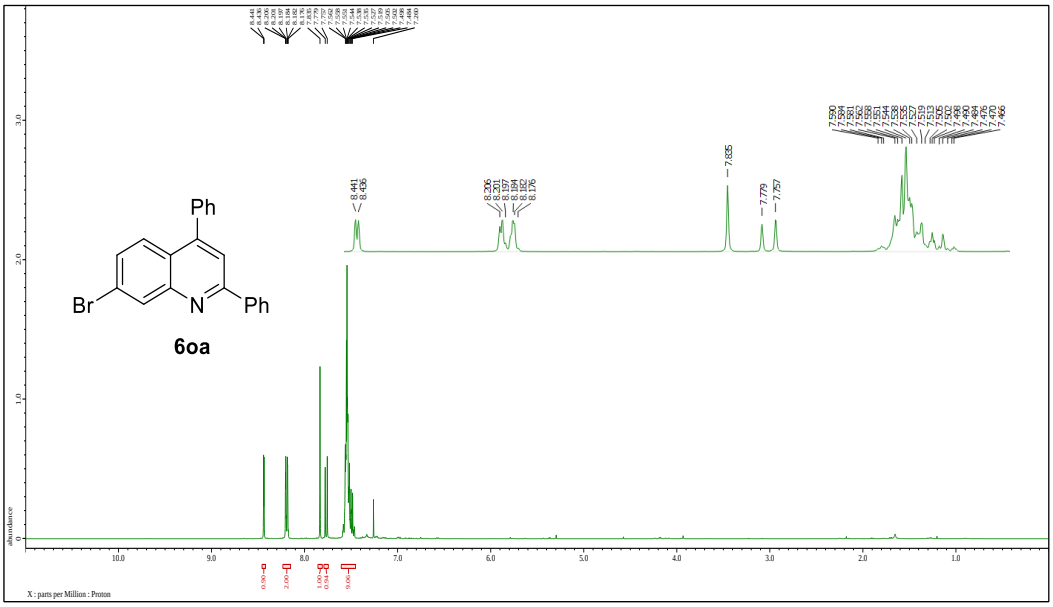
6na ^{1}H-NMR (400 MHz, $CDCl_3$)



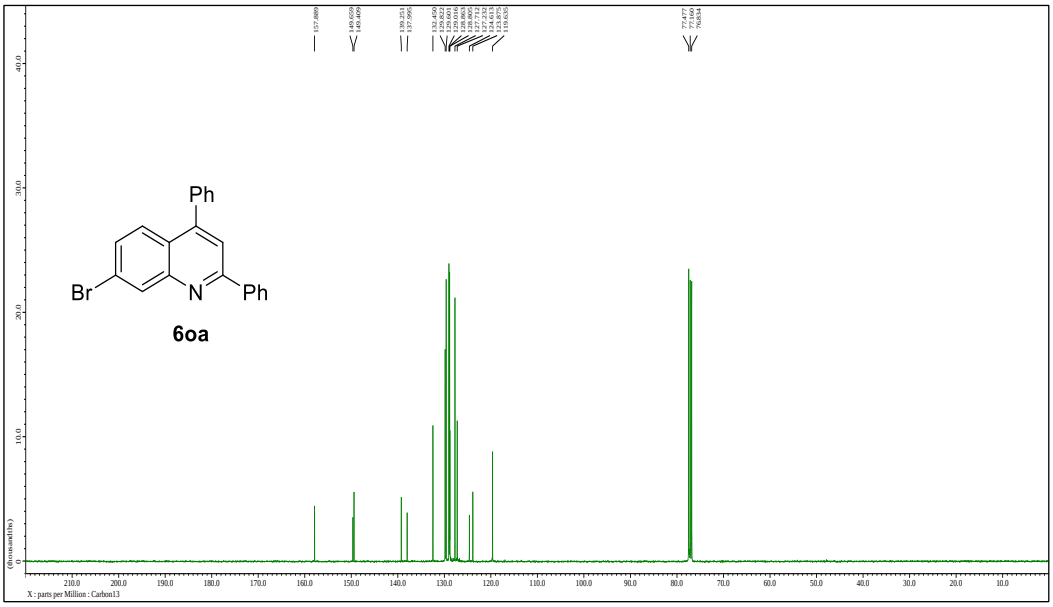
6na ^{13}C-NMR (100 MHz, $CDCl_3$)



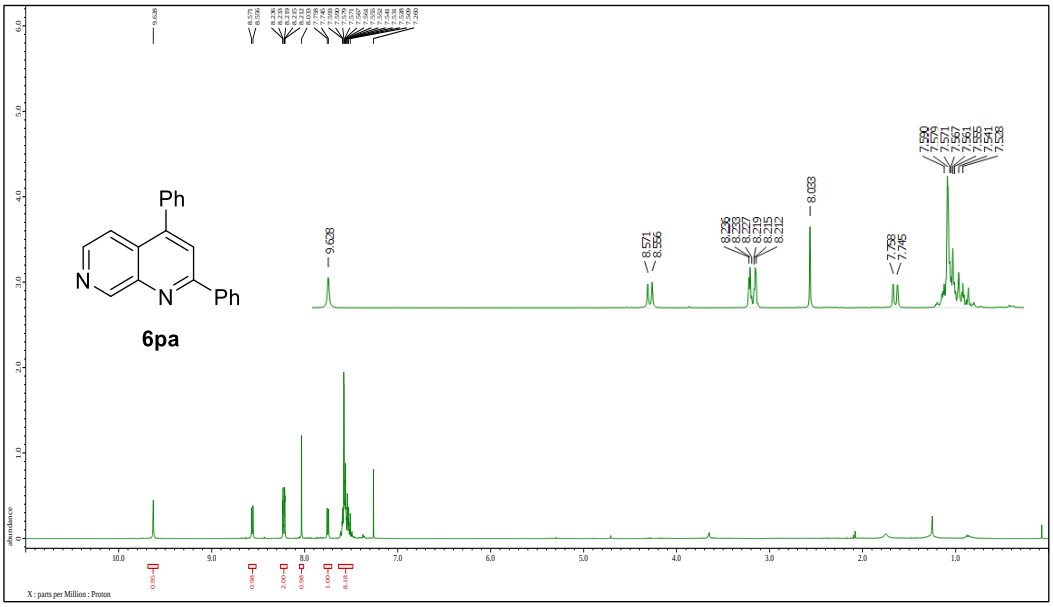
6oa ^{1}H-NMR (400 MHz, $CDCl_3$)



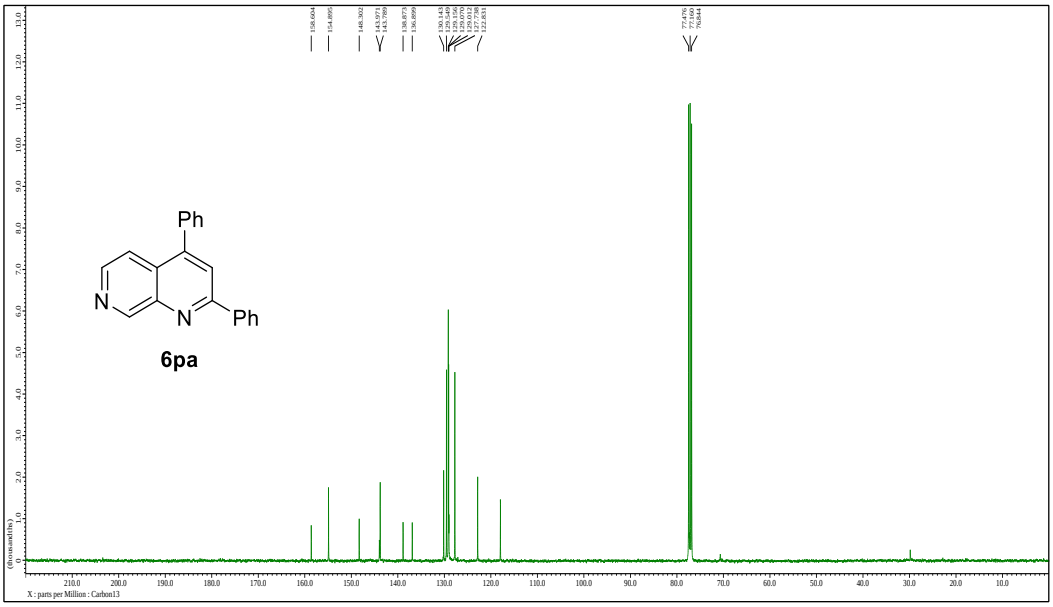
6oa ^{13}C-NMR (100 MHz, $CDCl_3$)



