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Metal-Free Synthesis of 4-Aryl-2-quinolone Derivatives by Iodine-Mediated Intramolecular C-H Amidation

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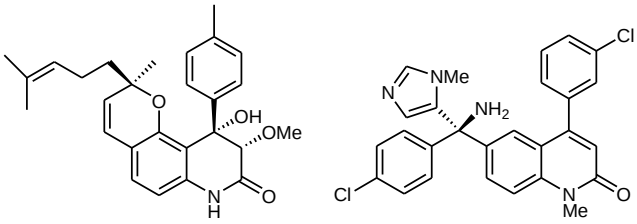
Abstract. A metal-free synthesis of a range of 4-aryl-2-quinolone derivatives has been developed which utilizes an iodine-mediated intramolecular C-H amidation of 3,3-diarylacryl amides as the key step. Electron-withdrawing or -donating substituents in either of the aryl rings display marginal influence on the course of the reaction. However, the presence of the diarylalkene moiety has been found to be crucial for the success of the reaction. The reaction proceeds in very good yield and is applicable to a range of substrates. Moreover, the methodology overcomes some of the difficulties associated with metal-mediated approaches such as regio-isomeric product formation, and *E-Z* isomerization. We propose a mechanism involving the *in situ* generation of hypoiodous acid as source of positive iodine.

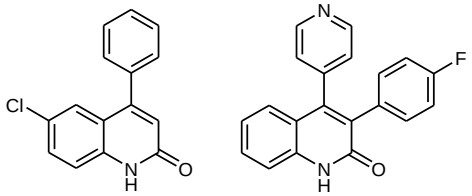
Keywords: C-H amidation; iodine; heterocycles; catalysis, synthetic methods

Introduction

4-Aryl-2-quinolones are important as naturally occurring compounds and pharmaceutically relevant structures since they exhibit a range of biological activities. For example, they have been found to inhibit the enzymes acyl coenzyme A and cholesterol acyl transferase, act as K-channel openers, and endothelin receptor antagonists.[1] Moreover, some of these derivatives (e.g. Tipifarnib, 2, Figure 1) also exhibit useful level of anti-cancer activity. [2] For this,



1, Yaequinolone **2**, Tipifarnib (zarnestra)



3, HBV inhibitor **4**, Kinase inhibitor

Figure 1. Structures of some important 4-aryl-2-quinolone derivatives

and other reasons, continuing efforts have been expended to develop new methodology towards the synthesis of this important heterocyclic motif.

Although classical cyclization methods such as Knöevenegal condensation[3]/ Knorr-type cyclization [4]/ Friedländer-type cyclization [5]/ protic and Lewis acid-mediated cyclization of *N*,3-diarylpropiolamides[6] are popular, several elegant transition metal catalyzed procedures have been developed in recent years. Among these, palladium-,[7] copper-[8] and gold-catalyzed[9] hydroarylation; transition metal-mediated[10]/transition metal-free carbonylation [11] of 2-alkenyl anilines; palladium-[12] / ruthenium-catalyzed C-H activation,[13] and Pd-catalyzed intramolecular amination[14] reactions, among others,[15] have emerged. Similarly, metal-catalyzed intramolecular amidation of 3,3-diarylacryl amides (**6**, Scheme 1), either pre-formed [16] or *in situ* generated from cinnamide **5** in a domino process[17] involving synergistic catalysis by Pd/Cu/Ag/Ir species has given fascinating results. Nonetheless, these have necessitated the use of sophisticated ligands, and simultaneous use of two or more heavy metal catalysts. Moreover, problems of electronic influence, compromise in regioselectivity and/or *E-Z* isomerization have occasionally been observed. In recent years, iodine-mediated heterocyclization reactions[18] have gained importance as metal-free variants[19] for heterocyclic synthesis. Herein, we describe a metal-free molecular iodine-mediated

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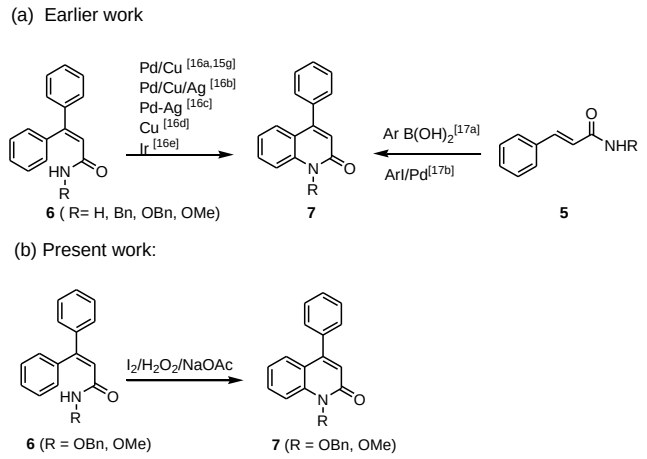
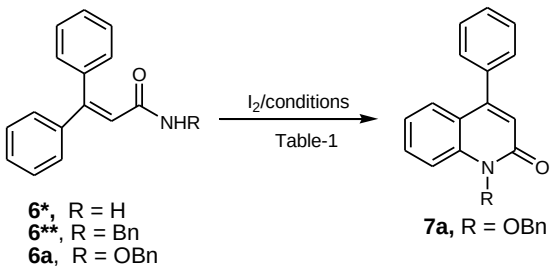
synthesis of the 4-aryl-2-quinolone ring system involving intramolecular C-H amidation of diarylacrylamides as the key step.



Scheme 1. Previous and present work

Results and Discussion

Iodine-mediated intramolecular amination has been carried out using hypervalent iodine compounds [20] under oxidative conditions. Iodine (III) reagents have also been recently used to prepare 2-quinolone ring system. [21] *N*-Iodosuccinimide[22] has been extensively used in heterofunctionalization reactions. In recent years, molecular iodine is being increasingly used [23] in heterocyclic synthesis because of its distinct advantage as a cyclization agent. However, molecular iodine-mediated synthesis of 2-quinolones is less well documented. Our initial attempts at molecular iodine mediated cyclization of diphenylacrylamide **6*** (Scheme 2) under a range of conditions proved to be unsuccessful. It is anticipated that simple amides are perhaps poor substrates for intramolecular amidation due to the weak nucleophilicity of the amide nitrogen. Similarly, the corresponding *N*-benzyl derivative **6**** proved to be resistant to cyclization. We wondered whether the corresponding *N*-hydroxyamides would be sufficiently nucleophilic for intramolecular substitution due to possible α-effect of the oxygen atom. Thus, we looked into iodine-mediated C-H amidation of the *N*-benzyloxy-3, 3-diphenylacryl amide **6a** in greater detail.



Scheme2. Conversion of 3,3-diphenylacrylamides to 4-phenyl-2-quinolones.

The required model substrate **6a** was prepared by EDCI-mediated amide bond formation of 3,3-diphenylacrylic acid (**8a**) with *O*-benzylhydroxyl amine in the conventional way (Scheme 3).

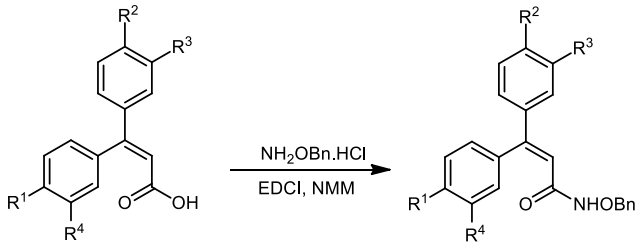
Iodine–mediated intramolecular C-H amidation of **6a** was initially attempted with some of the reported conditions. Compound **6a** when treated with equimolar mixture of molecular iodine and KI in refluxing toluene, almost no conversion was detected. Adding an equivalent of $NaHCO_3$ did induce the desired conversion to the quinolone derivative **7a** but the yield was very poor even after prolonged reflux. Changing the base to sodium acetate improved the yield to a minor extent (27%) but the starting material remained largely unreacted. Increasing the molar equivalents of each of the ingredients of the I_2/KI/NaOAC combination from 1 to 2.5 improved the yield significantly. Further increase of the equivalents of KI and NaOAc to 5 from 2.5 delivered an acceptable yield of 66% in refluxing toluene (entry 4). Changing the solvent to DMF slightly lowered the yield and also increasing the temperature had a further deleterious effect.

