Chapter III

Pd-NHC catalysed carbonylative Suzuki coupling reactions of aryl halides and arylboronic acids and its application towards the synthesis biologically active 4-quinolone scaffolds

III.A. Introduction

Biaryl ketones are found in numerous photosensitizers, advanced organic materials, natural products, and pharmaceutically apposite agents.[1] For instance Evista,[2] Tricor[3] and Sector[4], which contain biaryl ketone cores, are commonly prescribed medications, due to their extraordinary biological and therapeutic properties (e.g., in selective estrogen receptor modulation, cholesterol regulation, and anti-inflammation, respectively). Predictably, the development of methodologies towards the synthesis of functionally diverse biaryl ketones that are economical, practical, synthetically effective, and nonhazardous is of both great importance and interest to medicinal chemists. Traditionally, transition metal catalyzed cross-coupling methods, such as acylative Suzuki couplings, Friedel-Crafts acylations, and nucleophilic additions of an organometallic to a carbonyl moiety, are commonly used for the synthesis of aryl ketones. However, the cross coupling of arylboronic acids with carboxylic acid derivatives is far superior to these previous methods, not only with respect to the reaction's conditions and reagent compatibility, but also with regard to its regioselectivity and efficiency.[5] Bumagin and colleagues introduced Pd-catalyzed cross-coupling reactions of acid chlorides in 1997 for the synthesis of aryl ketones.[6] Later, this method was extended to acylative Suzuki couplings with anhydrides,[7] esters,[8] and carboxylic acids, in the presence of activating agents.[7c-9] More recently, a Pd-catalyzed thiol ester–boronic acid coupling towards the synthesis of biaryl ketones was developed by Liebeskind and Srogl.[10] Catalytic amount of Pd(0) salt and stoichiometric amount of Cu(I)TC [Copper(I)-thiophene-2-carboxylate], an expensive salt are essential requirements of this thioorganic–boronic acid coupling reaction.[10]

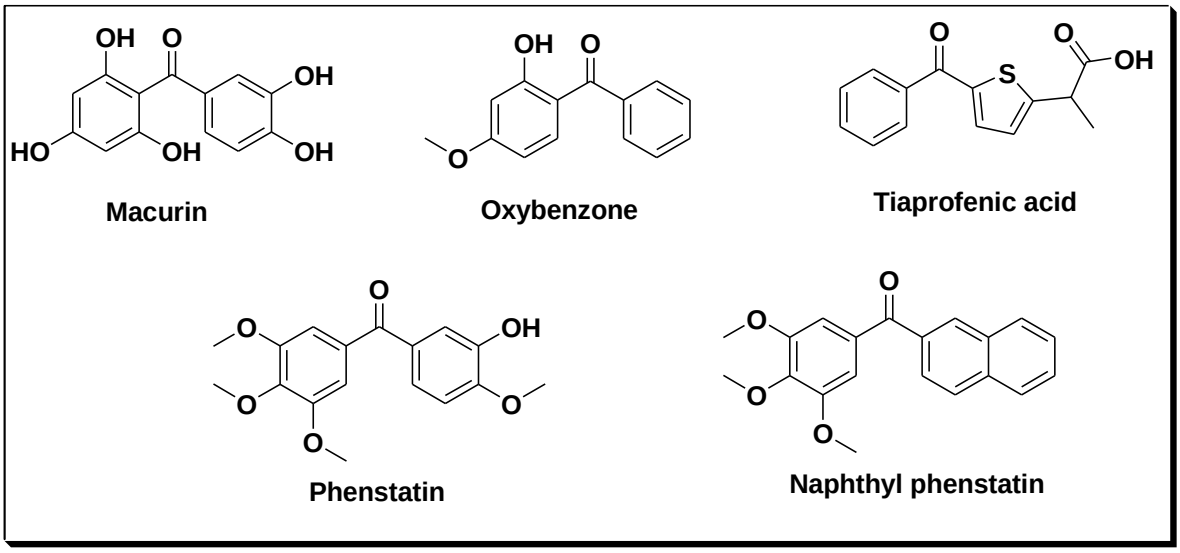
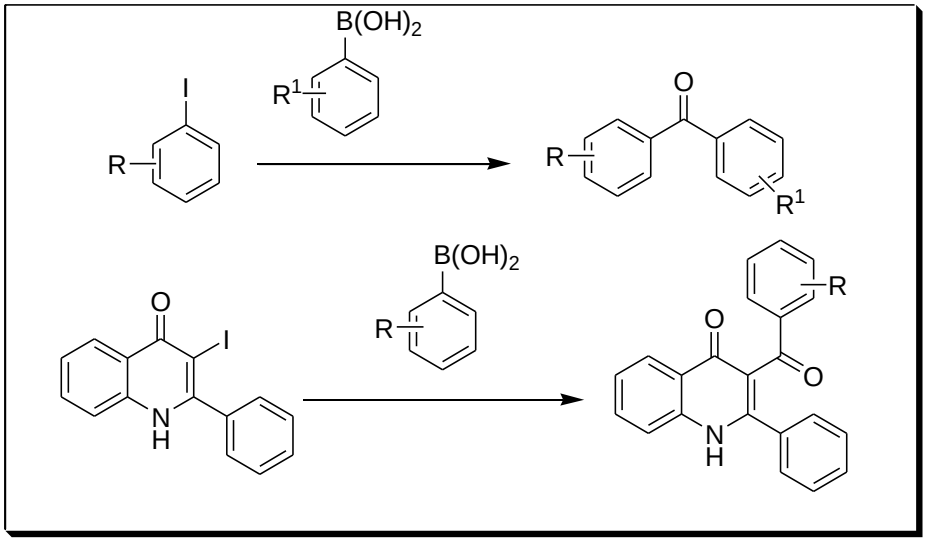


Fig: III.1. Some biologically active biaryl ketone compounds

III. B. Present work: Background & Objective:

However, the traditional transition metal catalysed carbonylative cross coupling reactions between aryl electrophiles, carbon monoxide and organometallic reagent is supposed to be the more convenient route for the synthesis of wide range of biaryl ketones. Several aryl metal reagents have been preferably used such as silicon[11], aluminium[12], tin [13]and magnesium [14]etc. The main disadvantage of this carbonylative cross coupling reaction is the formation several by products without carbon monoxide insertion, generally in the case of electron deficient aryl halides. Suzuki et.al firstly developed a facile protocol to synthesize the biaryl ketones from arylboronic acid, carbon monoxide and aryl halides in presence of palladium catalyst[15].In general, this method becomes quite effective due to the versatile nature of boronic acid which is non-toxic and stable to moisture and air. Afterwards, various research groups reported several methods for the synthesis of biaryl carbonyl scaffolds by using different palladium based catalyst such as $PdCl_2(PPh_3)_2$,[16]$PdCl_2(PPh_3)_2$/ $PdCl_2$(dppf),[17] $Pd(OAc)_2$-imidazolium salts,[18]$Pd(OAc)_2$/ N,N-bis(2,6-diisopropylphenyl)dihydroimidazolium chloride,[19] an MCM-41-supported bidentate phosphane palladium complex,[20] $Pd(OAc)_2$/di-1-adamantyl-n-butylphosphane[21][and Pd/thiourea,[22]. In spite of huge potential applicability, this method suffers from main disadvantage such as the use of air/moisture sensitive and expensive, phosphane donating ligands. Very recently, Bhanage et al. reported the Suzuki carbonylation of aryl and heterocyclic halides using palladacyle complex [23] and KCC-1supported palladium nanoparticles[24] using carbon monoxide gas as CO source. Applicability of CO gas at higher pressure reduces the formation of biaryl side products, but *insitu* generation of carbon monoxide in carbonylation process would much more effective in organic synthesis. In this context, several newly developed protocols are available in the literature such as formic acid, formates, formamides, chloroform, formic anhydride, and aldehydes, as well as metal carbonyls were used as CO source. Interestingly, the incorporation of carbon monoxide *via* metal carbonyl is much appealing and effective than any other methods.