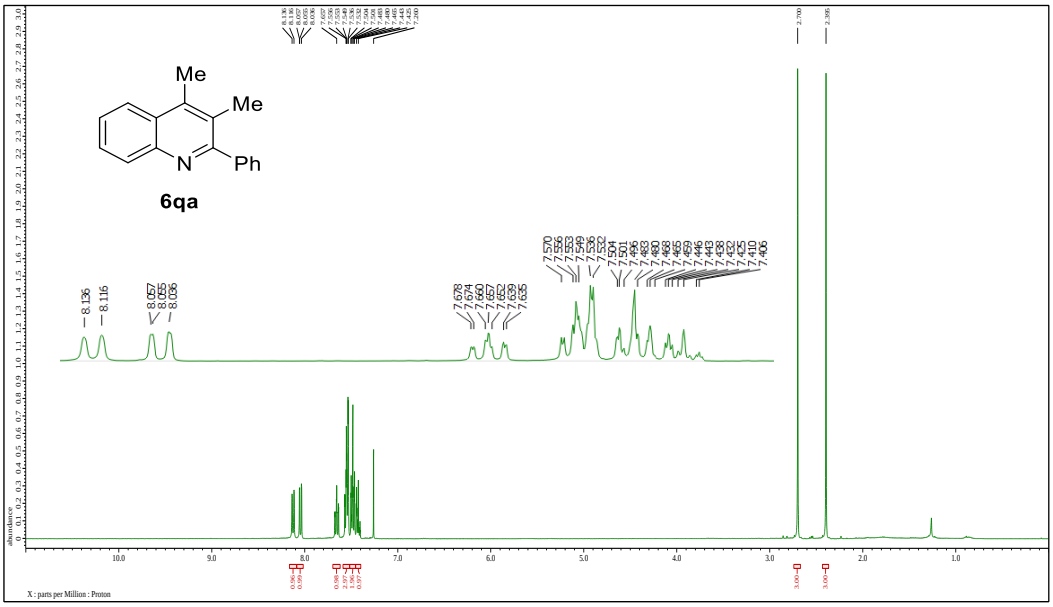
6pa ^{1}H-NMR (400 MHz, $CDCl_3$)



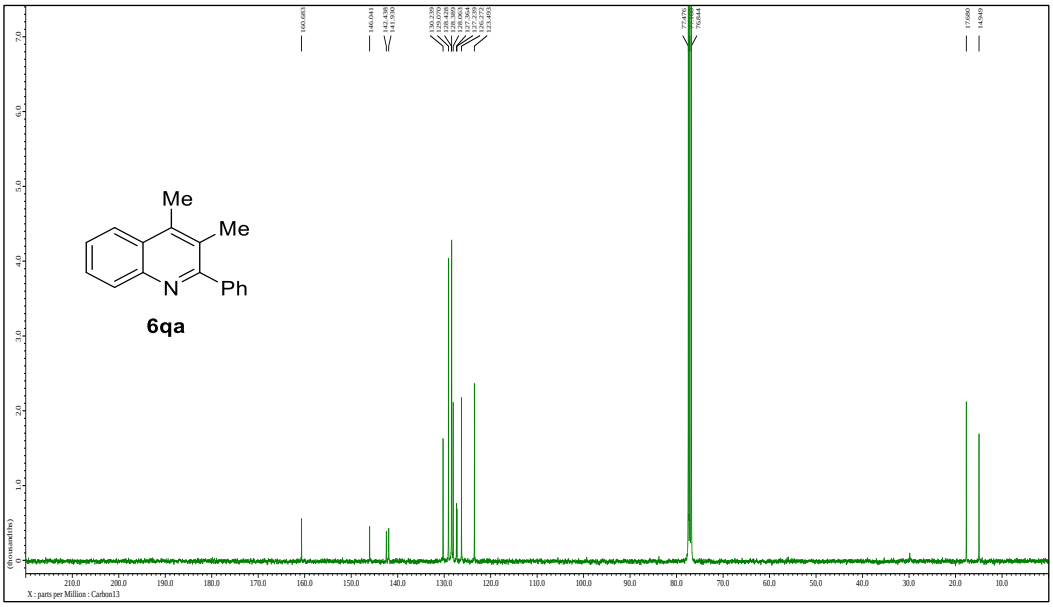
6pa ^{13}C-NMR (100 MHz, $CDCl_3$)



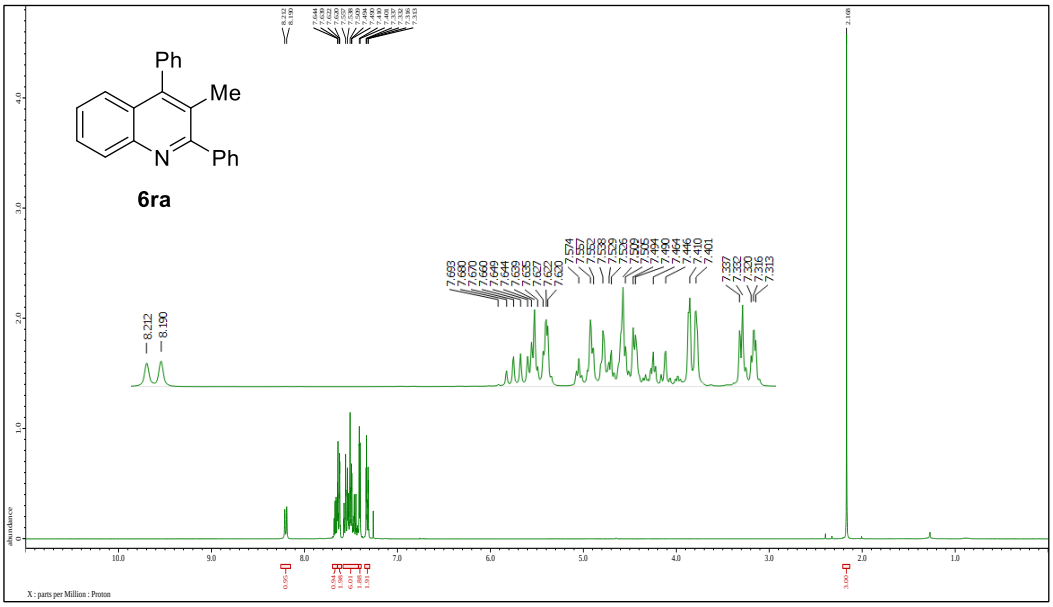
6qa ^{1}H-NMR (400 MHz, $CDCl_3$)



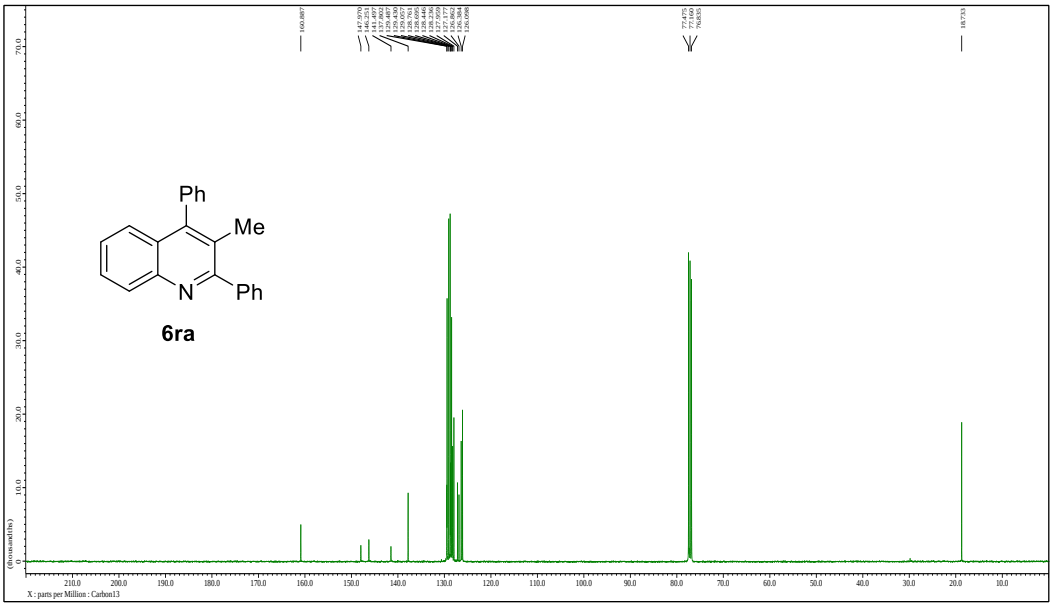
6qa ^{13}C-NMR (100 MHz, $CDCl_3$)



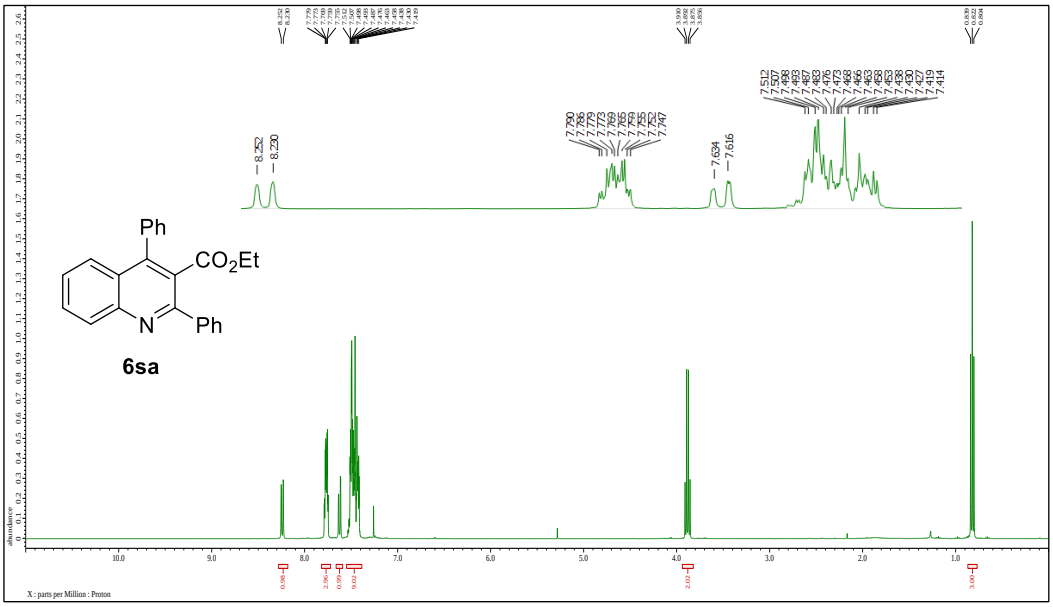
6ra ^{1}H-NMR (400 MHz, $CDCl_3$)