Table1. Optimization of the conversion **6a** → **7a**

Entry	Reagent (eqv)	Conditions	% **7a**
1	I_2 (1) /KI (1)	Toluene, reflux, 16h	trace
2	I_2 (1) /KI (1)/ $NaHCO_3$ (1)	Toluene, reflux, 16 h	14
3	I_2 (1)/KI (1)/NaOAc (1)	Toluene, reflux, 16 h	27
4	I_2 (2.5)/KI(5)/NaOAc (5)	Toluene, reflux, 24 h	66
5	I_2 (2.5)/KI(5)/NaOAc (5)	DMF, 140 ºC, 16 h	43
6	I_2 (2.5)/$nBu_4N^+I^-$ (5)/NaOAc (5)	Toluene, reflux, 16 h	9
7	NIS(2.5)/KI(5)/NaOAc (5)	Toluene, reflux, 16 h	33
8	I_2 (0.45)/H_2O_2 (8)	Toluene, 110 ºC, 24 h	21
9	I_2 (0.45)/H_2O_2 (8) /KI(5)	Toluene, reflux, 48 h	15
10	I_2 (0.45)/H_2O_2 (8) /NaOAc (5)	Toluene, 110 ºC , 24 h	95
11	I_2 (0.45)/H_2O_2 (8) /NaOAc (5)	Toluene, 80 ºC, 48 h	70
12	KI (5.0)/ H_2O_2 (8) /NaOAc (5)	Toluene, 110 ºC , 24 h	10

10.1002/adsc.201900530

Similarly, use of tetra-*n*-butylammonium iodide in place of KI was also found to be ineffective. Modest yield of the desired product **7a** was noticed when *N*-iodosuccinimide (entry 7) was used in place of molecular iodine. In an attempt to achieve the desired transformation using catalytic amount of iodine in combination with an oxidant, we opted to try the cheaper I_2/H_2O_2 combination for *in situ* generation of hypoiodous acid as possible source of electrophilic iodine. [24] After some experimentation, it was found that the reaction could be induced in the presence of at least 0.45 equivalent amount of I_2 but only when excess of hydrogen peroxide at elevated temperature was used (entry 8). Even an excess amount of KI had little influence (entry 9) on the course of the reaction; but, use of NaOAc (entry 10) significantly improved the yield to near completion (95%). The reaction was found to be slower at lower temperature, and longer time was required to achieve acceptable yield. Similarly, lesser equivalents of the base were of little use. Replacing iodine by KI (entry 12) keeping the other ingredients unchanged was also of no avail. We thus, followed the optimized condition (entry 10) to examine the substrate scope and generality of the reaction. To this end, compounds **6b-p** (Scheme 3) were prepared from corresponding known carboxylic acids **8b-p**, prepared following literature.



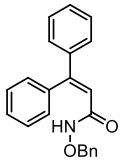
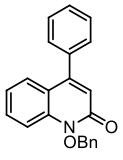
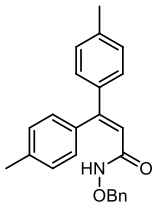
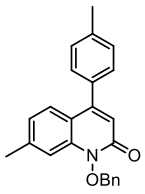
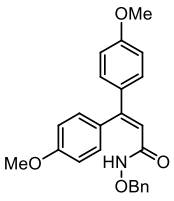
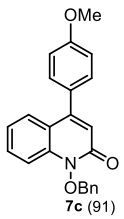
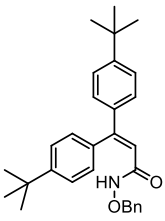
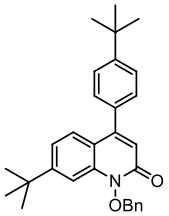
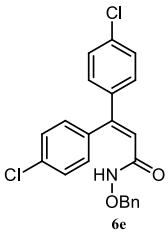
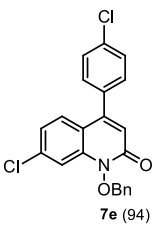
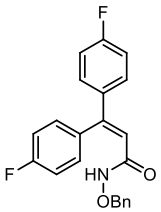
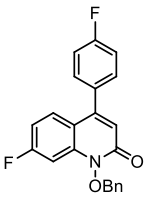
8a-p **6a-p**

Scheme 3. Preparation of N-benzyloxy- 3,3-diarylacrylamides **6a-p**

The symmetrical 4,4′-disubstituted diarylacrylamides **6b-f** having either electron-donating or electron-withdrawing substituents reacted with more or less equal facility under the developed conditions providing the respective products **7b-f** (Table 2) in very good yield.

The symmetrical 3,3′- disubstituted diarylacrylamides **6g-j** electronically behaved similarly (Table 3) with the added advantage that only one regioisomer (**7g-j**) was formed in each case. The isomeric products **7g***-**7**i* were not detected. It was earlier reported [17b] that in metal mediated C-H amidation reactions mixture of regioisomers were formed. The isomeric pair of products could be differentiated by observing the nature of the high field

Table 2. Products from symmetrical substrates

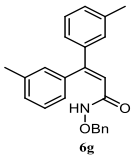
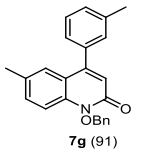
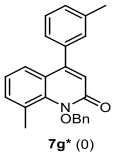
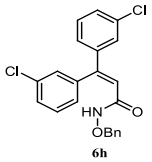
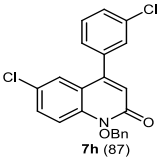
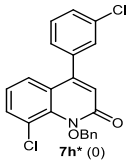
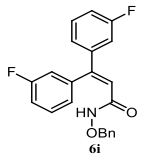
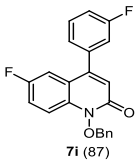
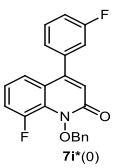
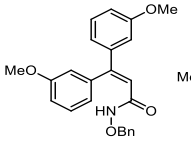
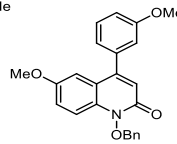
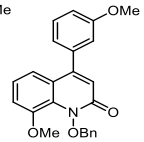
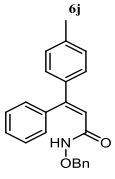
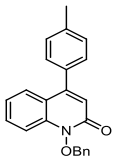
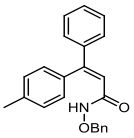
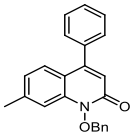
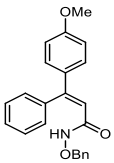
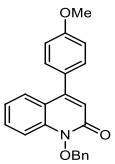
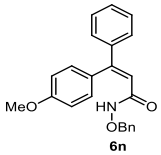
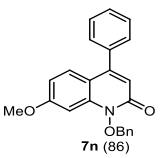
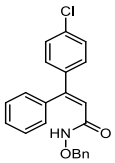
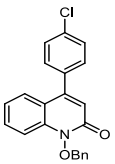
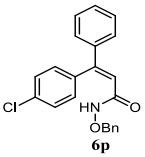
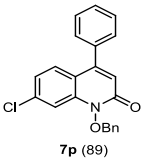
Entry	**6**	**7**(Yield %)
1	 **6a**	 **7a** (95)
2	 **6b**	 **7b** (92)
3	 **6c**	 **7c** (91)
4	 **6d**	 **7d**(93)
5	 **6e**	 **7e** (94)
6	 **6f**	 **7f** (95)

aromatic carbon C-8 (~112-114 ppm) in DEPT experiment wherein in compound **7g** it appeared as a C-H carbon as against a quaternary carbon that would appear from the alternative structure **7g***. Even more interesting was the behaviour of the singly substituted diarylacryl amides **6k-p** wherein only one of the two rings contains a substituent. In each of these cases, a

10.1002/adsc.201900530

single product (**7k-p**) was found to be formed in very good yield and with negligible electronic influence of the substituent.