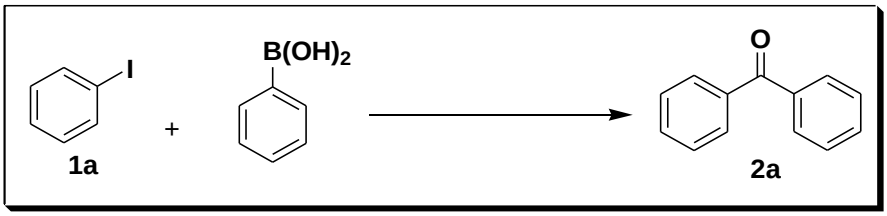


Scheme-III.1. Approach for the Biaryl ketones synthesis

Preliminary, we have focused our approach to insert the CO in situ in carbonylation process by using simple molybdenum hexacarbonyl as a solid handling reagent. Previously, Jafarpour et.al also reported the carbonylative Suzuki coupling of aryl halides and aryl boronic acid in presence of $Mo(CO)_6$ and Palladium acetate.[25]However, this method generally suffers from various disadvantages such as use high loading Pd catalyst (10 mol%), longer reaction time and high temperature. As a part of our ongoing efforts to develop the simple protocol for the formation of C-C bond, C-hetero atom bond formation, herein we explore the methodology of carbonylative Suzuki coupling reaction in between different aryl halides and arylboronic acids by using our pre-synthesized Pd-NHC[26] catalyst in low catalyst loading. Further, we apply this protocol to the biologically active 4-quinolone scaffold for developing its better pharmacokinetic properties. Our approach is free from microwave heating as well as using of toxic carbon monoxide gas.

III.B.1. Present work: Results and Discussion

Table-III.1. Optimization of the reaction condition for the carbonylative Suzuki coupling



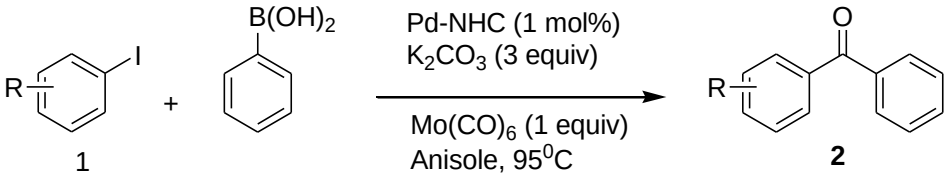
entry	Catalyst (mol %)	solvent	Base (equiv)	Temp (°C)	Time (h)	Yield (%)
1	Pd-NHC 1	DMF	K_2CO_3	95	24	15
2	Pd-NHC 1	THF	K_2CO_3	95	24	20
3	Pd-NHC 1	1,4-dioxane	K_2CO_3	95	24	NR
4	**Pd-NHC 1**	**anisole**	**K_2CO_3**	**95**	**1**	**85**
5	Pd-NHC 1	toluene	K_2CO_3	95	24	30
6	Pd-NHC 1	anisole	t-BuOK	95	24	10
7	Pd-NHC 1	anisole	DBU	95	24	NR
8	Pd-NHC 1	anisole	Cs_2CO_3	95	24	10
9	Pd-NHC 1	anisole	Et_3N	95	24	25
10	$Pd(OAc)_2$ 5	anisole	K_2CO_3	95	7	64
11	$PdCl_2$ 5	anisole	K_2CO_3	95	7	68
12	$Pd_2(dba)_3$ 5	anisole	K_2CO_3	95	7	73
13	Pd-NHC 1	anisole	K_2CO_3	80	4	65
14	Pd-NHC 1	anisole	K_2CO_3	60	12	52
15	Pd-NHC 1	anisole	K_2CO_3	120	1	84

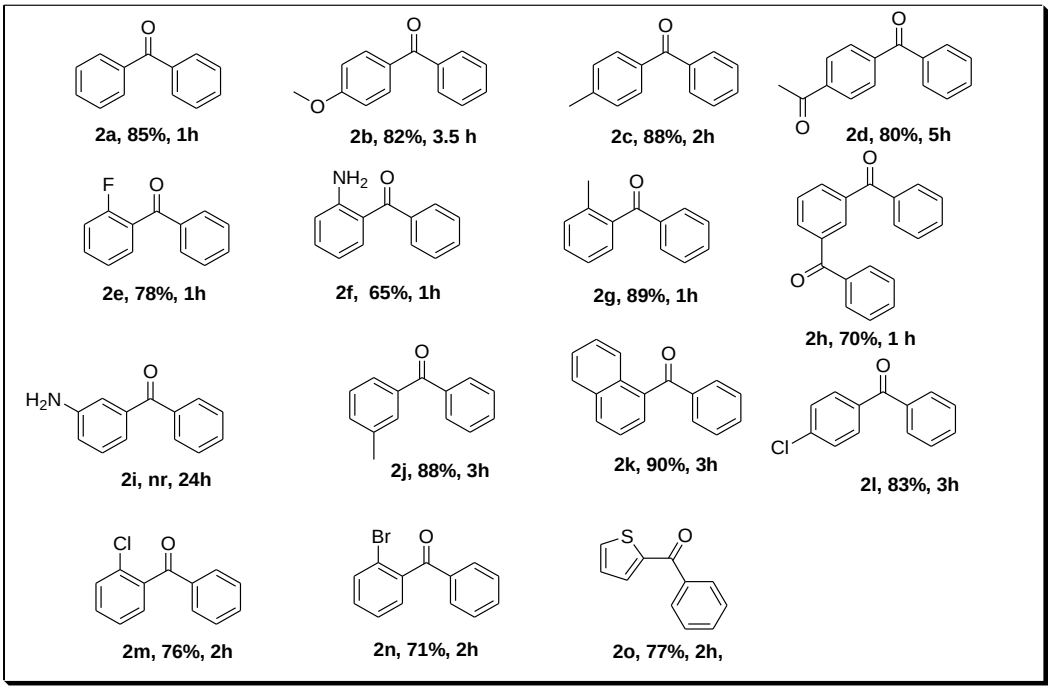
Reaction conditions: 0.25 mmol of iodobenzene, 0.375 mmol of phenylboronic acid, base (3 equiv), $Mo(CO)_6$ (1 equiv), were heated . Yield = Isolated yields.

To investigate the feasibility of the reaction, we commenced our journey *via* the carbonylative cross coupling reactions in between phenylboronic acid and iodobenzene using Pd-NHC (1 mol%) as catalyst in DMF in presence of K_2CO_3. However, only 15% yield of the desired biaryl ketone was obtained (Table-III.C.1; entry-1). Next, we screened the different solvents (Table-III.C.1; entry-1-5). Anisole as a solvent media served the better yields of

biaryl ketone whereas other solvents such as DMF, Toluene, 1, 4-dioxane and THF led to the biaryl as a predominant product. The combination of K_2CO_3/anisole proved to be the most suitable combination as base/ solvent for the carbonylative Suzuki coupling (Table-III.C.1; entry-4). Most surprisingly, the reaction completed within 1h only and yielded 85% of the desired product. We next turned our attention to choose the better base other than K_2CO_3. Inferior results of desired product was obtained by using several bases such as DBU, t-BuOK, Cs_2CO_3 and Et_3N (Table-III.C.1; entry-6-9). Further, we evaluated the catalytic activity of different palladium catalyst but not getting so much promising result as Pd-NHC (Table-III.C.1; entry 10-12). Rather, we also optimize the temperature and 95°C gave the best result (Table-III.C.1; entry-4). By lowering the temperature, the yield of the biaryl ketone decreases due to the low liberation of carbon monoxide (Table-III.C.1; entry 13, 14). By comparison, the same reaction, at 120°C resulted in only 84% yield of **2a** after 1h also (Table-III.C.1; entry 15). Eventually, the combination of Pd-NHC (1mol %) and K_2CO_3 (3 equiv), in DMF at 95 °C, was found to be optimal for the coupling of iodobenzene and arylboronic acids, leading to benzophenone in high yield (85%) after only 1h.