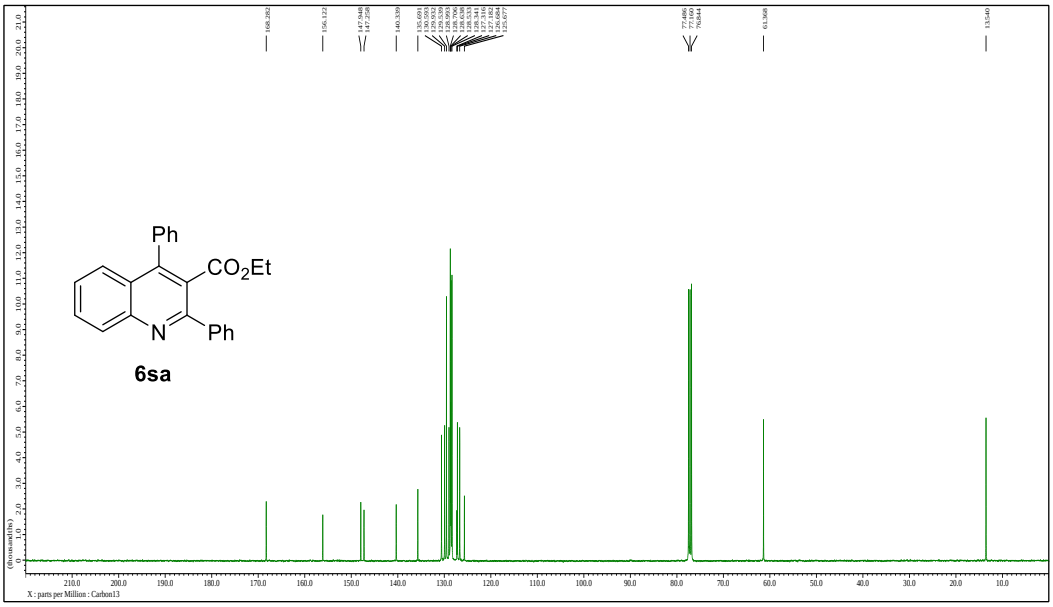
6ra ^{13}C-NMR (100 MHz, $CDCl_3$)



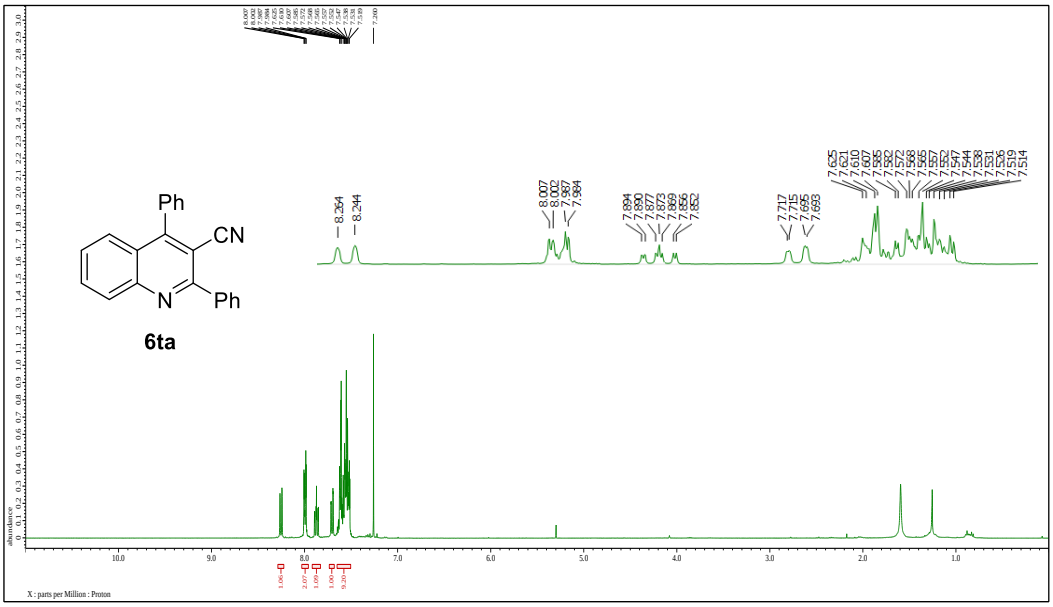
6sa ^{1}H-NMR (400 MHz, $CDCl_3$)



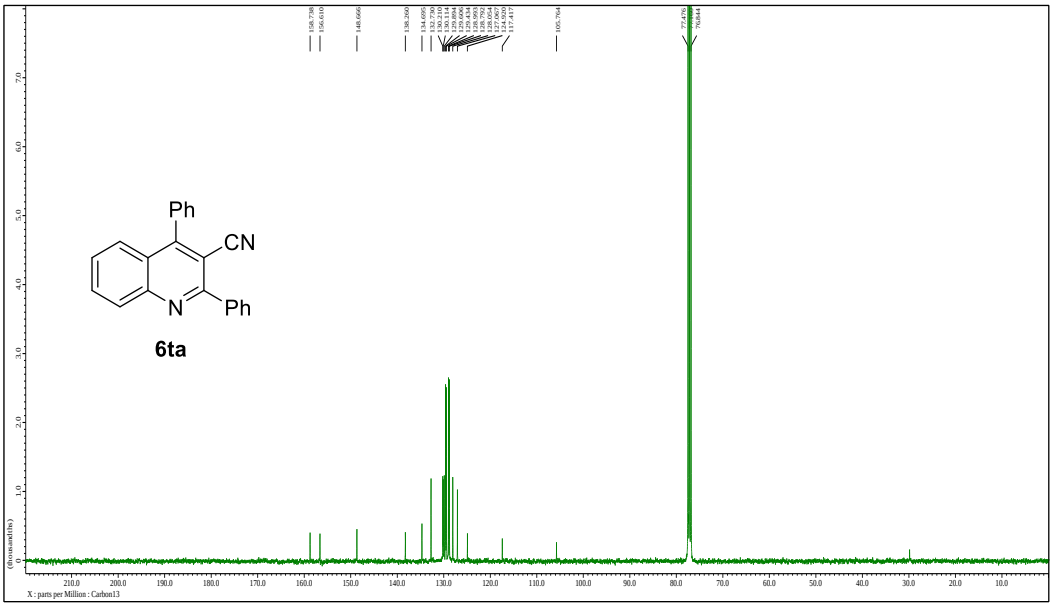
6sa ^{13}C-NMR (100 MHz, $CDCl_3$)



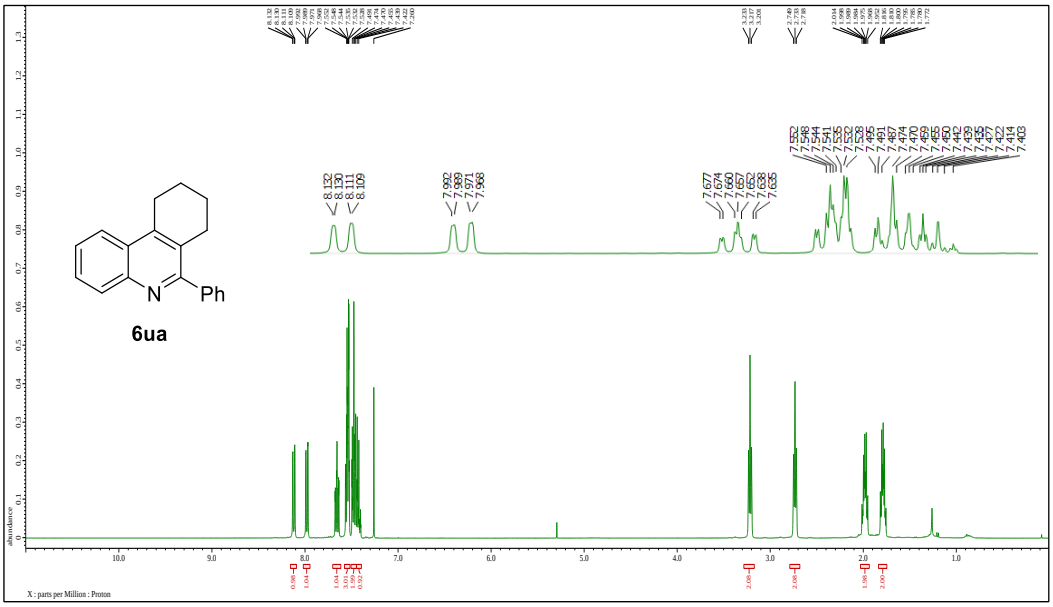
6ta ^{1}H-NMR (400 MHz, $CDCl_3$)