Table 3. Products from unsymmetrical substrates

Entry	6	7(Yield %)	7*(Yield %)
1	 **6g**	 **7g** (91)	 **7g*** (0)
2	 **6h**	 **7h** (87)	 **7h*** (0)
3	 **6i**	 **7i** (87)	 **7i*** (0)
4	 **6j**	 **7j** (88)	 **7j*** (0)
5	 **6k**	 **7k** (89)	
6	 **6l**	 **7l** (93)	
8	 **6m**	 **7m** (90)	
9	 **6n**	 **7n** (86)	
10	 **6o**	 **7o** (94)	
11	 **6p**	 **7p** (89)	

The identity of the isomeric pairs **7k/7l** and **7o/7p** could be ascertained following the splitting pattern of the designated C8-H which appears as a doublet (δ 7.68, J = ~2 Hz) with *meta*-coupling. For the pair **7m**/**7n**, even more diagnostic is the appearance of the C-8 at very high field at δ 95.7 ppm.

The direction of the cyclization in each case is dictated by preferred proximity of the amide group in the *Z*-substrate. It may be noted that during metal-promoted cyclization of unsymmetrical diarylacrylamides, an *E*/*Z*-isomerization leading to formation of mixture of products was observed. [15b, 16a, 17a, 17b] The present methodology thus appears to be of somewhat broader scope.

On the other hand, its limitations also were significant (Figure 2). Thus, neither of the *cis*- or *trans*- *N*-benzyloxycinnamides **9** and **10** underwent any conversion. Similarly, the corresponding saturated derivative **11** or its homologue **12** equally frustrated our attempts. The diarylpropanamide **13** also remained unchanged. The ß-methyl substituted cinnamide **14** (~ 2:1 mixture of E/Z-isomers) also proved to be unreactive. On the other hand, the *N*-methoxyacrylamide **6q** smoothly underwent conversion to the desired **7q**.

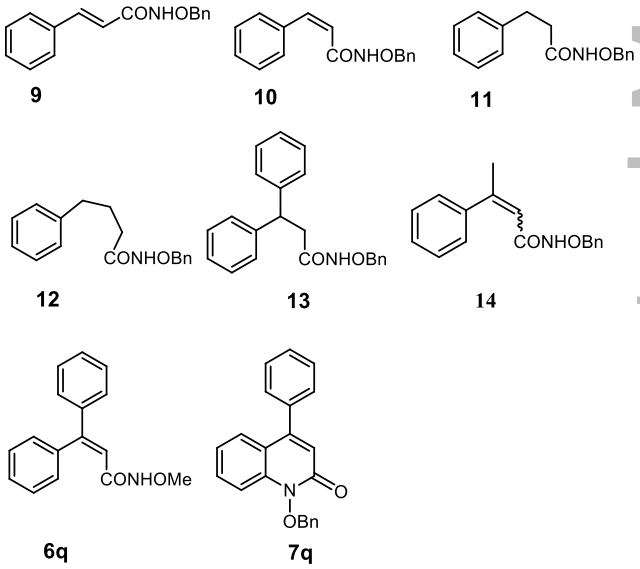
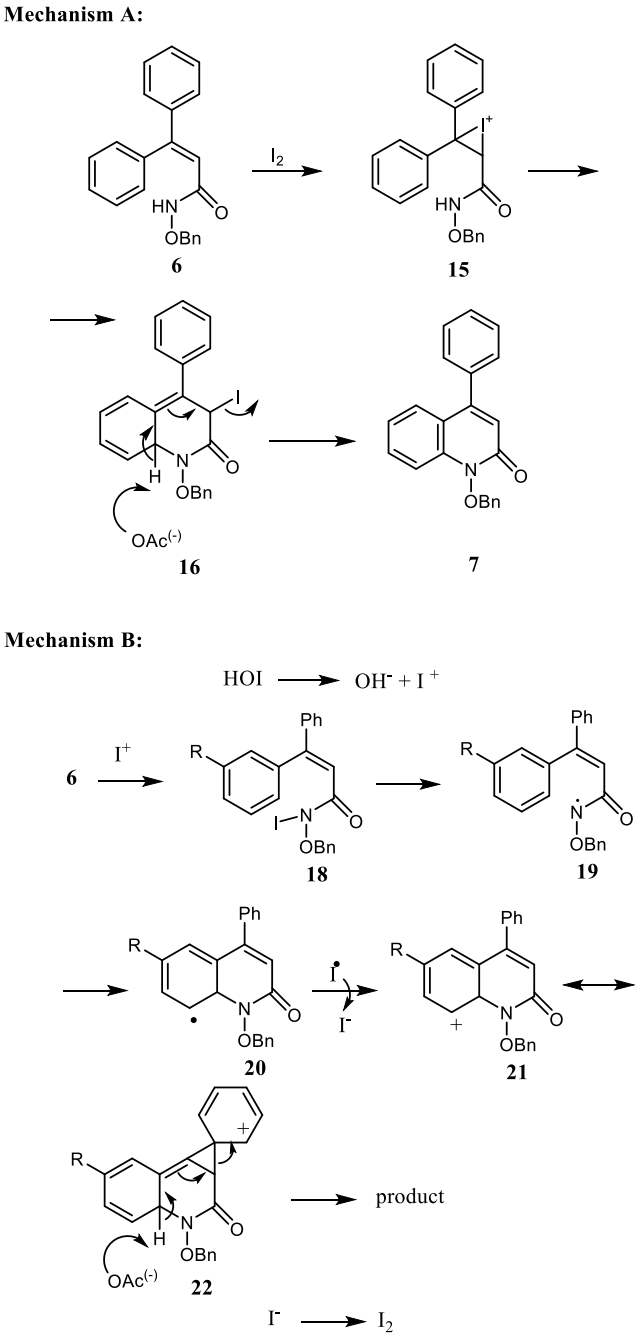


Figure 2. Limitations of the methodology

These studies led us to conclude that the presence of the diarylethylene linkage and a N-alkoxy substituent are crucial to the success of the reaction.

Based on the above experiments, a tentative mechanism [25] is proposed in Scheme 4. For the I_2/KI/NaOAc protocol, it may go through the formation of the iodonium intermediate **15** (mechanism A). Intramolecular nucleophilic capture by the proximal activated nitrogen and subsequent

base-mediated loss of HI leads to overall C(sp2)-H amidation. However, for the I_2/H_2O_2/NaOAc it is



Scheme 4. Suggested mechanisms for the formation of **4** under two different conditions.

more likely that a radical species may be involved. Iodine reacts with H_2O_2 to form hypoiodous acid. Being a source of I^+, this may lead to formation of the N-iodo derivative **18**. Homolytic cleavage of the later may form the N-centered radical **19**. Because of the proximity to the aryl ring, the radical **19** may undergo addition to it preferably at the sterically more accessible para-position due to the presence of the bulky N-substituent. In the highly redox environment, the newly formed radical **20** may undergo oxidation to the corresponding cation **21**, resonance stabilised to **22**. Base-mediated loss of proton leads to overall C(sp2)-H amidation. Oxidative regeneration of iodine may continue the catalytic cycle. The proposed mechanism may explain some of the observations e.g. the negligible E/Z-isomerization (as the double bond is not involved before cyclization), necessity of the extra aryl ring at C_4 (participation in resonance), and regio-selectivity in the meta-substituted case (predominant steric influence since there is little electronic influence). However, our attempts to trap the radical intermediate **19** using Tempo, and 2,6-di-tert-butyl-4-methylphenol did not meet with success, although somewhat lowering of yield (~20%) was observed in each case. Thus other mechanistic possibilities may exist. [26]

Conclusion

In conclusion, we have developed a metal-free procedure for the synthesis of the important 4-aryl-2-quinolone ring system involving the less explored I_2-H_2O_2 combination for an intramolecular C-H amidation. The reaction proceeds in very good yield and it also overcomes some of the difficulties associated with some related metal-mediated procedures. The developed methodology may thus complement the existing procedures and hence may find general application. It may also encourage the exploration of the intramolecular amidation of other substrates involving the *in situ* generation of hypoiodous acid.