Scheme-III.2. Scope of various iodobenzene in the carbonylative Suzuki coupling

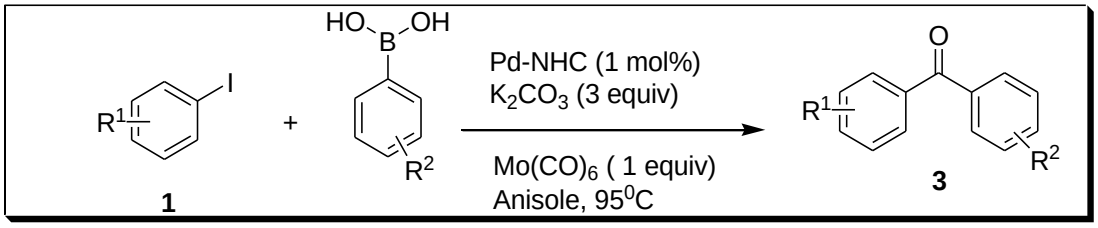


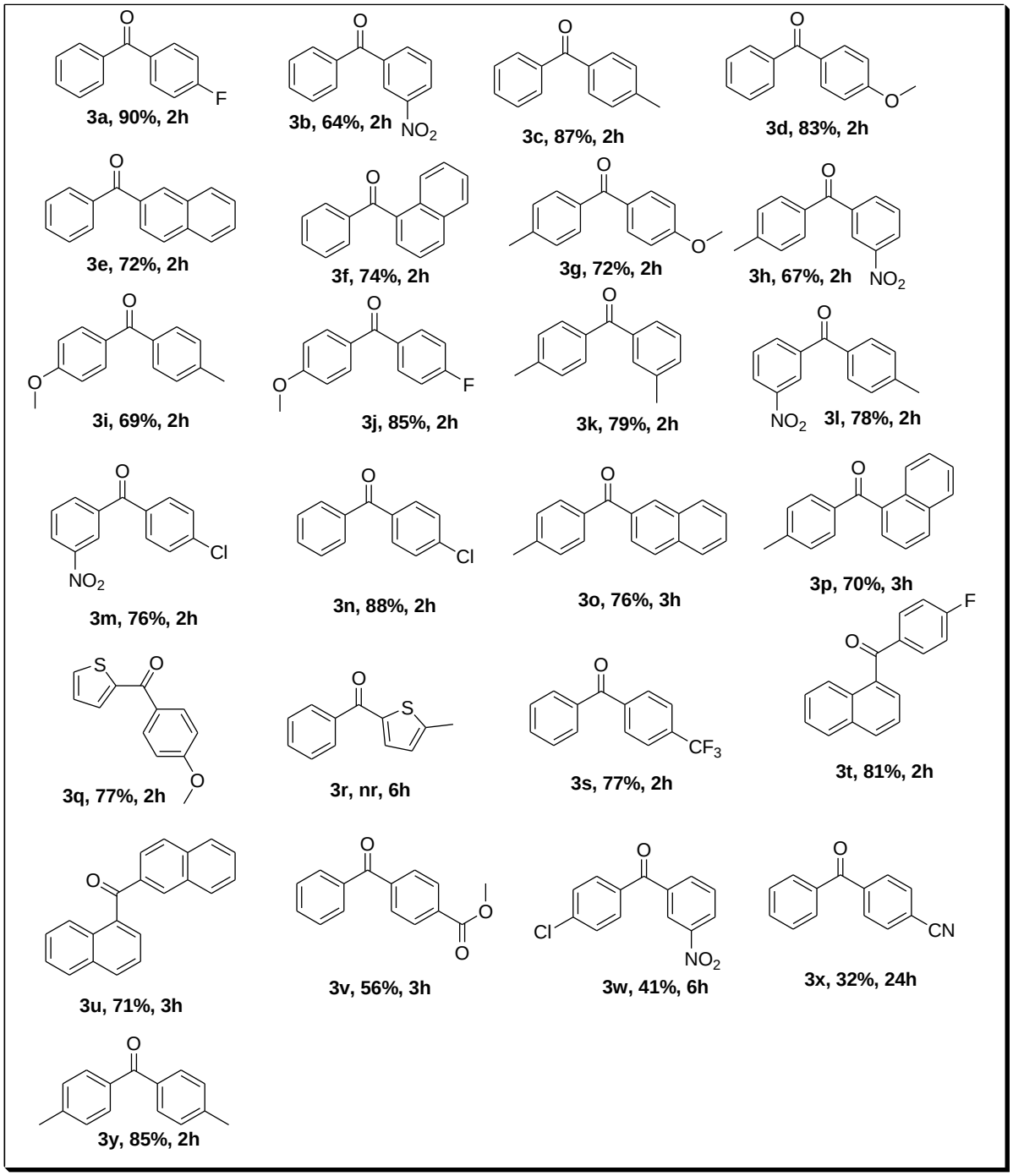


Reaction conditions: 0.25 mmol of various iodoarenes, 0.375 mmol of phenylboronic acid, base (0.75mmol,104mg) and Pd-NHC (3mg, 1mol%), $Mo(CO)_6$ (1 equiv), were heated in anisole . Yield = Isolated yield after column chromatography.

Encouraged by the above observation, the scope of the reaction with a broad range of aryl iodide was explored. Various iodoarenes possessing both electron withdrawing and electron releasing group participated in the reaction very well and afforded moderate to excellent yields (scheme-III.2; entry **2a-2o**). Iodobenzene reacted with phenyl boronicacid in a short span of time and resulted in 85% yield of benzophenone. Employment of *p*-methoxy and *p*-methyl substituted iodobenzene in carbonylative Suzuki coupling led to the promosing yield of the desired product (scheme-III.2, entry **2b, 2c**). 4-iodocetophenone took longer time and resulted 80% yield of the desired product. (scheme-III.2, entry **2d).** We also covered the aspect of steric hindrance in making the biaryl ketones via this coupling reaction. Such as ortho substituted -F, $-NH_2$,-Cl,-Br and –Me groups afforded the corresponding biaryl ketones in moderate to good yields respectively (scheme-III.2, entry **2e, 2f, 2g, 2m, 2n**). Whereas bulky 1-naphthyl iodoarenes responded very well and yielded 90% yield of the desired product in just 1h only. Nevertheless, 3-iodotoluene proved to be a good coupling partner for this coupling methodology (scheme-III.2, entry-**2j**). Surprisingly, 3-iodo aniline did not afford the corresponding biaryl ketone over 24h stirring (scheme-III.2, entry **2i**). Heterocyclic iodoarene (2-iodothiophene) was very prone to undergo the reaction and resulted 77% yield of the corresponding product (scheme-III.2, entry-**2o)**.

Scheme-III.3. Substrate scope of various iodoarenes and aryl(Het)boronic acid



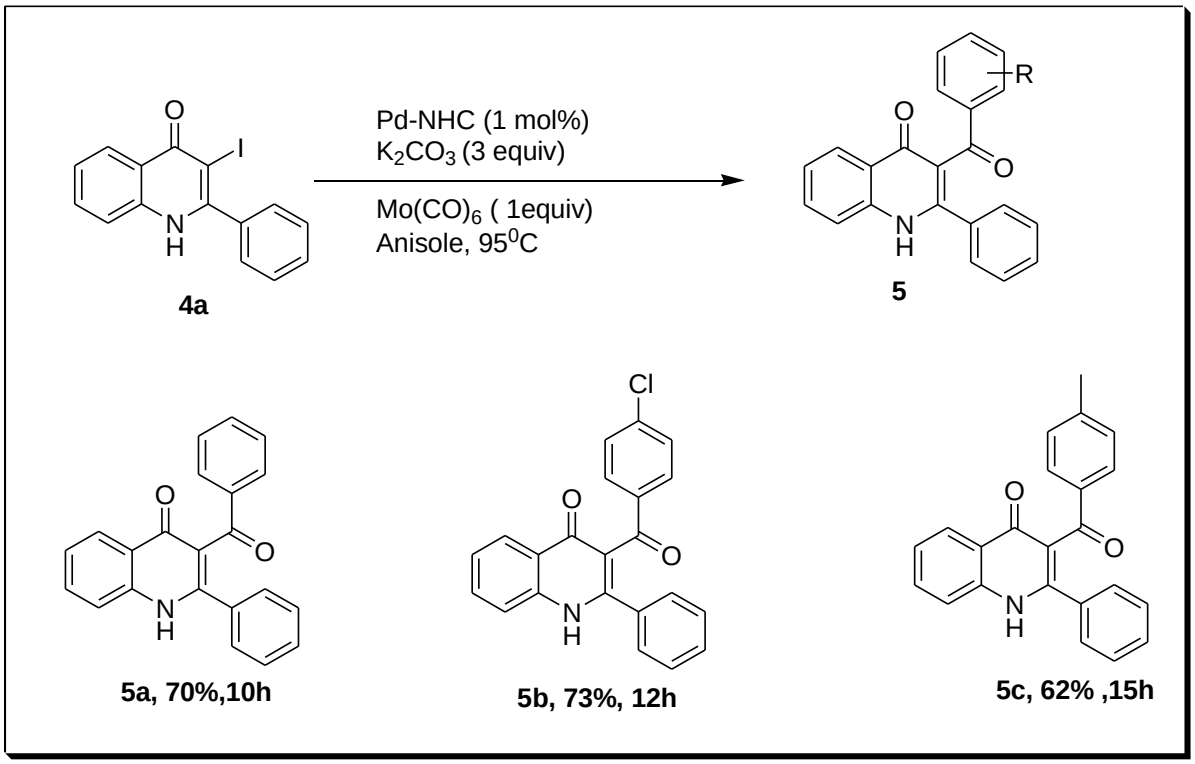


Reaction conditions: 0.25 mmol of various iodobenzene, 0.375 mmol of substituted arylboronic acid, base (3 equiv) and Pd-NHC (3mg, 1mol%), $Mo(CO)_6$ (66mg, 1 equiv), were heated in anisole . Yield = Isolated yields.