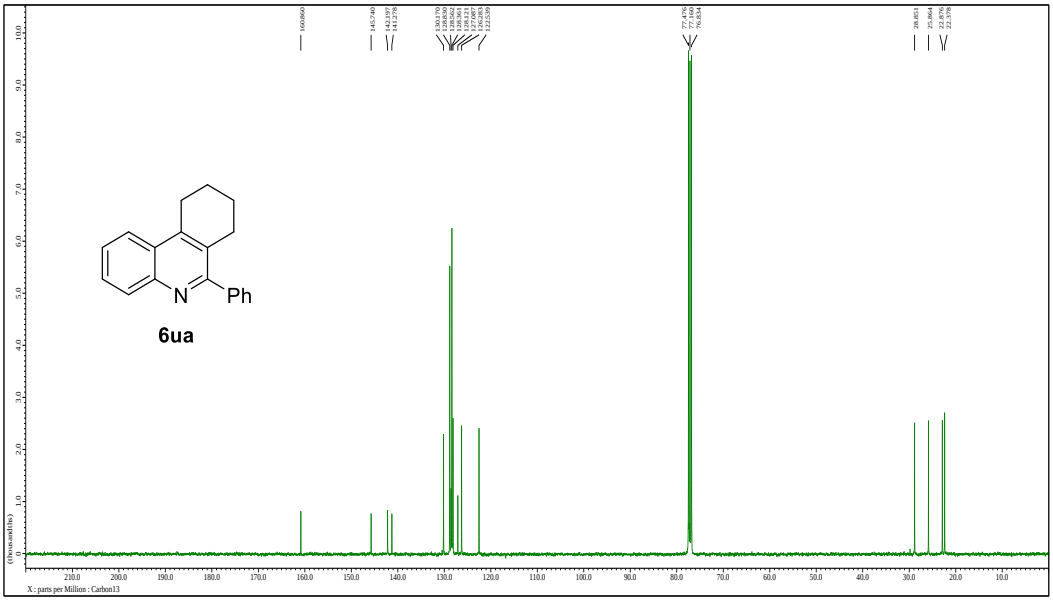
6ta ^{13}C-NMR (100 MHz, $CDCl_3$)



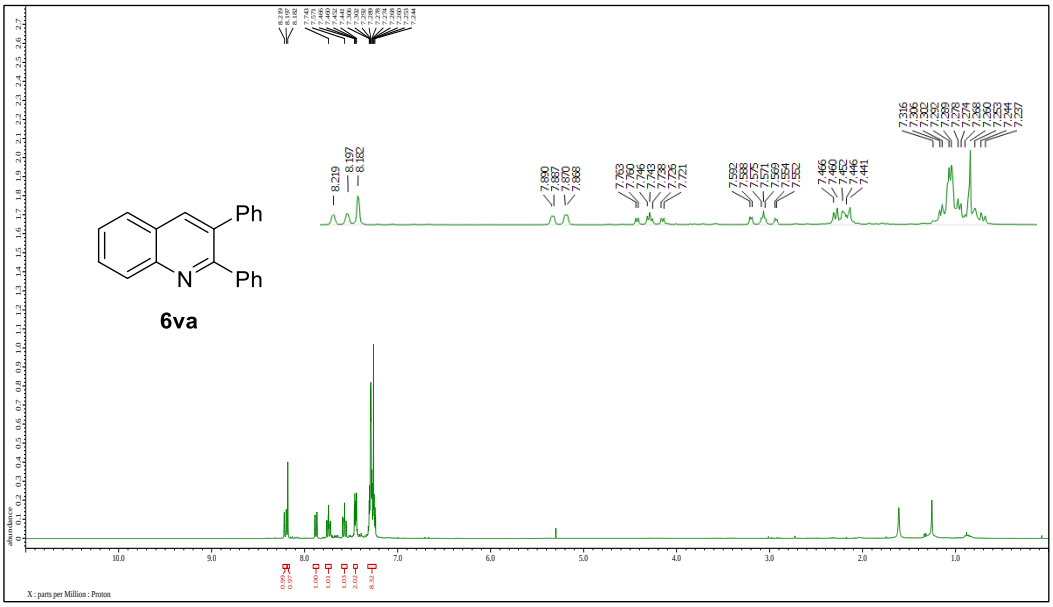
6ua ^{1}H-NMR (400 MHz, $CDCl_3$)



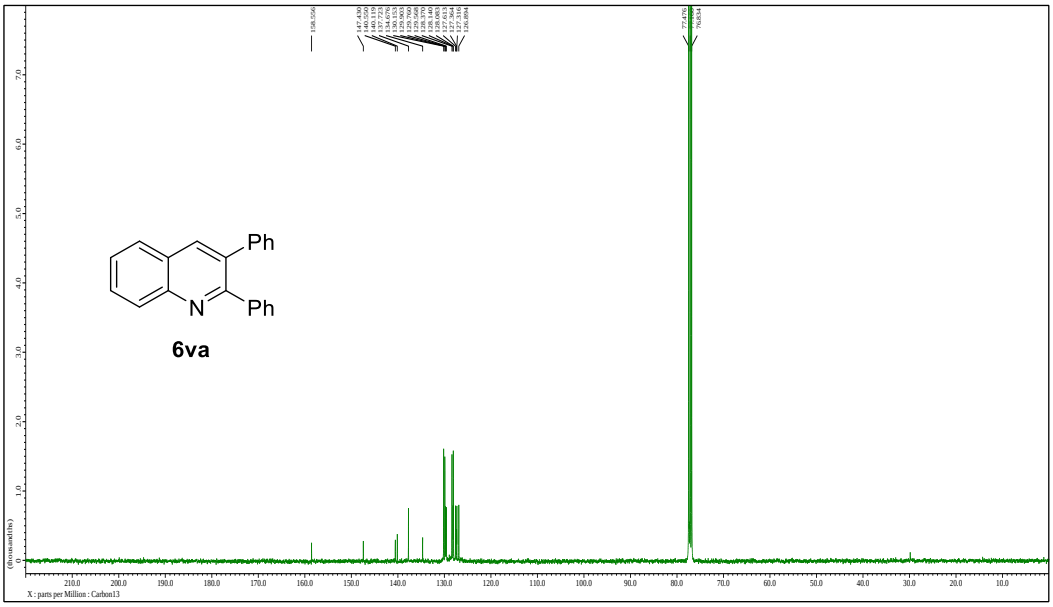
6ua ^{13}C-NMR (100 MHz, $CDCl_3$)



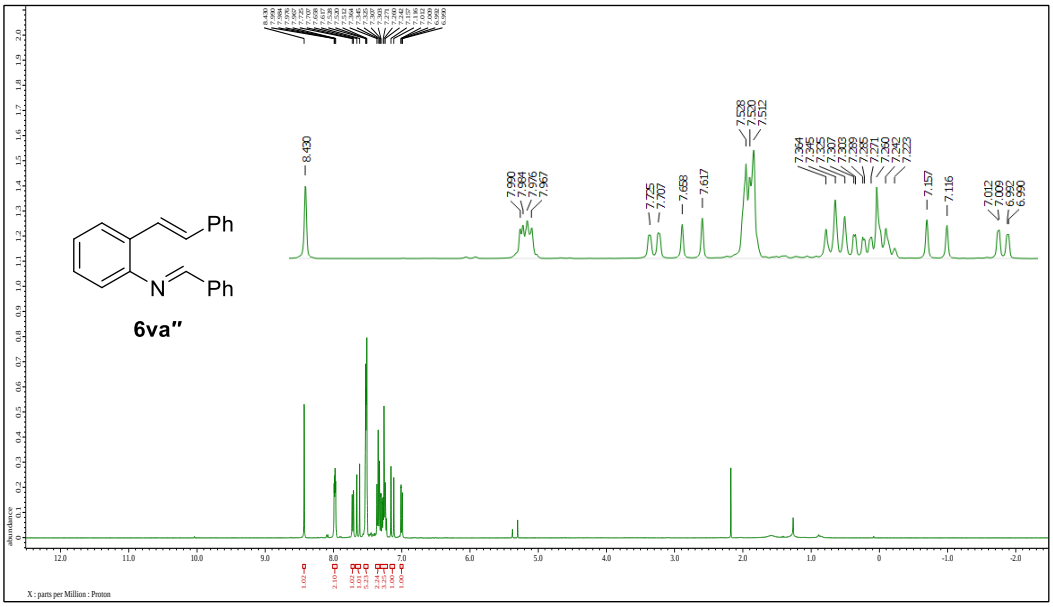
6va ^{1}H-NMR (400 MHz, $CDCl_3$)



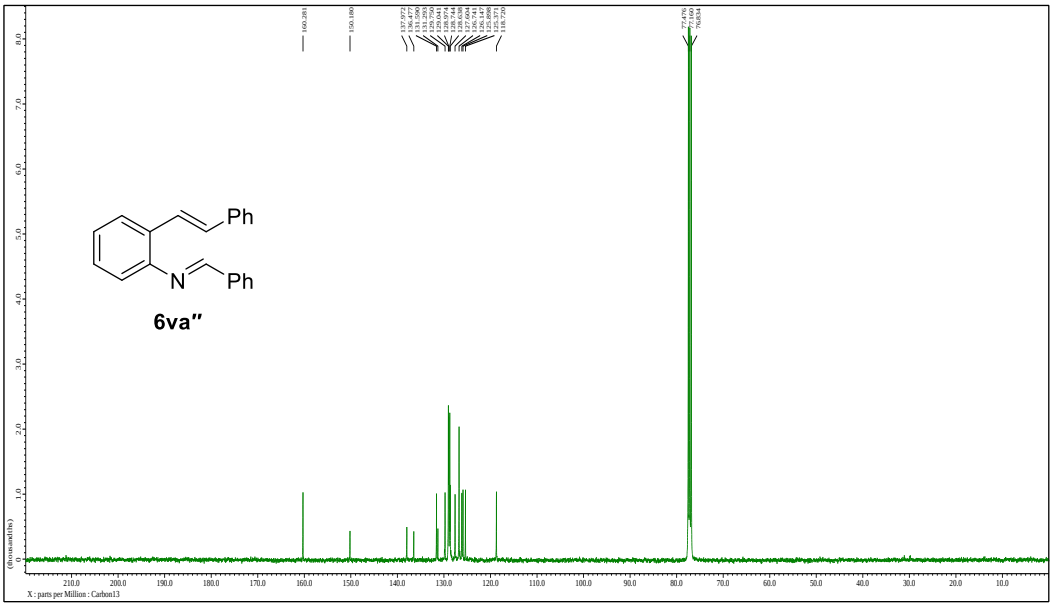
6va ^{13}C-NMR (100 MHz, $CDCl_3$)