Experimental Section

Experimental Details

Infrared spectra were recorded with a Perkin–Elmer Infrared Spectrometer model No L120–000A. ^1H and ^{13}C NMR spectra were recorded with a Bruker400 MHz Ultrashield NMR spectrometer purchased through a DST-FIST grant. Mass spectra were recorded with a Water Xevo QTOF mass spectrometer purchased through DST-PURSE grant. Elemental analysis was performed with a Perkin–Elmer 2400 series II Instrument. All solvents obtained from commercial sources were dried with appropriate drying agents and were immediately distilled before use. Column chromatography was performed with silica gel (230–400) purchased from Spectrochem India Pvt. Ltd. Thin-layer chromatography was performed with pre-coated silica plates and was visualized under a UV lamp or with an iodine spray. Melting points were determined in open capillaries and are uncorrected.

General procedure for the synthesis of N-(benzyloxy)-3,3-diarylacrylamides 6a-p

EDC.HCl (0.48 g, 2.5 mmol) was added portion wise to a stirred solution of 3,3-diphenylacrylic acid (0.33 g, 1.5 mmol) in dry DCM (10 mL) at 0 °C during 15 minutes. Then a solution of *O*-benzylhydroxylamine hydrochloride

(0.25 g, 1.5 mmol) and *N*-methylmorpholine (0. 15 mL, 1.5 mmol) in dry DCM (5 ml) was added dropwise over 10 min to the solution of the acid at the same temperature. The reaction mixture was allowed to come to rt and stirred for 16 h. It was then diluted with DCM (20 ml) and the combined organic solution was washed successively with saturated aqueous solution of $NaHCO_3$ (2 × 15 mL), HCl (2N, 2 × 10 ml), H_2O (1 × 20 mL), brine (1 × 20 mL), and then dried (Na_2SO_4).It was then concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using a mixture of petroleum ether: ethyl acetate (70:30) as eluent to provide the product **6a** (300 mg, 76%) as colourless viscous liquid.

N-(Benzyloxy)-3,3-diphenylacrylamide (6a) :

IR (neat): 3418, 2919, 1646, 1455 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.05 (1H, brs), 7.34-7.26 (9H, m), 7.23-7.19 (6H, m), 6.24 (1H, s), 4.71 (2H, s) . ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.9, 151.6, 140.5, 138.2, 135.3, 129.7, 129.3, 129.2, 129.0, 128.8, 128.5, 128.4, 128.1, 127.7, 118.9, 77.9. Elemental analyses: calcd for $C_{22}H_{19}NO_2$; C, 80.22; H, 5.81; N, 4.25; obsd, C, 80.12; H, 5.95; N, 4.32.

N-(Benzyloxy)-3,3-di-p-tolylacrylamide (6b) :

This was prepared from the acid **8b**[27a] and the product **6b** as an yellowish viscous liquid; yield 317 mg (71%); IR (neat): 3419, 2925, 1603, 1570, 1429 cm^{-1}. ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 8.23 (1H, brs), 7.18-7.13 (3H, m), 7.10 (2H, brs), 7.00-6.95 (8H, m), 6.08 (1H, s), 4.61 (2H, s), 2.23 (3H, s), 2.21 (3H, s) . ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.3, 151.8, 139.3, 138.6, 138.0, 135.4, 129.3, 129.1, 129.0, 128.8, 128.5, 128.4, 128.2, 125.8, 117.7, 77.9, 21.4, 21.3. Elemental analyses: calcd for $C_{24}H_{23}NO_2$; C, 80.64; H, 6.49; N, 3.92; obsd, C, 80.76; H, 6.37; N, 4.12.

N-(Benzyloxy)-3,3-bis(4-methoxyphenyl)acrylamide (6c):

This was prepared from the acid **8c**[27a] and the product **6c** was obtained as a yellowish viscous liquid ; yield 350 mg (75%); IR (neat) 3217, 2947, 1657, 1624 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.78 (1H, s), 7.33-7.31 (3H, m), 7.26-7.25 (2H, m), 7,17-7.11 (4H, m), 6.87-6.80 (4H, m), 6.14 (1H, brs), 4.78 (2H, s), 3.82 (3H, s), 3.80 (3H, s). 13C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.7, 160.5, 160.0, 151.1, 135.4, 133.3, 130.8, 130.4, 129.7, 129.0, 128.5, 116.7, 114.0, 113.7, 77.9, 55.3, 55.2. Elemental analyses: calcd for $C_{24}H_{23}NO_4$; C, 74.02; H, 5.95; N, 3.60; obsd. C, 74.14 ; H, 5.79; N, 3.72.

N-(Benzyloxy)-3,3-bis(4-tert-butylphenyl)acrylamide (6d):

This was prepared from the acid **8d** [27b] and the product **6d** obtained as a colourless viscous liquid ; yield 360 mg (68%); IR (neat): 3409, 2918, 2120, 1640, 1431 cm^{-1} . ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.54 (1H, brs), 7.31-7.24 (8H, m), 7.12-7.07 (5H, m), 6.21 (1H, s), 4.64 (2H, s), 1.27 (9H, s), 1.23 (9H, s) . ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.7, 151.9, 150.7, 138.9, 136.4, 136.2, 129.6, 129.2, 128.8, 128.0, 125.7, 125.0, 118.4, 77.2, 34.8, 31.6, 31.5. Elemental analyses: calcd for $C_{30}H_{35}NO_2$; C, 81.59; H, 7.99; N, 3.17; obsd, C, 81.67; H, 7.86; N, 3.28.

N-(Benzyloxy)-3,3-bis(4-chlorophenyl)acrylamide (6e):

This was prepared from the acid **8e** [27c] and the product **6e** was obtained as a yellowish viscous liquid ; yield 284 mg (66%); IR (neat): 3738, 3184, 1648, 1611, 1590 cm^{-1} . ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.26 (1H, s), 7.47-7.41 (4H, m), 7.39-7.35 (5H, m), 7.25 (2H, d, J = 8.4Hz), 7.18 (2H, d, J = 8.4Hz), 6.73 (1H, s), 4.74 (2H, m). 13C NMR (100 MHz, DMSO-d_6): δ (ppm) 162.5, 148.1, 139.3, 137.1, 135.8, 133.8, 132.7, 131.0, 129.4, 128.7, 128.6, 128.3, 127.9, 119.7, 76.8. Elemental analyses: calcd for $C_{22}H_{17}Cl_2NO_2$; C, 66.34; H, 4.30; N, 3.52; obsd. C, 66.22; H, 4.42; N, 3.69.

N-(Benzyloxy)-3,3-bis(4-fluorophenyl)acrylamide (6f):

This was prepared from the acid **8f** [27c] and the product **6f** was obtained as a colourless viscous liquid ; yield 331 mg (72%); IR (neat): 3738, 3419, 2923, 2346, 1639, 1602, 1539 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) : δ 11.24 (1H, s), 7.41-7.38 (5H, m), 7.33-7.21 (8H, m), 6.33 (1H, s), 4.76 (2H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.8 (d, $1J_{C,F}$ = 60 Hz), 163.2, 161.4 (d, $1J_{C,F}$ = 58 Hz), 148.8, 137.8, 136.4, 135.2, 131.9 (d, $3J_{C,F}$ = 8 Hz), 130.3 (d, $3J_{C,F}$ = 8 Hz), 129.2, 128.8, 128.7, 119.5, 116.0 (d, 2JC,F = 21 Hz), 115.4 (d, 2JC,F = 21 Hz), 77.2 . Elemental analyses: calcd for $C_{22}H_{17}F_2NO_2$; C, 72.32; H, 4.69; N, 3.83; obsd, C, 72.43; H, 4.57; N, 3.95.