To further investigate the scope, we extensively surveyed the carbonylative Suzuki coupling with various iodoarenes and arylboronic acids under our optimized reaction condition. A broad array of arylboronic acid possessing both electron donating and electron releasing group were well tolerated in this reaction. Our protocol was quite compatible with various functional groups like methoxy, chloro, fluoro, ester and cyano. Bulky naphthylboronic acid (1-naphthyl and 2-naphthyl) were quite effectively coupled with iodobenzene and 4-

iodoarenes and afforded the desired products with much higher yields (scheme-III.3; entry **3e**, **3f**, **3o**, **3p**). We were also pleased to find that a heterocyclic iodoarenes (2-iodo thiophene) coupled with 4-methoxyphenyl boronic acid effectively (scheme-III.3; entry-**3q**). Importantly, 1-iodonaphthalene quite successfully underwent the carbonylative Suzuki coupling with 2-naphthylboronic acid and 4-fluoro phenylboronic acid (scheme-III.3; entry **3t**, **3u**). Surprisingly, 4-cyano phenylboronic acid afforded only 32% yield of the desired biaryl ketone when it coupled with normal iodobenzene (scheme-III.3; entry **3x**). To our delight, iodoarene possessing nitro group at meta position did not hamper the process and coupled with both electron deficient and electron rich arylboronic acid (scheme-III.3; **3l**, **3m**). More interestingly, 4-iodotoluene coupled with *p*-tolylboronic acid excellently and furnished the corresponding product **3y** (85%) in a very short span.

Scheme-III.4. Scope of the carbonylative Suzuki coupling in 4-quinolone scaffold



Reaction conditions: 0.25 mmol of 3-iodo substituted 4-quinolone (86mg), 0.375 mmol of substituted arylboronic acid, base (3 equiv) and Pd-NHC (3mg, 1mol%), $Mo(CO)_6$ (66mg, 1 equiv), were heated in anisole . Yield = Isolated yields.

Next, we explored the scope of the reaction into the biologically active 4-quinolone scaffold. Very recently, Alfonsi et.al synthesized the 3-Aroylquinolin-4(1*H*)-ones which act as a inhibitors of the Hedgehog Signaling Pathway.[27]3-iodo-2-aryl substituted 4-quinolone participated well in this carbonylative Suzuki coupling. Both electron withdrawing and electron donating arylboronic acid effectively underwent the reaction and resulted in the desired products respectively (scheme-III.4; entry **5b** and **5c**).

III.C. Conclusion

In summary, we have developed a simple mild protocol for the synthesis of biaryl ketones via carbonylative Suzuki coupling. Notably, this method offers various advantages such as free of toxic CO gas, shorter reaction time, good to excellent yield of the desired product and broad substrate scope availability. Several functional groups (-COMe, -COOMe,-F,_Cl) were well tolerated in this reaction. This approach was quite effective in the biological active 4-quinolone scaffold to synthesize the 3-Aroylquinolin-4(1*H*)-ones.

III.D. Experimental section:

III.D.1. General Information:

Unless stated otherwise, all reagents such as various Iodoarenes, aryl(Het)boronic acid, K_2CO_3, Anisole, $Mo(CO)_6$ and solvents were used as received from commercial suppliers. NMR spectra were recorded on 300 MHz spectrometer at 298 K with calibration done on the basis of solvent residual peak. Products were purified using column chromatography on silica gel (60-120 mesh). Ethyl acetate and petroleum ether ($60\text{-}80^0$C) were used as eluents. Progress of reaction was monitored using silica gel TLC.

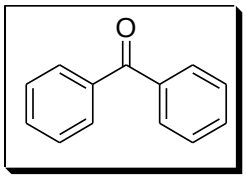
III.D.2. Preparation of Biaryl ketones from the carbonylative Suzuki coupling of various iodoarenes and arylboronic acids:

Initially, various iodoarenes (0.25 mmol), aryl(Het) boronicacid (0.375 mmol), K_2CO_3 (0.75 mmol, 103.5 mg) $Mo(CO)_6$ (0.25 mmol, 66mg), Pd-NHC (1 mol%, 2.5mg) and anisole (2 ml) were taken in a sealed tube under N_2 atmosphere and heated at 95°C. The reaction was continued for 1h to several hours for completion of the reaction. After monitoring the TLC analysis, the reaction mixture was diluted with 30 ml water and the organic layer was extracted with DCM (30 ml). Then, it was dried over anhydrous sodium

sulphate and concentrated under reduced pressure. The crude residue was purified through column chromatography using pet.ether and ethyl acetate as an eluents.

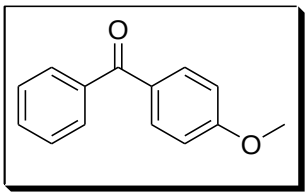
III.D.3. Physical characteristics and spectral data of compounds:

1**. Benzophenone (2a)**[28]



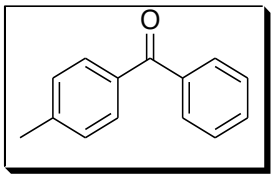
White solid, Melting point: 47-48 °C, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47-7.53 (m,4H), 7.58-7.64 (m, 2H), 7.80-7.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 128.3, 130.1, 132.4, 137.6, 196.8.

2. **(4-methoxy phenyl) phenyl methanone (2b and 3d)**[28]



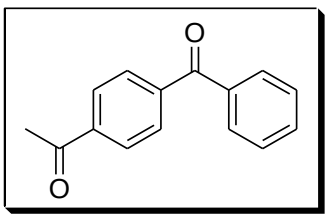
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (s, 3H), 6.95-6.98 (m, 2H), 7.44-7.49 (m, 2H), 7.53-7.59 (m, 1H), 7.73-7.76 (m, 2H), 7.77-7.84 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.5, 113.6, 128.2, 129.7, 130.2, 131.9, 132.5, 138.3, 163.2, 195.6.

3. **Phenyl (*p*-tolyl)methanone (2c and 3c)**[28]



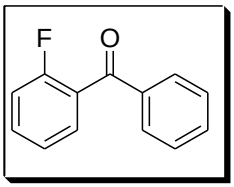
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.44 (s, 3H), 7.26-7.30 (m, 2H), 7.44-7.50 (m, 2H), 7.54-7.60 (m,1H), 7.70-7.74 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6,128.3, 129.0, 129.9, 130.3, 132.1, 134.9, 138.0, 143.2, 196.5.

5. 1-(4-Benzoylphenyl)ethan-1-one (2d)[29a]



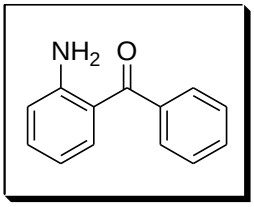
yellow oil, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.69 (s, 3H), 7.50-7.55 (m, 2H), 7.62-7.65 (m, 1H), 7.81-7.84 (m, 2H), 7.87-7.90 (m, 2H), 8.07-8.09 (m, 2H),^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.8, 128.1, 128.4, 130.0, 130.1, 132.9, 136.9, 139.6, 141.4, 195.9, 197.5.

6. (2-fluoro phenyl)(phenyl)methanone (2e)[30]



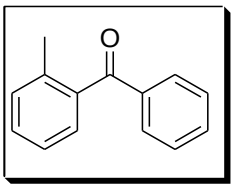
Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53-7.57 (m, 2H), 7.69-7.73 (m, 1H), 7.82 (s, 2H), 7.93 (s, 2H), 8.20 (d, *J* = 8.0Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.0, 125.3, 128.8, 129.0, 130.6, 134.8, 134.9, 162.0, 189.6.

7. (2-aminophenyl)(phenyl)methanone (2f)[30]



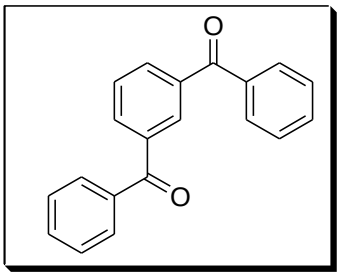
Yellow solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.00 (s, 2H), 6.57-6.72 (m, 1H), 6.73-6.75 (m, 1H), 7.26-7.32 (m, 1H), 7.43-7.65 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 115.5, 117.0, 118.2, 128.1, 129.1, 131.1, 134.2, 134.6, 140.1, 150.9, 199.1.

8. phenyl(o-tolyl)methanone (2g)[28]



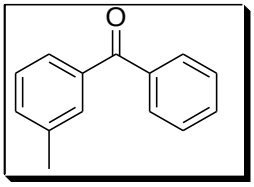
Colorless liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.33 (s, 3H), 7.24-7.35 (m, 3H), 7.37 (t, *J* = 7.5Hz, 1H), 7.44 (t, *J* = 7.5Hz, 2H), 7.57 (t, *J* = 7.5Hz, 1H), 7.78 (d, *J* = 7.5Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.5, 124.7, 127.8, 128.1, 129.5, 129.7, 130.5, 132.7, 136.3, 137.3, 138.3, 197.9.