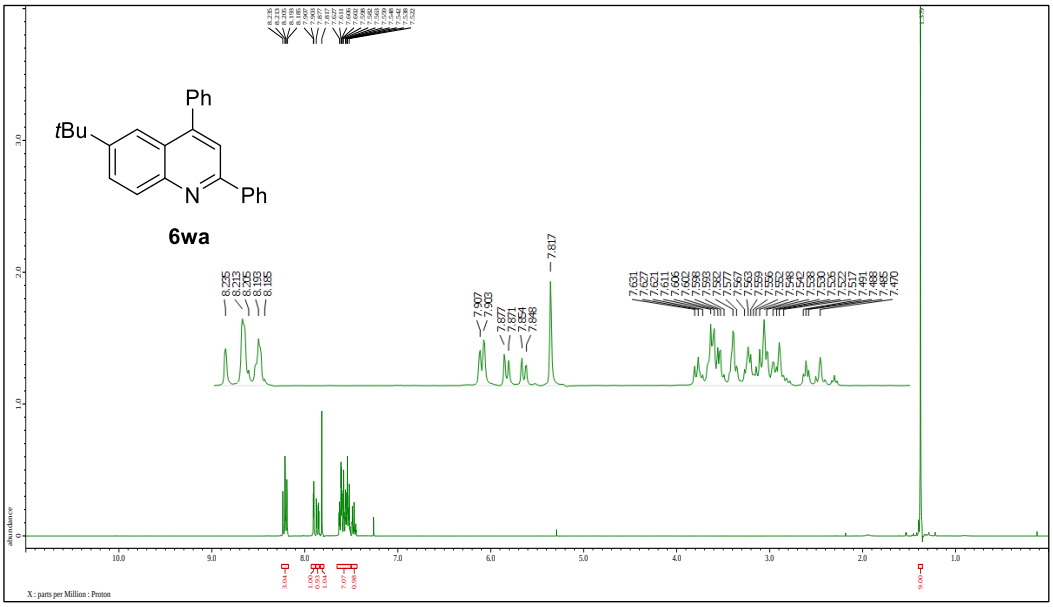
6va″ ^{1}H-NMR (400 MHz, $CDCl_3$)



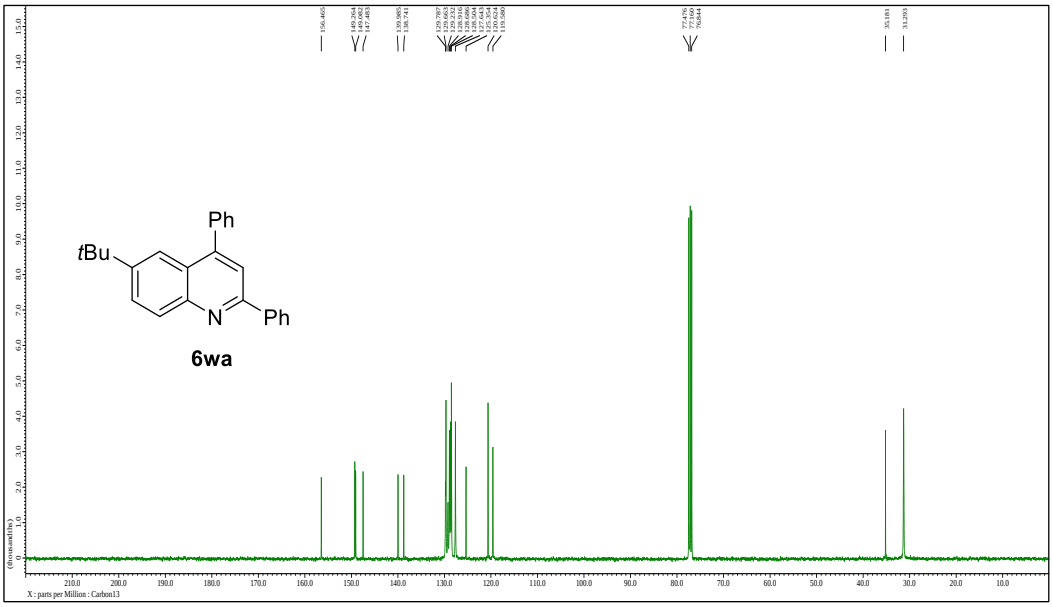
6va″ ^{13}C-NMR (100 MHz, $CDCl_3$)



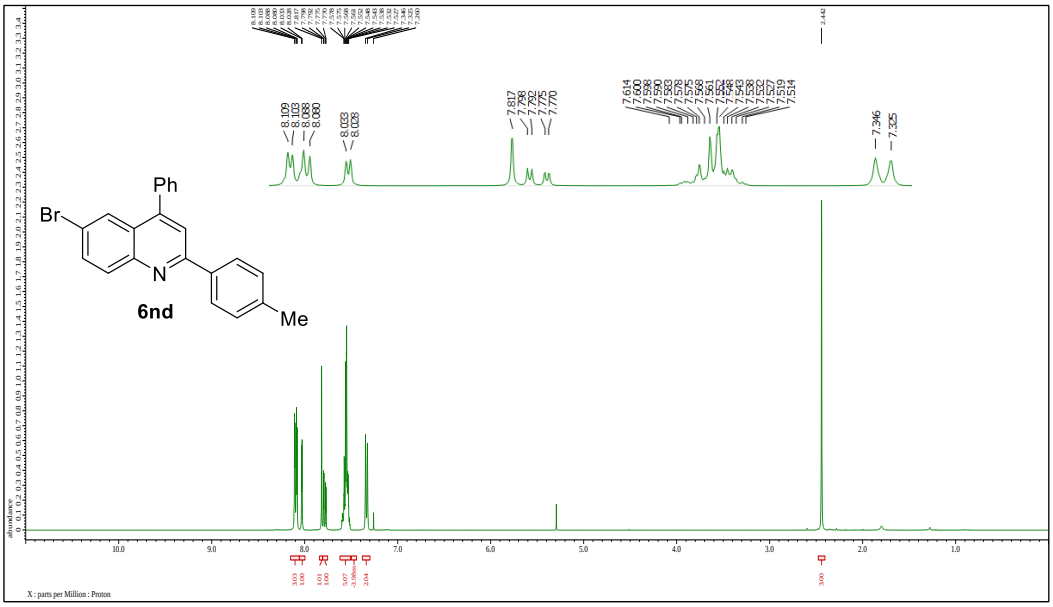
6wa ^{1}H-NMR (400 MHz, $CDCl_3$)



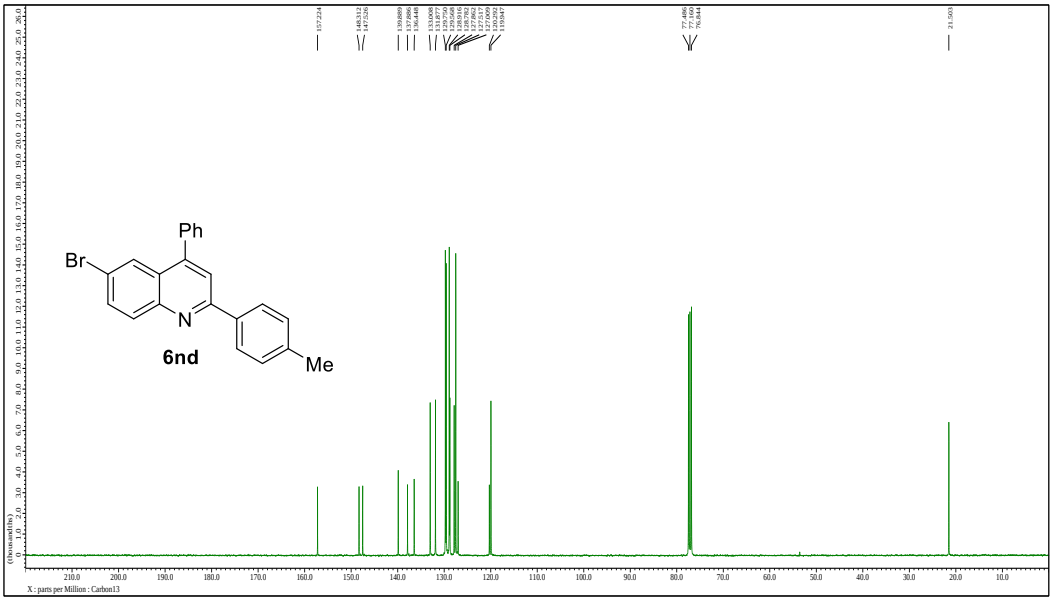
6wa ^{13}C-NMR (100 MHz, $CDCl_3$)