N-(Benzyloxy)-3,3-di-m-tolylacrylamide (6g):

This was prepared from the acid **8g**[27c] and the product **6g** was obtained as a colourless viscous liquid. Yield 299 mg (67%). IR (neat): 3419, 2925, 1603, 1570, 1429 cm^{-1}. ^1H NMR (400 MHz,DMSO-d_6): δ (ppm) 11.14 (1H, s), 7.36-7.33 (3H, m), 7.31-7.27 (2H, m),7.24 (2H, dd, J = 7.6, 2Hz), 7.17-7.15 (2H, m) 7.05 (1H, brs), 6.97-6.94 (3H, m) , 6.29 (1H, s), 4.66 (2H, s), 2.28 (3H, s), 2.26 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.6, 151.1, 141.5, 139.1, 138.1, 137.4, 137.2, 136.3, 130.0, 129.9, 129.2, 129.0, 128.8, 128.7, 128.5, 128.2, 126.8, 125.5, 119.1, 77.2, 21.5, 21.4. Elemental analyses: calcd for $C_{24}H_{23}NO_2$; C, 80.64; H, 6.49; N, 3.92; obsd, C, 80.57; H, 6.62; N, 3.78.

N-(Benzyloxy)-3,3-bis(3-chlorophenyl)acrylamide (6h):

This was prepared from the acid **8h**[27c] and the product **6h** was obtained as a colourless viscous liquid ; yield 258 mg (60%) ; IR (neat): 3728, 3149, 2925, 1657, 1603, 1547 cm^{-1}. ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.87 (1H, s), 7.40 7.33 (7H, m), 7.27-7.16 (3H, m), 7.11-7.08 (2H, m), 6.99 (1H, d, J = 7.2Hz), 6.14 (1H, s) , 4.71 (2H, s) . ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.1, 149.3, 139.3, 135.1, 134.6, 129.9, 129.8, 129.5, 129.1, 128.9, 128.8, 128.0, 127.5, 127.0, 126.3, 120.1, 78.1. Elemental analyses: calcd for $C_{22}H_{17}Cl_2NO_2$; C, 66.34; H, 4.30; N, 3.52; obsd, C, 66.45; H, 4.17; N, 3.61.

N-(Benzyloxy)-3,3-bis(3-fluorophenyl)acrylamide (6i):

This was prepared from the acid **8i**[27c] and the product **6i** was obtained as a colourless viscous liquid ; yield 56%. IR (neat): 3449, 2928, 1619, 1610, 1523 cm^{-1}. 1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.07 (1H, brs), 7.32-7.16 (10H, m), 6.98-6.90 (4H, m), 6.81 (2H, dd, J = 1.6, 6.4Hz), 6.16 (1H, brs), 4.69 (2H, s). ^{13}C NMR (100 MHz,$CDCl_3$): δ (ppm) 164.2, 163.9, 161.7, 161.5, 161.4, 149.4, 142.2, 135.1, 130.4, 130.3, 130.1, 130.0, 129.3, 128.9, 128.7, 128.6, 125.0, 125.0, 124.2,123.7, 119.8, 116.4, 116.3, 116.2, 116.1, 115.8, 115.1, 114.9, 78.08; Elemental analyses: calcd for $C_{22}H_{17}F_2NO_2$; C, 72.32 ; H, 4.69; N, 3.83; obsd, C, 72.43 ; H, 4.57; N, 3.95.

N-(Benzyloxy)-3,3-bis(3-methoxyphenyl)acrylamide (6j):

This was prepared from the acid **8j**[27c] and the product **6j** was obtained as a colourless viscous liquid ; yield 285 mg (61%) ; IR (neat): 3118, 2928, 1649, 1614 cm^{-1} . ^1H NMR (400 MHz,$CDCl_3$) δ (ppm): 7.77 (1H, brs), 7.24-7.23 (3H, m), 7.19-7.12 (4H, m), 6.80 (2H, dt, J = 8.0, 2.0 Hz), 6.75-6.69 (3H, m), 6.65 (1H, brs), 6.21 (1H, s), 4.65 (2H, s), 3.67 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.9, 159.7, 159.5, 150.7, 141.5, 139.3, 135.2, 129.9, 129.4, 128.9, 128.5, 121.4, 120.6, 119.4, 114.7, 114.6, 114.3,

113.7, 77.9, 55.3, 55.2 . Elemental analyses: calcd for $C_{24}H_{23}NO_4$; C, 74.02; H, 5.95; N, 3.60; obsd, C, 74.14; H, 5.86; N, 3.69.

(E)-N-(Benzyloxy)-3-phenyl-3-p-tolylacrylamide (6k):

This was prepared from the acid **8k**[27d] and the product **6k** was obtained as a colourless viscous liquid ; yield 259 mg (63%); IR (neat): 3427, 2915, 1637, 1603, 1429 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 11.12 (1H, s), 7.37-7.31 (8H, m), 7.18-7.09 (6H, m), 6.26 (1H, s), 4.67 (2H, s), 2.30 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.0, 150.4, 138.8, 138.4, 138.1, 135.9, 129.2, 129.0, 128.9, 128.7, 128.3, 128.2, 127,7, 127.6, 117.9, 76.7, 20.7. Elemental analyses: calcd for $C_{23}H_{21}NO_2$; C, 80.44; H, 6.16; N, 4.08; obsd, C, 80.53; H, 6.27; N, 3.98.

(Z)-N-(Benzyloxy)-3-phenyl-3-p-tolylacrylamide (6l):

This was prepared from the acid **8l**[27d] and the product **6l** was obtained as a yellowish viscous liquid. Yield 263 mg (64%). IR (neat): 3438, 2818, 1647, 1613 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 11.18 (1H, s), 7.41-7.36 (8H, m), 7.26-7.21 (4H, m), 7.09 (2H, d, J = 8Hz), 6.28 (1H, s), 4.75 (2H, s), 2.39 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.6, 150.9, 141.7, 137.6, 136.4, 136.2, 129.7, 129.5, 129.2, 128.9, 128.7, 128.6, 128.2, 128.1, 119.1, 77.2, 21.3. Elemental analyses: calcd for $C_{23}H_{21}NO_2$; C, 80.44; H, 6.16; N, 4.08; obsd, C, 80.33; H, 6.31; N, 4.01.

(E)-N-(Benzyloxy)-3-(4-methoxyphenyl)-3-phenylacrylamide (6m):

This was prepared from the acid **8m**[27d] and the product **6m** was obtained as a colourless viscous liquid ; yield 341 mg (79%); IR (neat): 3488, 3136, 1667, 1610, 1517 cm^{-1}. ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.73 (1H, s), 7.27-7.23 (6H, m), 7.20-7.08 (4H, m), 7.08-7.04 (2H, m), 6.78-6.72 (2H, m), 6.14 (1H, brs), 4.64 (2H, s), 3.71 (3H, s) . ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.2, 160.0, 151.1, 138.4, 135.3, 132.7, 130.8, 130.2, 129.5, 129.2, 129.0, 128.5, 128.4, 127.0, 117.1, 113.8, 78.0, 55.3. Elemental analyses: calcd for $C_{23}H_{21}NO_3$; C, 76.86; H, 5.89; N, 3.90; obsd, C, 76.94; H, 5.78; N, 3.97.

(Z)-N-(Benzyloxy)-3-(4-methoxyphenyl)-3-phenylacrylamide (6n):

This was prepared from the acid **8n**[27e] and the product **6n** was obtained as an yellowish viscous liquid ; yield 288 mg (67%). IR (neat): 3188, 2932, 1647, 1604, 1510 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.74(1H, brs), 7.28-7.22 (6H, m), 7.21-7.13 (4H, m), 7.07 (2H, d, J = 8.4Hz), 6.78 (2H, d, J = 8.8 Hz), 6.12 (1H, brs) , 4.71 (2H, s), 3.75 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.8, 159.5, 150.7, 142.0, 136.4, 131.2, 129.2, 128.9, 128.7, 128.3, 118.7, 113.7, 77.2, 55.5. Elemental analyses: calcd for $C_{23}H_{21}NO_{23}$; C, 76.86; H, 5.89; N, 3.90; obsd, C, 76.73; H, 5.92; N, 3.74.