9. (2h) [28]



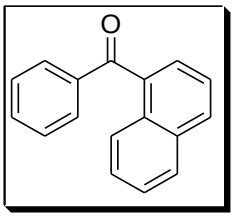
White solid, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.57-7.62 (m, 1H), 7.68-7.70 (m, 3H), 7.79-7.82 (m, 4H), 8.00-8.04 (m, 1H), 8.05-8.08 (m, 2H), ^{13}C NMR (DMSO-d_6, 75 MHz) δ 129.1, 129.7, 130.2, 131.2, 133.5, 133.9, 136.9, 137.5, 195.5.

10. Phenyl (m-tolyl)methanone (2j)[28]:



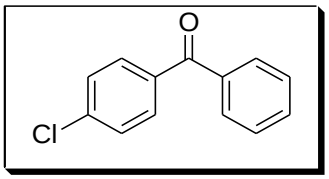
Colourless liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 7.39-7.40 (m 2H), 7.49-7.51 (m, 2H), 7.57-7.64 (m, 3H), 7.79-7.82 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.8, 126.8, 127.6, 127.7, 129.5, 130.0, 131.8, 132.6, 137.2, 137.3, 137.6, 196.4.

11. (Naphthalen-2-yl)(phenyl)methanone (2k and 3f)[28]:



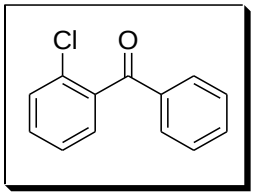
Colourless oil, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45-7.64 (m, 7H), 7.88-7.97 (m, 3H), 8.01-8.03 (m, 1H), 8.10-8.14 (m,1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.4, 125.7, 126.5, 127.3, 127.97, 128.4, 128.51, 130.5, 131.0, 131.4, 133.3, 133.7, 138.3, 198.1.

12. (4-chloro phenyl)(phenyl) methanone (2l and 3n)[28]



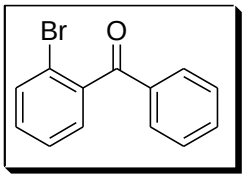
White solid, 1H NMR ($CDCl_3$, 300 MHz) δ 7.44-7.52 (m, 4H), 7.58-7.63 (m, 1H), 7.74-7.79 (m, 4H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 128.4, 128.6, 129.9, 131.5, 132.6, 135.9, 137.2, 138.9, 195.2.

13. (**2-chlorophenyl)phenyl methanone (2m)[30]:**



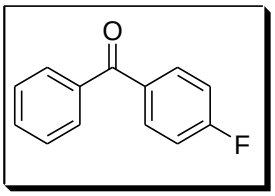
Colourless oil, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83-7.85 (d, *J* =7.8 Hz, 2H), 7.60-7.65 (t, *J* =7.5 Hz, 1H), 7.46-7.51 (m, 4H), 7.38-7.44 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 129.1, 128.6, 126.7,128.6, 129.1, 130.1, 130.2, 131.1, 131.3, 133.7, 136.4, 138.5, 195.4.

14. (2-bromophenyl)(phenyl)methanone (2n)[31]:



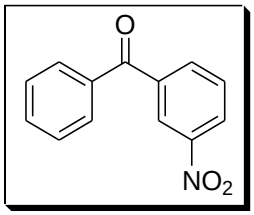
Yellow solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.50 (m, 5H), 7.58-7.66(m, 2H), 7.80-7.83(m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 119.5, 127.2, 128.6, 129.0, 130.2, 131.2, 133.2, 133.8, 136.1, 140.7, 195.9.

15. **4-Fluoro phenyl) phenyl methanone (3a)[31]**



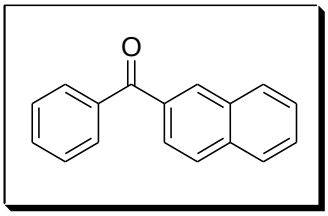
Yellow oil, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13-7.20 (m, 2H), 7.46-7.51 (m, 2H), 7.57-7.62 (m, 1H), 7.75-7.79 (m, 2H), 7.82-7.87 (m, 2H),^{13}C NMR ($CDCl_3$, 75 MHz) δ 115.3, 115.6, 127.5, 128.3, 128.7, 129.2, 129.8, 132.4, 132.6, 132.7, 133.8, 137.5, 163.7, 167.1, 195.2.

16. (3-nitrophenyl)(phenyl)methanone (3b)[32]:



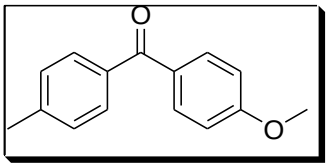
Yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53-7.57 (m, 2H), 7.64-7.74 (m, 2H), 7.79-7.83 (m, 2H), 8.15 (td, *J*= 3.0 Hz, 1.2Hz, 1H), 8.45 (m, 1H), 8.62 (t, *J*=1.8Hz, 1H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.3, 126.3, 128.3, 129.2, 129.6, 133.0, 135.0, 138.7, 147.7, 193.7.

17. (Naphthalen-3-yl)(phenyl) methanone (3e)[28]



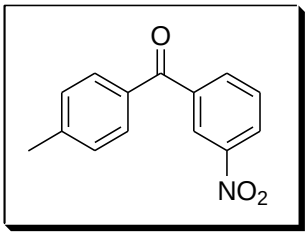
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41-7.60 (m, 7H), 7.84-7.92 (m, 3H), 7.97-7.99 (m,1H), 8.07-8.10 (m, 2H),^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.4, 125.7, 126.5, 127.3, 127.8, 128.4, 128.5, 130.4, 131.0, 131.3, 133.3, 133.7, 136.4, 138.3, 198.1.

18. 4-methoxy phenyl(p-tolyl) methanone (3g & 3i)[28]



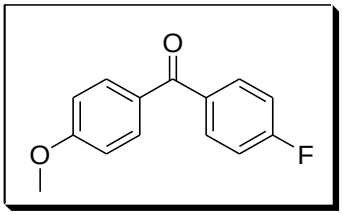
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 3.88 (s, 3H), 6.95 (dt, *J* =4.8Hz, 2.7Hz, 2H), 7.26-7.29 (m, 2H), 7.67 (dd, *J*=8.1Hz, 1.8Hz, 2H), 7.78-7.82 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 55.5, 113.5, 128.9, 130.0, 130.5, 132.5, 135.5, 142.6, 163.0, 195.4.

19. (3-nitrophenyl)(p-tolyl)methanone (3h and 3l)[33]



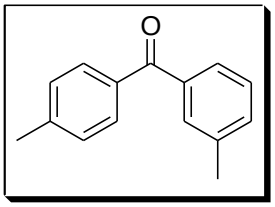
Yellow solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.47 (s, 3H), 7.32-7.34 (m, 2H), 7.67-7.73 (m, 3H), 8.12 (td, *J* =2.7Hz, 1.5Hz, 1H), 8.43 (qd, *J* = 3.6Hz, 1.2Hz, 1H), 8.60(t, *J* =1.8Hz, 1H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 124.6, 126.4, 129.4, 129.5, 130.2, 133.6, 135.3, 139.5, 144.4, 148.1, 193.8.

20. (4-fluorophenyl)(4-methoxyphenyl)methanone (3j)



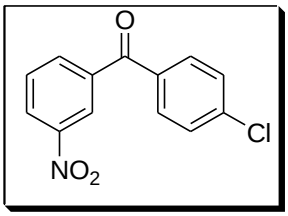
White solid, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.08-7.11(m, 2H), 7.38 (dt, *J* = 6.9Hz, 1.8Hz, 2H), 7.72-7.79 (m, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 56.0, 114.4, 115.8, 116.1, 129.7, 132.6, 132.7, 134.6, 134.7, 163.1,163.4, 166.4, 193.5.

21. *m*-tolyl(*p*- tolyl) methanone (3k)[34]



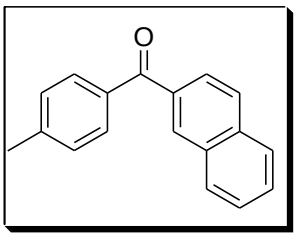
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 3H), 7.25-7.38 (m, 4H), 7.53-7.60 (m, 2H), 7.70-7.73 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 21.6, 127.2, 128.0, 128.9, 130.3, 130.3, 132.9, 135.1, 138.0, 138.1, 143.1, 196.7.

22. (4-chloro phenyl)(m-nitro) methanone (3m)[35]



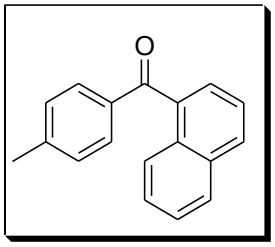
Yellow solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51(td, *J*=4.2Hz, 2,1Hz, 2H), 7.70-7.78 (m, 3H), 8.12 (td, *J* =3.0Hz, 1.5Hz, 1H), 8.46 (qd, *J* =2.4Hz, 1.2Hz, 1H), 8.59 (t, *J*=1.8Hz, 1H),^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.6, 126.9, 129.1, 129.4, 129.8, 131.4, 134.5, 135.3, 138.7, 140.0, 148.1, 193.0.