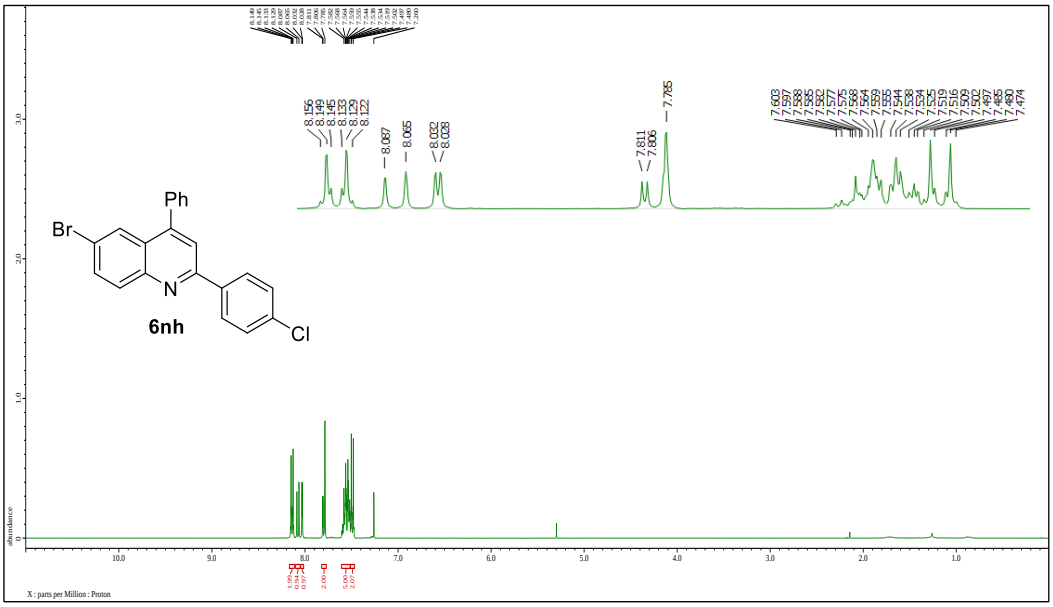
6nd ^{1}H-NMR (400 MHz, $CDCl_3$)



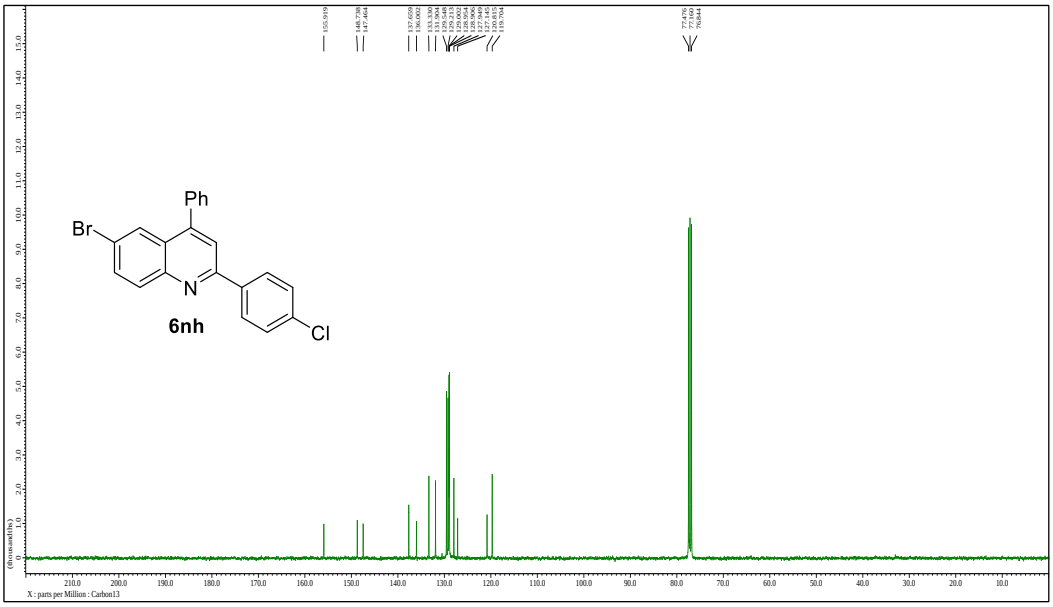
6nd ^{13}C-NMR (100 MHz, $CDCl_3$)



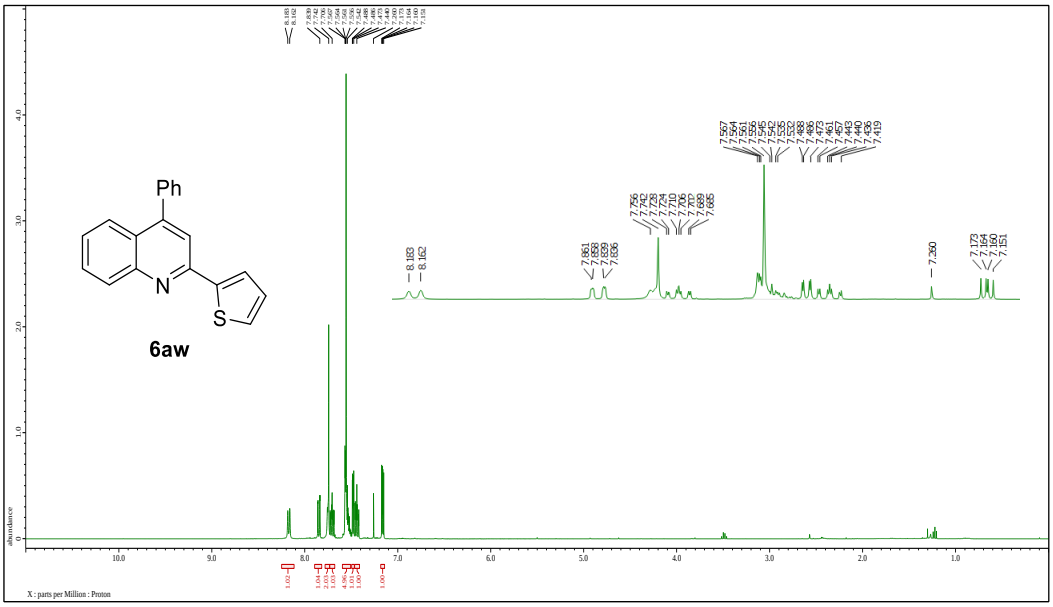
6nh ^{1}H-NMR (400 MHz, $CDCl_3$)



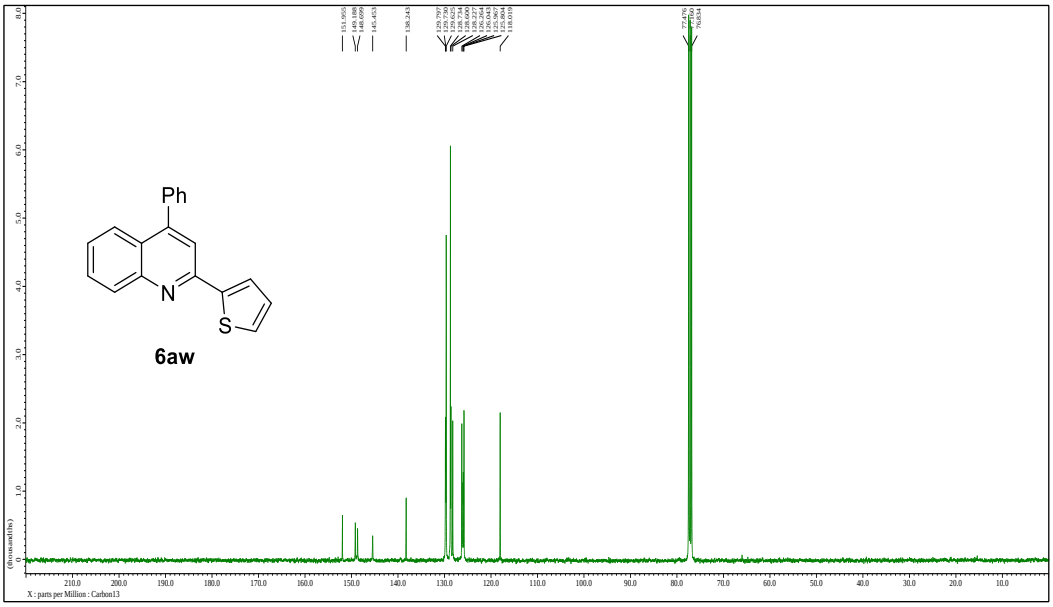
6nh ^{13}C-NMR (100 MHz, $CDCl_3$)