(E)-N-(Benzyloxy)-3-(4-chlorophenyl)-3-phenylacrylamide (6o):

This was prepared from the acid **8o**[27d] and the product **6o** was obtained as a colourless viscous liquid ; yield 283 mg (65%); IR (neat): 3422, 2919, 1663, 1589 cm^{-1}. ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.41 (1H, brs), 7.36-7.28 (4H, m), 7.25 (3H, brs), 7.21-7.16 (2H, m), 7.12-7.11 (3H, m), 7.08-7.06 (2H, m), 6.17 (1H,s), 4.66 (2H, s) . ^{13}C NMR (100 MHz, $CDCl_3$) : δ (ppm) 164.7, 150.2, 138.9, 137.7, 135.3, 134.6, 130.7, 130.1, 129.4, 129.2, 128.9, 128.7, 128.6, 128.0, 119.3, 78.0 ; Elemental analyses: calcd for $C_{22}H_{18}ClNO_2$; C, 72.62 ; H, 4.99; N, 3.85; obsd, C, 72.54; H, 5.09; N, 3.76.

(Z)-N-(Benzyloxy)-3-(4-chlorophenyl)-3-phenylacrylamide (6p):

This was prepared from the acid **8p**[27c] and the product **6p** was obtained as a colourless viscous liquid ; yield 296 mg (68%); IR (neat): 3447, 2851, 1666, 1604 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) : δ 7.70 (1H, s), 7.34-7.22 (10H, m), 7.13-7.07 (4H, m), 6.15 (1H, s), 4.74 (2H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 163.3, 150.1, 140.9, 137.9, 136.2, 133.0, 131.5, 129.6, 129.3, 129.2, 129.1, 128.8, 128.4, 128.1, 119.4, 77.3. Elemental analyses: calcd for $C_{22}H_{18}ClNO_2$; C, 72.62; H, 4.99; N, 3.85; obsd, C, 72.74; H, 4.84; N, 3.92

N-Methoxy-3,3-diphenylacrylamide (6q):

This was prepared from the acid **8a** following the general procedure but using *O*-methylhydroxylamine hydrochloride as the coupling partner. The product was purified using a mixture of hexane: ethyl acetate (60:40) as eluent to give **6q** as a colourless viscous liquid; yield: 230 mg (76%). IR (neat): 3231, 2924, 1655, 1603, 1578 cm^{-1}. NMR (400 MHz, $CDCl_3$): δ (ppm) 7.93 (1H, s), 7.33-7.31 (3H, m), 7.29-7.22 (3H, m), 7.22-7.17 (4H, m), 6.21 (1H, s), 3.45 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.1, 151.4, 140.3, 138.2, 129.3, 129.2, 128.9, 128.7, 128.4, 128.1, 119.0, 64.0. Elemental analyses: calcd for $C_{16}H_{15}NO_2$; C, 75.87; H, 5.97; N, 5.53; obsd, C, 75.98; H, 5.79; N, 5.65.

General procedure for the synthesis of 4-aryl-2-quinolones 7a-p:

To a round bottom flask (25 mL) fitted with a condenser containing a solution of compound **6a** (100 mg, 0.30 mmol) in toluene (3.0 mL) was added sequentially molecular iodine (34 mg, 0.13 mmol), NaOAc (124 mg, 1.51 mmol) and H_2O_2 (0.8 mL, 30%, 4 equiv) at room temperature. Then, the round bottom flask was placed in a pre-heated oil bath at 110 °C under gentle relux for 16 h. The flask was lifted from the bath, cooled to rt, and then another lot of H_2O_2 (0.4 mL, 30%, 2 equiv) was added. Heating was continued for an additional 8 h. The reaction mixture was allowed to cool to room temperature, diluted with water (10 mL) and then extracted with EtOAc (2× 25 ml). The combined organic extract was washed with saturated aqueous solution of $Na_2S_2O_3$ (2 × 10 mL), water (20 mL), brine (20 mL), and then dried ($MgSO_4$). It was filtered and the filtrate was concentrated under reduced pressure to leave a residue which was passed through a short pad of silica using a mixture of hexane-ethyl acetate (4:1) as eluent to afford **7a** (94 mg, 0.28 mmol, 95%) as a colourless solid. Compounds **7b-q** were prepared analogously.

1-**(Benzyloxy)-4-phenylquinolin-2(1H)-one (7a):**

M.p 140-141 °C (Lit.[16b] viscous oil). IR (neat): 3424, 2923, 2847, 1669, 1608, 1512 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.72 (1H, d, J = 8.4Hz), 7.66-7.42 (2H, m), 7.60-7.54 (3H, m), 7.51-7.49 (3H, m), 7.45-7.35 (5H, m), 7.18 (1H, t, J = 7.2 Hz), 6.74 (1H, s), 5.32 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.6, 150.8, 138.7, 136.7, 133.9, 131.0, 129.9, 129.3, 128.9, 128.7, 128.6, 127.5, 122.6, 122.0, 119.6, 112.5, 77.3(overlapped); HRMS (TOF MS ES+): m/z [M + H]+ calcd. for $C_{22}H_{18}NO_2$ 328.1338; found 328.1396.

1-(Benzyloxy)-7-methyl-4-p-tolylquinolin-2(1H)-one (7b):

This was prepared from the amide **6b** and the product **7b** was obtained as a pale yellow solid; yield 91 mg (92%); m.p 150-152 °C; IR (neat): 3423, 2917, 2855, 1662, 1614, cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$):δ (ppm) 7.66-7.64 (2H, m), 7.48 (2H, d, *J* = 8Hz), 7.45-7.41 (3H, m), 7.34-7.32 (4H, m), 6.99 (1H, d, J = 8Hz), 6.66 (1H, s), 5.30 (2H, s), 2.47 (3H, s), 2.45 (3H, s) ;^{13}C NMR (100 MHz, $CDCl_3$): δ

(ppm) 157.9, 150.7, 141.8, 138.8, 138.7, 134.1, 134.0, 129.9, 129.3, 129.2, 128.8, 128.7, 127.4, 124.0, 120.6, 117.5, 112.5, 76.8, 22.0, 21.3; HRMS (TOF MS ES+): m/z [M+H]+ calcd. for $C_{24}H_{22}NO_2$ 356.1651; found 356.1641.

1-(Benzyloxy)-7-methoxy-4-(4-methoxyphenyl)quinolin-2(1H)-one (7c):

This was prepared from the amide **6c** and the product **7c** was obtained as a colourless solid; yield 90 mg (91%); m.p 159-160 ºC; IR (neat): 3421, 2922, 2840, 1747, 1657, 1606 cm^{-1} ; ^1H NMR (400 MHz,$CDCl_3$) δ (ppm) 7.55-7.52 (2H, m), 7.40 (1H, d, *J* = 8.8Hz), 7.35-7.33 (3H, m), 7.28 (2H, d, J = 8.8Hz), 7.01 (1H, d, J = 2Hz), 6.94 (2H, d, J = 8.8Hz), 6.66 (1H, dd, J = 8.8,2.4Hz), 6.48 (1H, s), 5.24 (2H, s), 3.80 (3H, s), 3.75 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.1, 160.1, 158.3, 150.4, 140.5, 134.2, 130.2, 129.9, 129.3, 129.0, 128.8, 118.5, 114.0, 113.6, 111.4, 95.6, 77.5, 55.6, 55.4 ; Elemental analyses: calcd for $C_{24}H_{21}NO_4$; C, 74.40; H, 5.46; N, 3.62; obsd, C, 74.29 ; H, 5.64; N, 3.53.