23. (Naphthalen-2-yl)(*p*-tolyl)methanone (3o)[36]



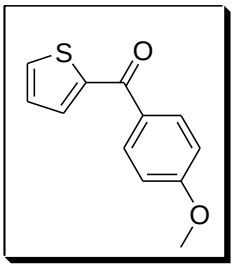
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.47 (s,3H), 7.32 (d, *J*=8.1Hz, 2H), 7.54-7.63 (m, 2H), 7.78 (dd, *J*=1.8Hz, 2H), 7.90-7.93 (m, 4H), 8.25 (s, 1H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 125.9,126.7, 127.8, 128.1, 128.2, 129.1, 129.4, 130.4, 131.5, 132.4, 135.2, 135.3, 143.2, 196.5.

24. (**Naphthalen-1-yl)(*p*-tolyl)methanone (3p)**[28]**



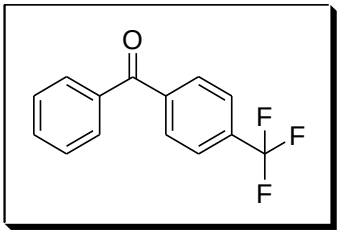
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.41(s, 3H), 7.22-7.25 (m, 2H), 7.44-7.56 (m, 4H), 7.77 (d, *J*=8.1Hz, 2H), 7.90 (dd, *J*=7.5Hz, 2.4Hz, 1H), 7.96-7.98 (m, 1H), 8.02-8.06 (m, 1H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.8, 124.4, 125.7, 126.4, 127.1, 127.4, 128.4, 129.2, 130.6, 130.9, 131.0, 133.7, 135.7, 136.8, 144.2, 197.8.

25. (4-methoxyphenyl)(thiophen-2-yl)methanone (3q)[24]



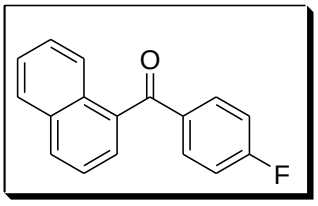
white solid, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.89 (s, 3H), 6.99 (dd, *J* = 4.8Hz, 2.1Hz, 2H), 7.14-7.17 (m, 1H), 7.64-7.70 (m, 2H), 7.90 (dd, *J* = 4.8 Hz, 2.1Hz, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 55.5, 113.7, 127.8, 130.7, 131.6, 133.4, 134.0, 143.8, 163.1, 186.9.

26. 4-trifluoromethyl-benzophenone (3s)[31]



white solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (t, *J* = 7.5Hz, 2H), 7.64 (t, *J* = 7.2Hz, 1H), 7.75 (d, *J* = 8.4Hz, 2H), 7.81 (d, *J* = 7.2Hz, 2H), 7.90 (d, J = 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 123.7, 125.4, 128.5, 130.1, 133.1, 133.7, 136.7, 140.7, 195.6.

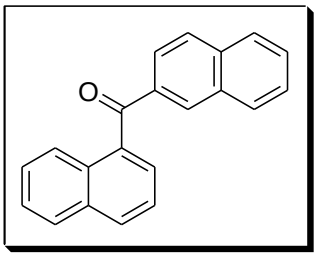
27. (4-fluorophenyl)(naphthalene-4-yl)methanone (3t)[23]



white solid, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.35-7.41 (m, 2H), 7.55-7.64 (m, 4H), 7.83-7.92 (m, 3H), 8.06-8.09 (m, 1H), 8.16-8.19 (m,1H); ^{13}C NMR

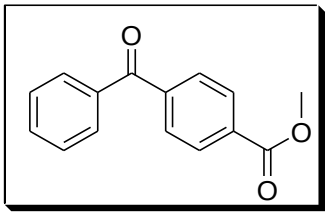
(DMSO-d_6, 75 MHz) δ 116.3, 116.5, 125.2, 126.2, 127.1, 127.9, 128.6, 129.1, 130.5, 131.7, 133.3, 133.4, 133.7, 134.7, 134.7, 136.0, 164.0, 167.3, 196.2.

28. (napthalen-2-yl)(napthalen-5-yl)methanone (3u)[37]



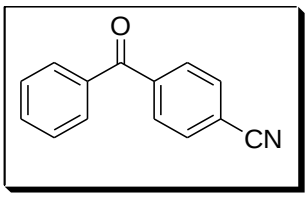
white solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48-7.54 (m, 4H), 7.57-7.66 (m, 2H), 7.83 (d, *J* = 8.1Hz, 1H), 7.89-7.97 (m, 3H), 8.03-8.13 (m, 3H), 8.24 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 124.4, 125.4, 125.7, 126.5, 126.8, 127.3, 127.7, 127.8, 128.4, 128.5, 128.7, 129.7, 131.0, 13 1.2, 132.4, 132.9, 133.8, 135.6, 135.7, 136.6, 198.0.

29. Methyl-4-benzoylbenzoate (3v)[29b].



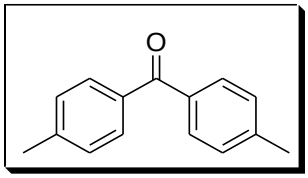
white solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.96 (s, 3H), 7.47-7.52 (m, 2H), 7.59-7.61 (m, 1H), 7.78-7.85 (m, 4H), 8.13-8.16 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.5, 128.5, 129.5, 129.8, 130.2, 133.0, 133.2, 136.9, 141.3, 166.3, 196.0.

30. (4-cyano phenyl) (phenyl) methanone (3x)[28]



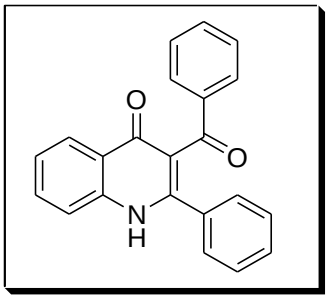
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.54 (m, 2H), 7.62-7.64 (m, 1H), 7.71-7.81(m, 4H), 7.86-7.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 115.7, 118.0, 128.6, 130.1, 130.2, 132.2, 133.3, 136.3, 141.2, 195.0.

31. di(*p*-tolyl)methanone (3y)[28]



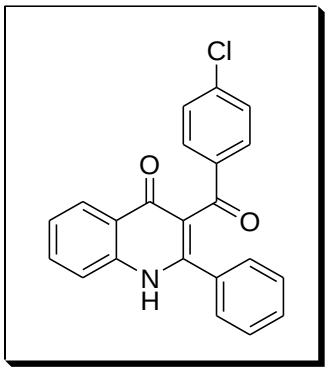
White solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.45 (s, 6H), 7.26 (d, J = 8.4Hz, 4H), 7.70 (d, J = 8.1Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.5, 128.8, 130.1, 135.2, 142.8, 196.2.

32. 3-benzoyl-2-phenyl-quinolin-4-(1*H*)-one (5a) [38]



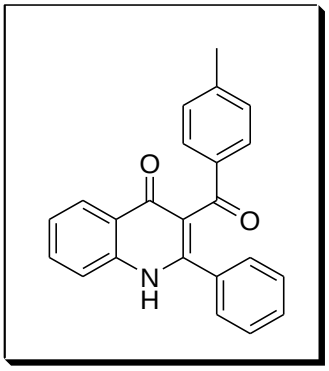
white solid, melting point:>260°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.38-7.53 (m, 8H), 7.56 (t, *J* = 7.5Hz, 1H), 7.75-7.79 (m, 4H), 8.10 (d, *J* = 8.1Hz, 1H), 12.2 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 119.3, 120.7, 124.5, 125.2, 125.3, 128.9, 129.0, 129.1, 129.4, 130.5, 132.9, 133.5, 134.0, 138.4, 140.3, 149.9, 175.5, 196.2.