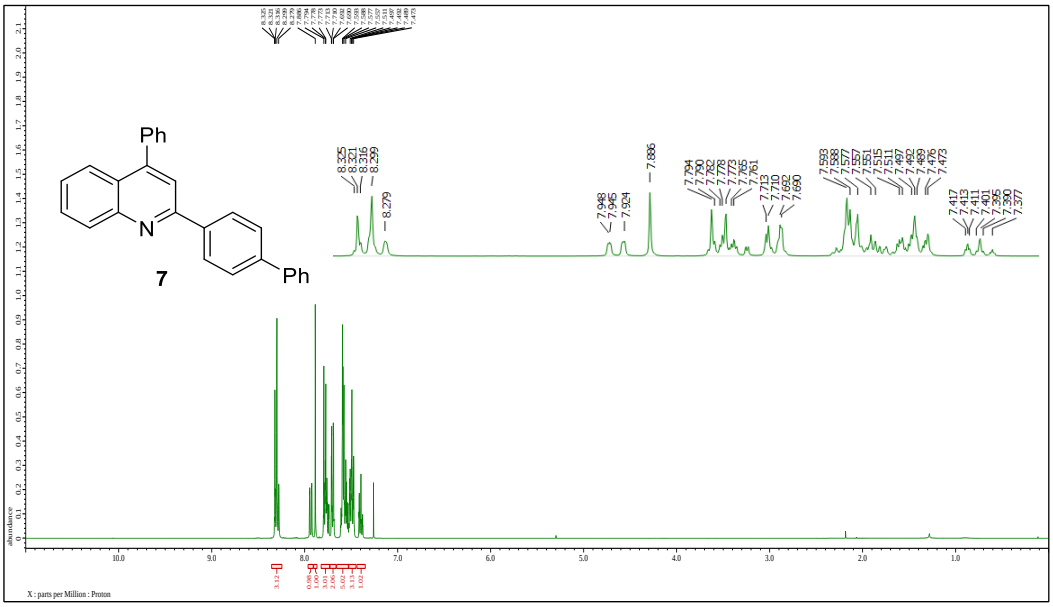
6aw ^{1}H-NMR (400 MHz, $CDCl_3$)



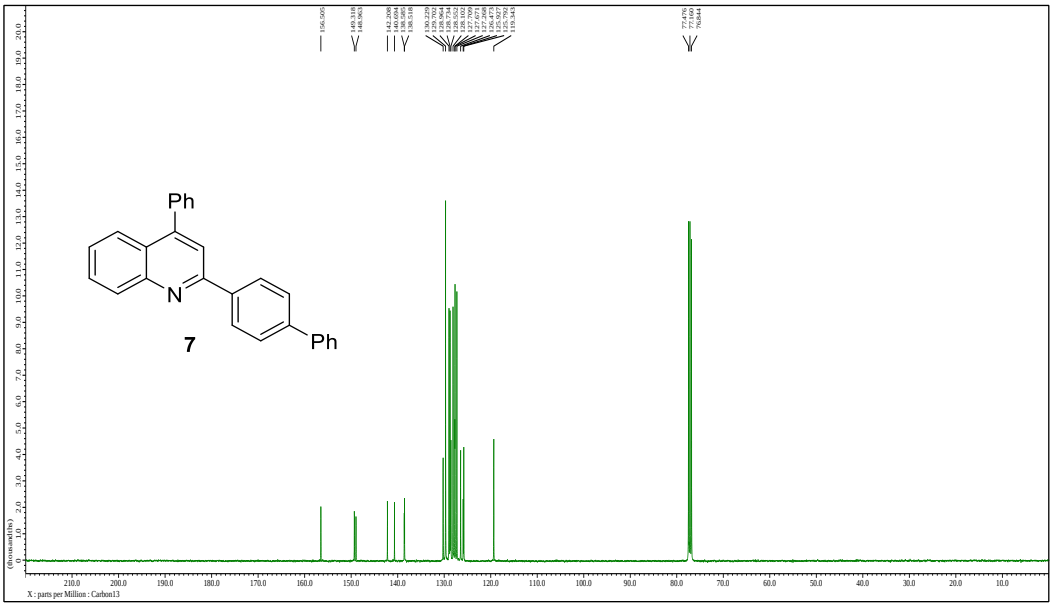
6aw ^{13}C-NMR (100 MHz, $CDCl_3$)



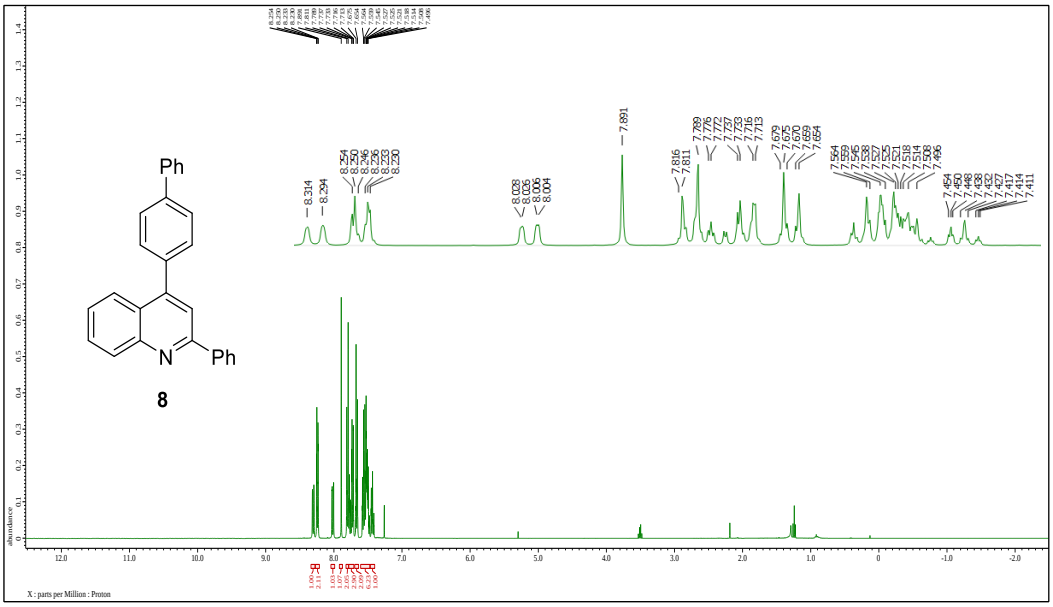
7 ^{1}H-NMR (400 MHz, $CDCl_3$)



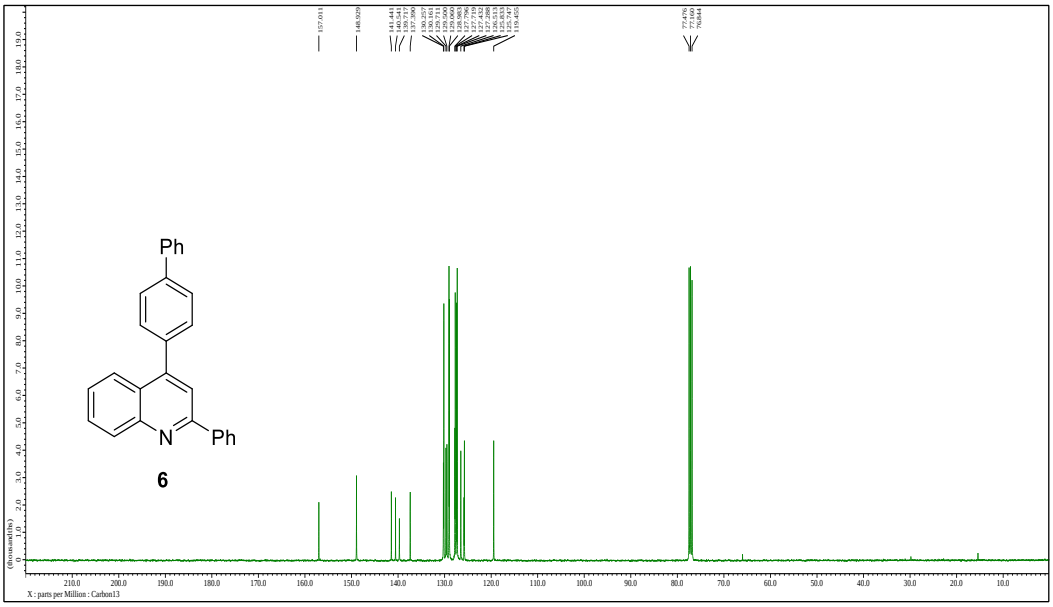
7 ^{13}C-NMR (100 MHz, $CDCl_3$)



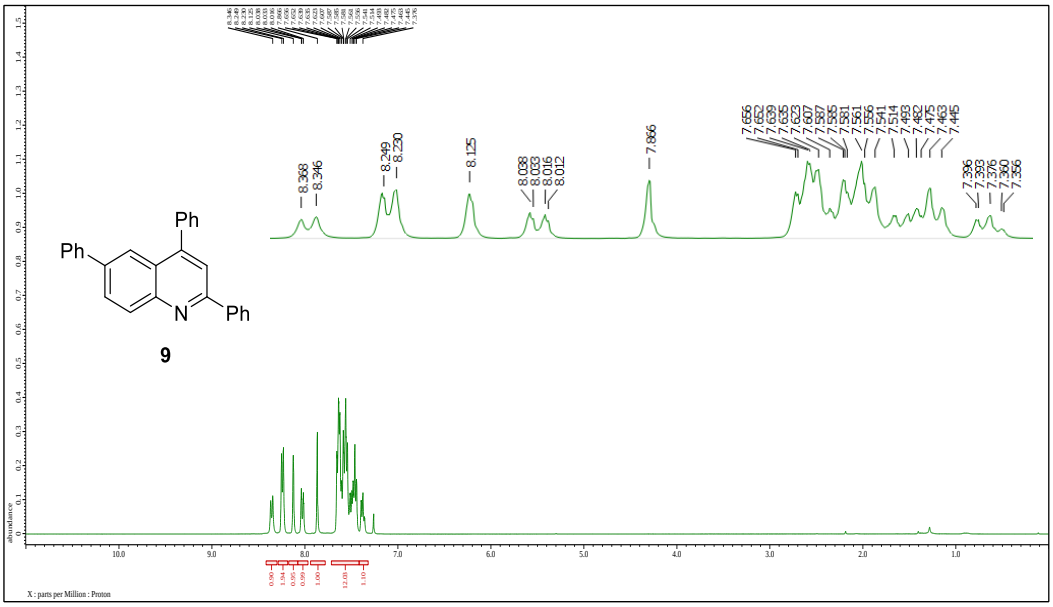
8 ^{1}H-NMR (400 MHz, $CDCl_3$)