1-(Benzyloxy)-7-tert-butyl-4-(4-tert-butylphenyl)quinolin-2(1H)-one (7d):

This was prepared from the amide **6d** and the product was **7d** was obtained as a colourless solid; yield 92 mg (93%); m.p 110-111 ºC; IR (neat): 3439, 2925, 2309 2, 1645, 1528, cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.67 (1H, d, J = 1.6Hz), 7.63-7.61 (2H, m), 7.55-7.50 (3H, m), 7.44-7.41 (3H, m), 7.40-7.36 (2H, m), 7.22 (1H, dd, J = 8.8,2Hz), 6.70 (1H, s), 5.33 (2H, s), 1.39 (9H, s), 1.34 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.1, 154.8, 152.0, 150.6, 138.6, 134.1, 133.9, 130.1, 129.3, 128.8, 128.6, 127.3, 125.5, 120.8, 120.5, 117.4, 109.1, 77.5, 35.3, 34.8, 31.3, 31.2; HRMS (TOF MS ES+): m/z [M + H]+ calcd. for $C_{30}H_{34}NO_2$ 440.2590; found 440.2592.

1-**(Benzyloxy)-7-chloro-4-(4-chlorophenyl)quinolin-2(1H)-one (7e):**

This was prepared from the amide **6e** and the product **7e** was obtained as a colourless solid; yield 93 mg (94%); m.p 199-200 ºC; IR (neat): 3418, 2921, 2852, 1663, 1587 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.59 (1H, d, J = 1.6Hz), 7.56-7.54 (2H, m), 7.42 (2H, d, J = 8.4Hz), 7.39-7.26 (6H, m), 7.06 (1H, dd, J = 8.4,1.6Hz), 6.62 (1H, s), 5.23 (2H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$) : δ (ppm) 157.4, 149.1, 139.5, 137.7, 135.4, 134.6, 133.5, 130.1, 130.0, 129.5, 129.1, 128.8, 128.4, 123.2, 122.1, 117.7, 112.7, 77.6 . Elemental analyses: calcd for $C_{22}H_{15}Cl_2NO_2$; C, 66.68; H, 3.82; N, 3.53; obsd. C, 66.87; H, 4.04; N, 3.72.

1-(Benzyloxy)-7-fluoro-4-(4-fluorophenyl)quinolin-2(1H)-one (7f):

This was prepared from the amide **6f** and the product **7f** was obtained as a colourless solid; yield 94 mg (95%); m.p 168-169 ºC; IR (neat): 3424, 2921, 1679, 1664, 1621 cm^{-1} ; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.64-7.61 (2H, m), 7.49-7.35 (7H, m), 7.24-7.19 (2H, m), 6.91 (1H, dt, J = 2.4, 8Hz), 6.66 (1H, s), 5.31 (2H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.1 (d, $J_{C,F}$ = 36 Hz), 162.6 (d, JC,F = 33 Hz), 157.7, 149.4, 140.4, 140.3, 133.5, 132.5, 130.7 (d, JC,F = 8 Hz), 130.0, 129.7 (d, $J_{C,F}$ = 10 Hz), 129.5, 128.8, 121.0, 116.0 (d, JC,F = 21 Hz) , 111.1 (d, $J_{C,F}$ = 24 Hz), 99.7 (d, $J_{C,F}$ = 28 Hz), 77.5 ; Elemental analyses: calcd for $C_{22}H_{15}F_2NO_2$; C, 72.72; H, 4.16; N, 3.85; obsd, C, 72.88 ; H, 4.07; N, 3.92.

1-(Benzyloxy)-8-methyl-4-m-tolylquinolin-2(1H)-one (7g):

This was prepared from the amide **6g** and the product **7g** was obtained as a colourless viscous liquid; yield 90 mg (91%); IR (neat): 3428, 2881, 1645, 1589 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.58-7.52 (3H, m), 7.38-7.31 (5H, m), 7.23 (2H, d, J = 8Hz), 7.15 (2H, d, J = 8.8Hz), 6.62 (1H, s), 5.23 (2H, s), 2.37 (3H, s), 2.27 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.5 (C), 150.7 (C), 138.4(C), 136.8(C), 136.7(C), 134.0 (C),, 132.3(CH), 132.2(C), 129.9(CH), 129.5(CH), 129.2(CH), 128.7(CH), 128.4(CH), 127.2(CH), 126.0(CH), 121.9(CH), 119.7 (C), 112.4 (CH), 77.3 (CH2), 21.5 (CH3), 20.9 (CH3) ; Elemental analyses: calcd for $C_{24}H_{21}NO_2$; C, 81.10; H, 5.96; N, 3.94; obsd, C, 81.27 ; H, 6.12; N, 3.85.

1-(Benzyloxy)-7-chloro-4-(3-chlorophenyl)quinolin-2(1H)-one (7h):

This was prepared from the amide **6h** and the product **7h** was obtained as a colourless solid; yield 86 mg (87%); m.p 126-127 ºC; IR (neat): 3423, 2917, 2855, 1662, 1614 cm^{-1}; 1H NMR (400 MHz,$CDCl_3$) δ (ppm) 7.63-7.58 (3H, m), 7.52 (1H, d, J = 2Hz), 7.50-7.47 (2H, m), 7.45-7.41 (4H, m), 7.29 (1H, td, J = 1.6, 6.8 Hz), 6.75 (1H, s), 5.31 (2H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.0 (C), 148.3(C),137.7(C),137.3(C),134.9(C),133.5(C), 131.4(CH), 130.2(CH),130.0(CH), 129.5(CH), 129.4(CH), 128.8(CH),128.5 (C) 126.9(CH), 126.3(CH), 123.5(CH), 120.2(C), 114.3(CH), 77.6 (CH2). Elemental analyses: calcd for $C_{22}H_{15}Cl_2NO_2$; C, 66.68; H, 3.82; N, 3.53; obsd, C, 66.97; H, 3.93; N, 3.66.

1-(Benzyloxy)-7-fluoro-4-(3-fluorophenyl)quinolin-2(1H)-one (7i):

This was prepared from the amide **6i** and the product was **7i** was obtained as a colourless solid; yield 86 mg (87%); m.p 166-167 ºC; IR (neat): 3447, 2958, 2857, 1659, 1601 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.65 (1H, dd, J = 9.2, 4.8 Hz), 7.62-7.59 (2H, m), 7.50 (1H, dt, J = 6, 8 Hz), 7.45-7.42 (3H, m), 7.30 (1H, dq, J = 2.4, 8 Hz), 7.24-7.19 (2H, m), 7.16 (1H, d, J = 2.4 Hz), 7.14 (1H, dd, J = 9.2, 2.0 Hz), 6.78 (1H, s), 5.32 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.0 (d, $J_{C,F}$ = 250 Hz), 159.5 (d, $J_{C,F}$ = 244 Hz), 157.0, 148.5, 138.2, 135.4, 133.6, 130.7 (d, $J_{C,F}$ = 7 Hz), 129.9, 129.4, 128.8, 125.5, 123.6, 120.2 (d, $J_{C,F}$ = 9 Hz), 119.3 (d, $J_{C,F}$ = 20 Hz), 116.2 (d, $J_{C,F}$ = 20 Hz), 115.9 (d, $J_{C,F}$ = 23 Hz), 114.5, 112.6 (d, $J_{C,F}$ = 24 Hz), 77.6 . Elemental analyses: calcd for $C_{22}H_{15}F_2NO_2$; C, 72.72; H, 4.16; N, 3.85; obsd, C, 72.93 ; H, 4.24; N, 3.69.

1-(Benzyloxy)-8-methoxy-4-(3-methoxyphenyl)quinolin-2(1H)-one (7j):

This was prepared from the amide **6j** and the product **7j** was obtained as a pale yellow solid; yield 87 mg (88%); m.p 152-153 ºC; IR (neat): 3402, 2923, 1657, 1593, cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.64-7.62 (3H, m), 7.44-7.04 (4H, m), 7.19 (1H, dd, J = 9.2, 2.8Hz), 7.03-7.01 (3H, m), 6.97 (1H, t, J = 1.6 Hz), 6.75 (1H, s), 5.31 (2H, s), 3.86 (3H, s), 3.73 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.7 (C), 157.2(C), 155.1(C), 149.9(C), 138.1(C), 133.9(C), 133.3(C), 129.9(CH), 129.8(CH), 129.3(CH), 128.7(CH), 122.6(CH), 121.1(CH), 120.4(C), 119.5(CH), 114.5(CH), 114.3(CH), 113.9(CH), 109.7(CH), 77.3(CH2), 55.7(CH3), 55.4(CH3); Elemental analyses: calcd for $C_{24}H_{21}NO_4$; C, 74.40; H, 5.46; N, 3.62; obsd, C, 74.61 ; H, 5.37; N, 3.78.