33. 3-benzoyl-(4-chlorophenyl)-quinolin-4-(1*H*)-one (5b) [38]



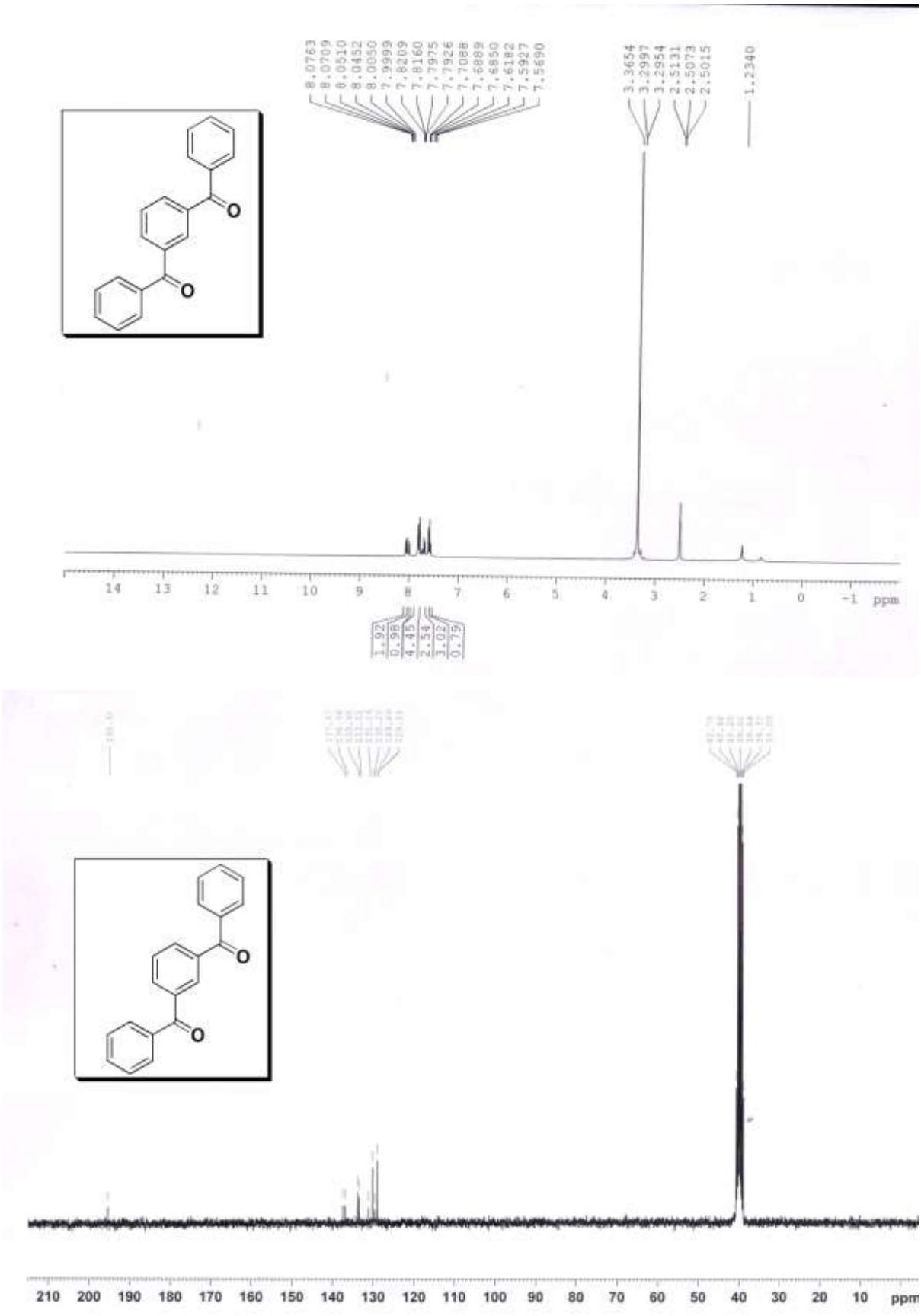
Pale yellow solid, melting point:>260°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.41-7.51 (m, 8H), 7.75-7.81 (m, 4H), 8.10 (d, *J* = 8.1Hz, 1H), 12.2 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 119.4, 120.2, 120.2, 124.5, 125.3, 129.0, 129.1, 129.2, 130.5, 131.3, 133.0, 134.0, 137.2, 138.3, 140.4, 150.5, 175.5, 195.1.

34. 3-(4-Methylbenzoyl)-2-phenylquinolin-4(1*H*)-one (5c)[38]