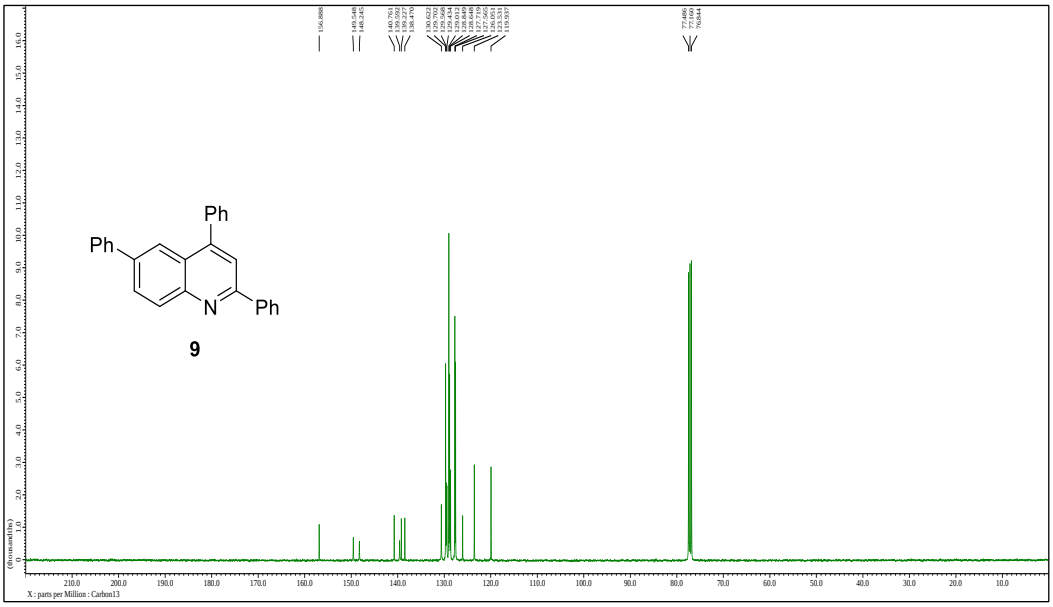
8 ^{13}C-NMR (100 MHz, $CDCl_3$)



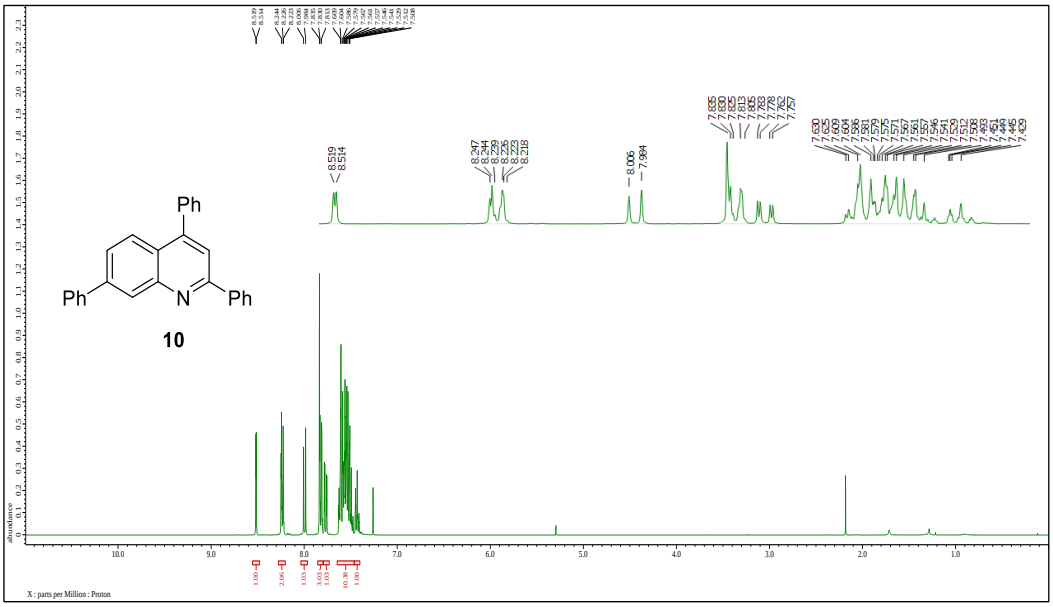
9 ^{1}H-NMR (400 MHz, $CDCl_3$)



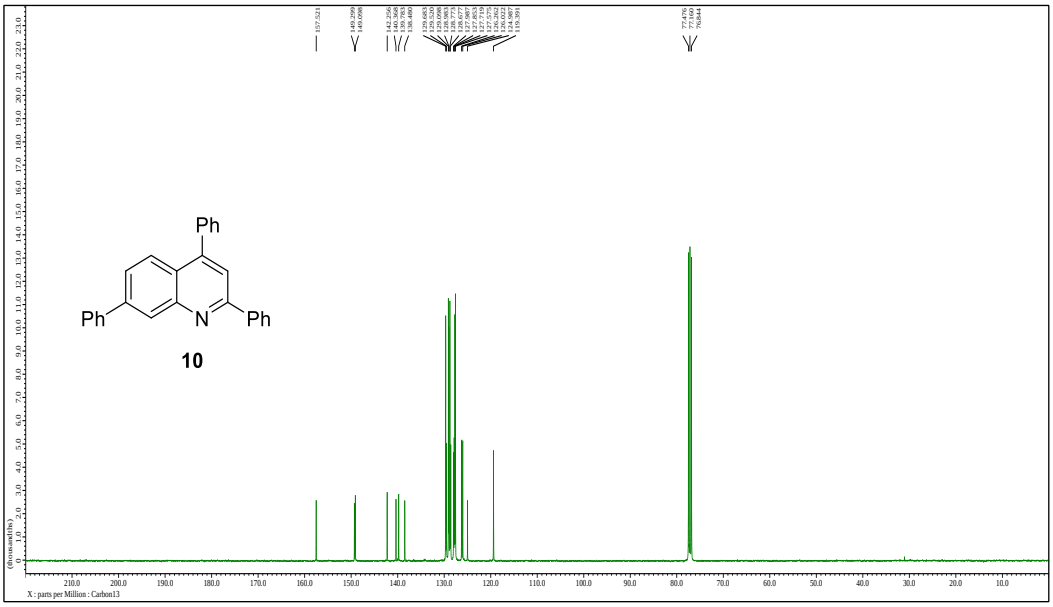
9 ^{13}C-NMR (100 MHz, $CDCl_3$)



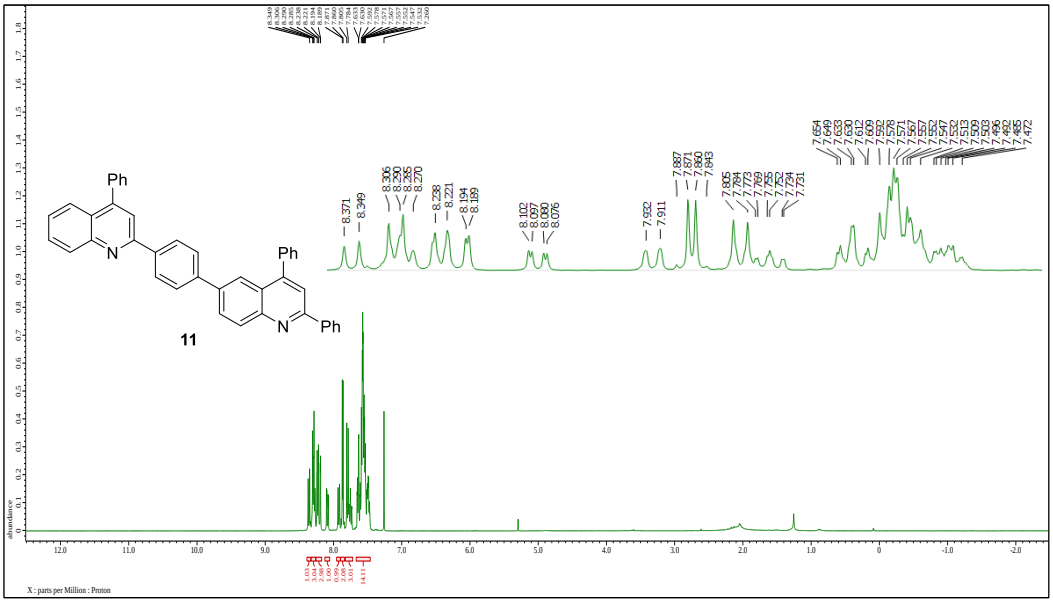
10 ^{1}H-NMR (400 MHz, $CDCl_3$)



10 ^{13}C-NMR (100 MHz, $CDCl_3$)



11 ^{1}H-NMR (400 MHz, $CDCl_3$)



11 ^{13}C-NMR (100 MHz, $CDCl_3$)