1-(Benzyloxy)-4-p-tolylquinolin-2(1H)-one (7k):

This was prepared from the amide **6k** and the product **7k** was obtained as a colourless solid; yield 88 mg (89%); m.p 168-170 ºC; IR (neat): 3425, 2920, 2852, 1660, 1593, 1510 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (1H, d, J = 8.4Hz), 7.59-7.57 (2H, m), 7.52-7.48 (2H, m), 7.39-7.34 (3H, m), 7.28-7.23 (4H, m), 7.11 (1H, dt, J = 0.8, 7.6 Hz), 6.66 (1H, s), 5.24 (2H, s), 2.38 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.7, 150.8, 138.9, 138.7, 133.9, 133.8, 130.9, 129.9, 129.3, 129.2, 128.8, 128.7, 127.6, 122.5, 121.9, 119.7, 112.5, 21.3; HRMS (TOF MS ES+):

m/z [M+H]+ calcd. for $C_{23}H_{20}NO_2$ 342.1494; found 342.1491.

1-(Benzyloxy)-7-methyl-4-phenylquinolin-2(1H)-one (7l):

This was prepared from the amide **6l** and the product **7l** was obtained as a colourless solid; yield 92 mg (93%); m.p 166-167 ºC; IR (neat): 3426, 2919, 2851, 1655, 1613 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.69-7.67 (2H, m), 7.54-7.50 (4H, m), 7.49-7.44 (6H, m), 7.01(1H, d, J = 8.4Hz), 6.70 (1H, s), 5.33 (2H, s), 2.50 (3H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.9, 150.7, 141.9, 138.7, 136.9, 134.0, 129.9, 129.2, 128.9, 128.8, 128.7, 128.6, 127.3, 124.0, 120.8, 117.4, 112.5, 77.4, 22.0 ; Elemental analyses: calcd for $C_{23}H_{19}NO_2$; C, 80.92; H, 5.61; N, 4.10; obsd, C, 80.79 ; H, 5.74; N, 4.03.

1-(Benzyloxy)-4-(4-methoxyphenyl)quinolin-2(1H)-one (7m):

This was prepared from the amide **6m** and the product **7m** was obtained as a colourless solid; yield 89 mg (90%); m.p 150-151 ºC; IR (neat): 3415, 2921, 1621, 1338, cm^{-1};^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (1H, d, J = 8.4Hz), 7.58-7.48 (4H, m), 7.39-7.38 (3H, m),7.33-7.30 (2H, m), 7.12 (1H, t, J = 7.2Hz), 6.96 (2H, d, J = 8.4Hz), 6.65 (1H, s), 5.24 (2H, s), 3.82 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) :δ (ppm) 160.2, 157.7, 150.5, 138.7, 133.9, 130.9, 130.2, 129.9, 129.2, 129.0, 128.7, 127.5, 122.5, 121.8, 119.8, 114.1(two signals overlapped), 112.5, 55.4; HRMS (TOF MS ES+): m/z [M + H]+ calcd. for $C_{23}H_{20}NO_3$ 358.1443; found 358.1442.

1-(Benzyloxy)-7-methoxy-4-phenylquinolin-2(1H)-one (7n):

This was prepared from the amide **6n** and the product **7n** was obtained as a colourless solid; yield 82 mg (86%); m.p 147-148 ºC; IR (neat): 3439, 2953, 1645, 1510, cm^{-1}. ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.55-7.54 (2H, m), 7.44-7.41 (3H, m), 7.38-7.32 (6H, m), 7.03 (1H, d, J = 2.4), 6.67 (1H, dt, J = 2.4,9.2Hz), 6.51 (1H, s), 5.26 (2H, s), 3.76 (3H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.1, 158.2, 150.7, 140.5, 137.0, 134.1, 130.2, 129.9, 129.3, 129.0, 128.8, 128.7, 128.6, 118.8, 113.5, 111.5, 95.6, 77.5, 55.6. Elemental analyses: calcd for $C_{23}H_{19}NO_3$; C, 77.29; H, 5.36; N, 3.92; obsd, C, 77.47; H, 5.45; N, 4.03.

1-(Benzyloxy)-4-(4-chlorophenyl)quinolin-2(1H)-one (7o):

This was prepared from the amide **6o** and the product **7o** was obtained as a colourless solid; yield 93 mg (94%); m.p 189-190 ºC; IR (neat): 3418, 2857, 1648, 1589 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.64 (1H, d, J = 8.4Hz), 7.57-7.49 (3H, m), 7.43-7.41 (3H, m), 7.37-7.35 (3H, m), 7.30 (2H, d, J = 8.4Hz), 7.12 (1H, t, J = 7.6Hz), 6.65 (1H, s), 5.23 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.4, 149.5, 138.7, 135.1, 135.0, 133.8, 131.3, 130.2, 129.9, 129.3, 129.0, 128.7, 127.2, 122.8, 122.2, 119.3, 112.6. HRMS (QTOF, ES+): m/z = 362.0998 [M + H] calcd. for $C_{22}H_{17}ClNO_2$, 362.0948; found 362.0998.

1-(Benzyloxy)-7-chloro-4-phenylquinolin-2(1H)-one (7p):

This was prepared from the acid **6p** and the product **7p** was obtained as colourless solid; yield 90 mg (89%); m.p 184-186 ºC; IR (neat): 3447, 2957, 1654, 1545 cm^{-1}; ^1H NMR (400 MHz,$CDCl_3$): δ (ppm) 7.60-7.55 (3H, m), 7.45-7.38 (3H, m), 7.36-7.30 (6H, m), 7.05 (1H, dd, J = 2,8.8Hz), 6.65 (1H, s), 5.25 (2H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.6, 150.3, 139.4, 137.5, 136.2, 133.5, 130.2, 130.0, 129.9, 129.5, 129.1, 129.0, 128.8, 127.2, 123.1, 121.9, 118.0, 112.5, 77.6 . Elemental analyses: calcd for $C_{22}H_{16}ClNO_2$; C, 73.03; H, 4.46; N, 3.87; obsd, C, 72.94; H, 4.57; N, 3.76.

1-Methoxy-4-phenylquinolin-2(1H)-one (7q):

This was prepared from the acid **6q** and the product **7q** was obtained as a colourless solid; yield 92 mg (93%). M.p. 96-97 ºC (Lit.[17a] 97-98 ºC). IR (neat): 3383, 2931, 1661, 1589 cm^{-1}. NMR (400 MHz,$CDCl_3$): δ (ppm) 7.62 (1H, d, J = 8.4Hz), 7.54 (1H, t, J = 8Hz), 7.47 (1H, d, J = 8Hz), 7.42-7.40 (3H, m), 7.33-7.32 (2H, m), 7.12 (1H, t, J = 7.6Hz), 6.62 (1H, s), 4.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.3, 150.7, 138.1, 136.6, 131.2, 128.9, 128.8, 128.7, 127,7, 122.7, 121.9, 119.7, 112.1, 62.9.

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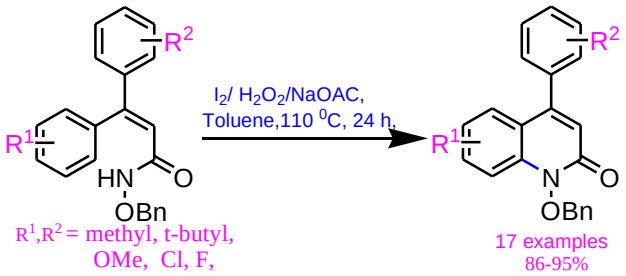
FULL PAPER

Metal-Free Synthesis of 4-Aryl-2-quinolone Derivatives by Iodine-Mediated Intramolecular C-H Amidation



Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Subhankar Ghosh and Shital K Chattopadhyay*