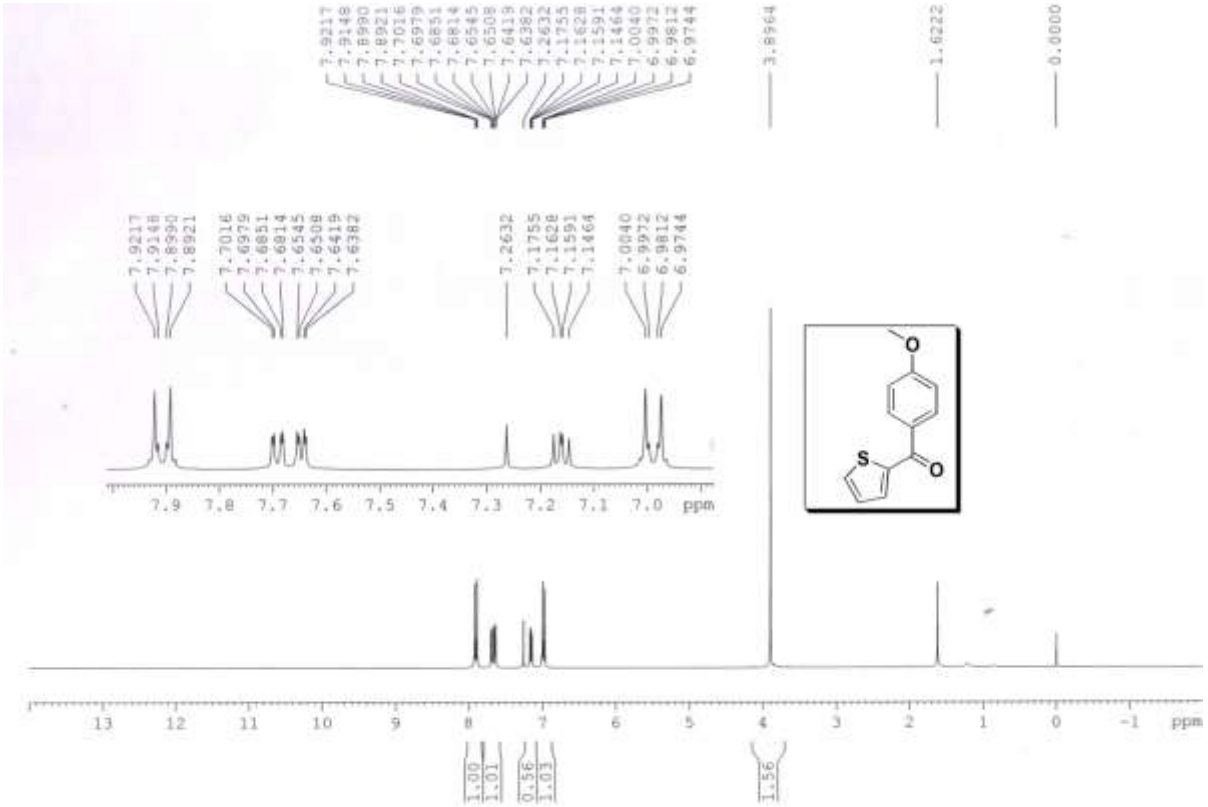


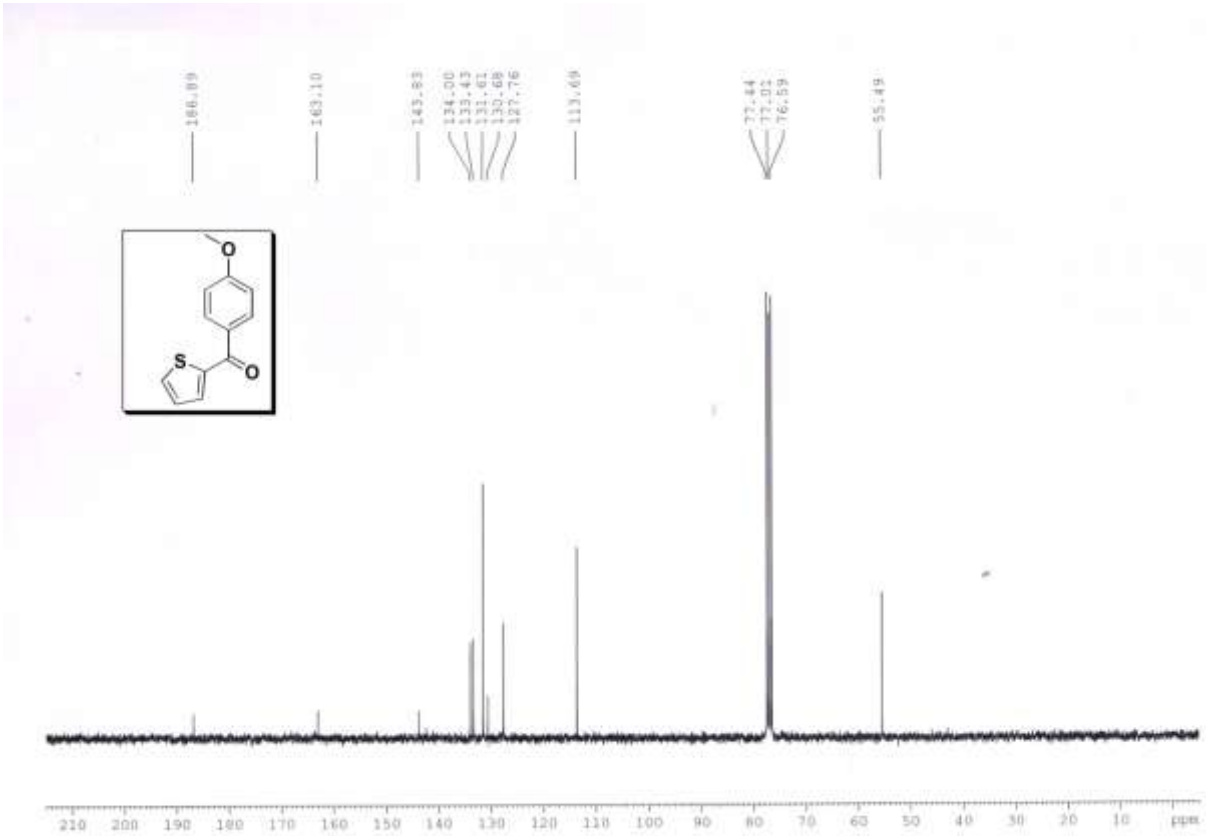
Brown solid, melting point: >260°C, ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.33 (s, 3 H),7.22 (d, *J* = 8.0 Hz, 2 H), 7.40−7.49 (m, 6 H),7.67 (d, *J* = 8.0 Hz, 2 H), 7.75−7.79 (m, 2 H), 8.10 (d, *J* = 8.0 Hz, 1 H), 12.12 (s, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 21.5, 119.3, 120.7, 124.5, 125.2, 125.3, 128.9, 129.0, 129.1, 129.4, 130.5, 132.9, 133.5, 134.0, 138.4, 140.3, 149.9, 175.5, 196.2.

^{1}H and ^{13}C NMR spectra of entry 2h (Scheme-III.2.) in DMSO-d_6

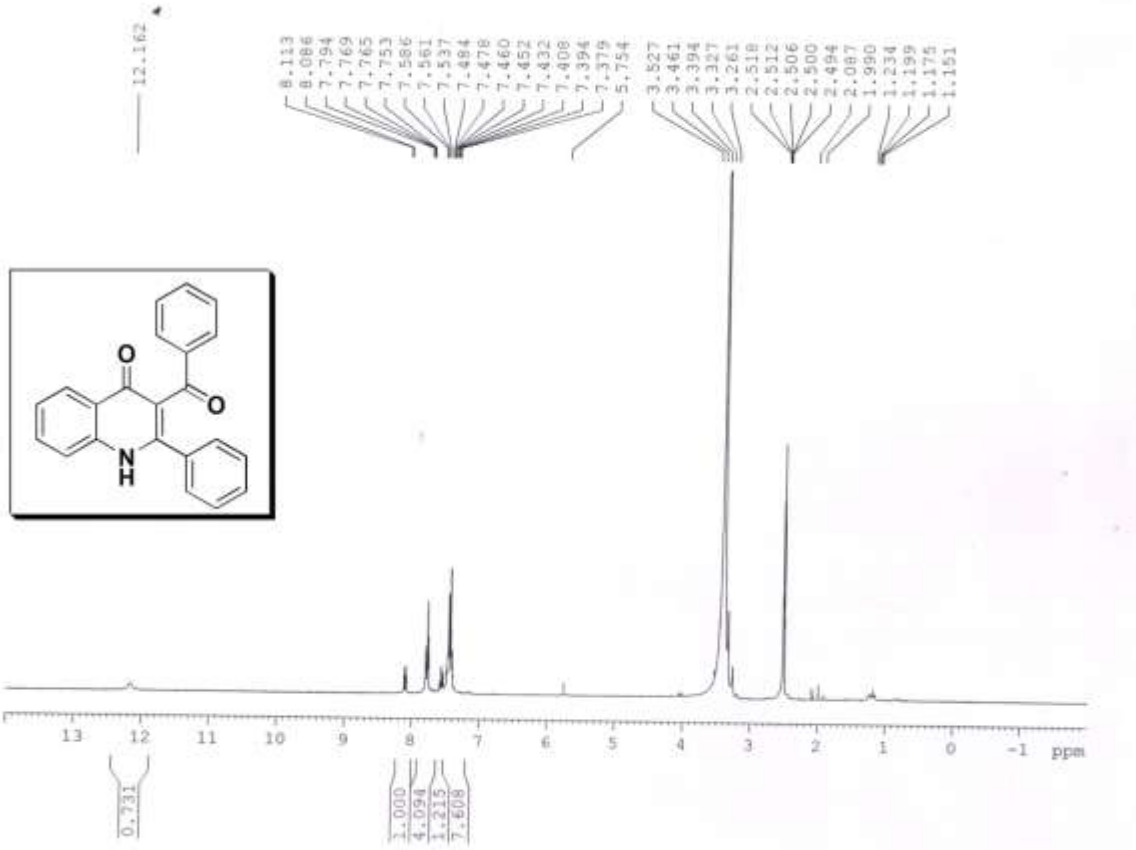


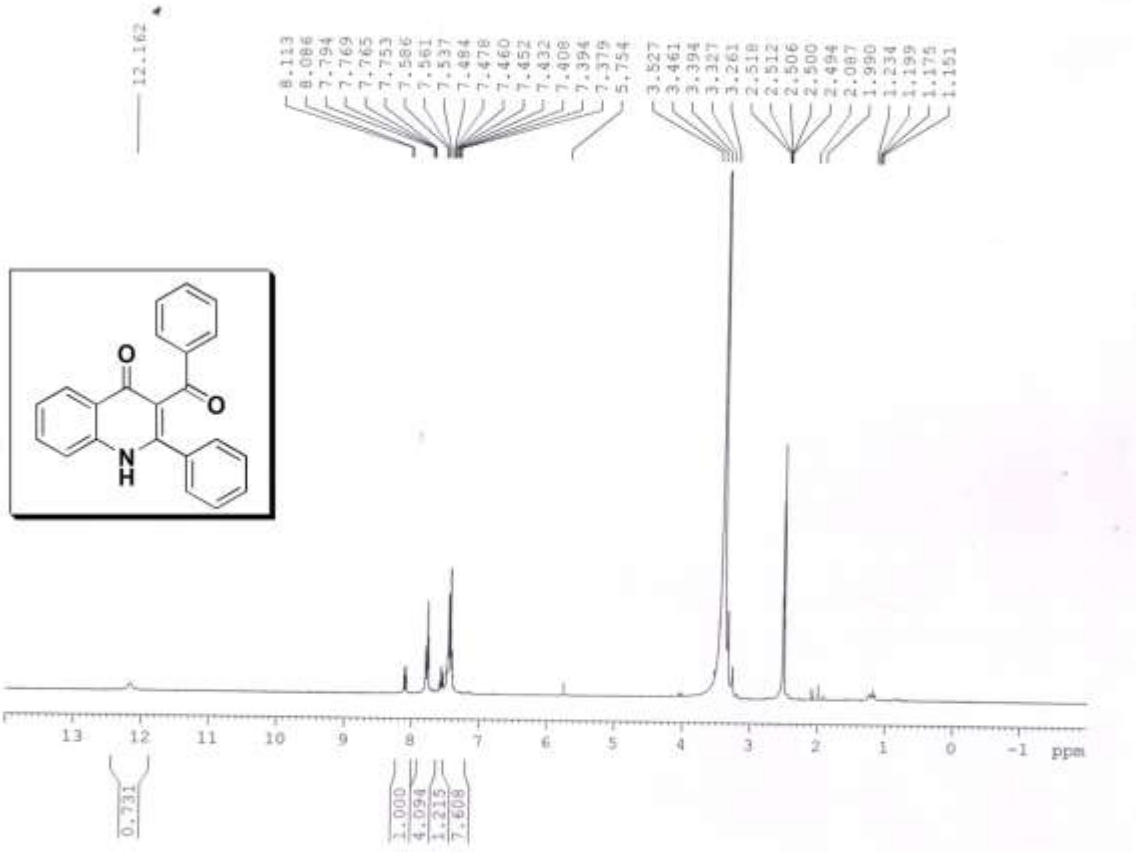
^{1}H and ^{13}C NMR spectra of entry 3q (Scheme-III.3.) in DMSO-d_6





^{1}H and ^{13}C NMR spectra of entry 5a (Scheme-III.4.) in DMSO-d_6





III.E. References

References are given in BIBLIOGRAPHY under Chapter III (pp-229-231)