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# Chemoselective Synthesis of pyrrolo[2,3,4-kl]acridin-1-ones using Copper(I)/DBU Catalyst as an efficient and recoverable catalyst under thermal irradiation

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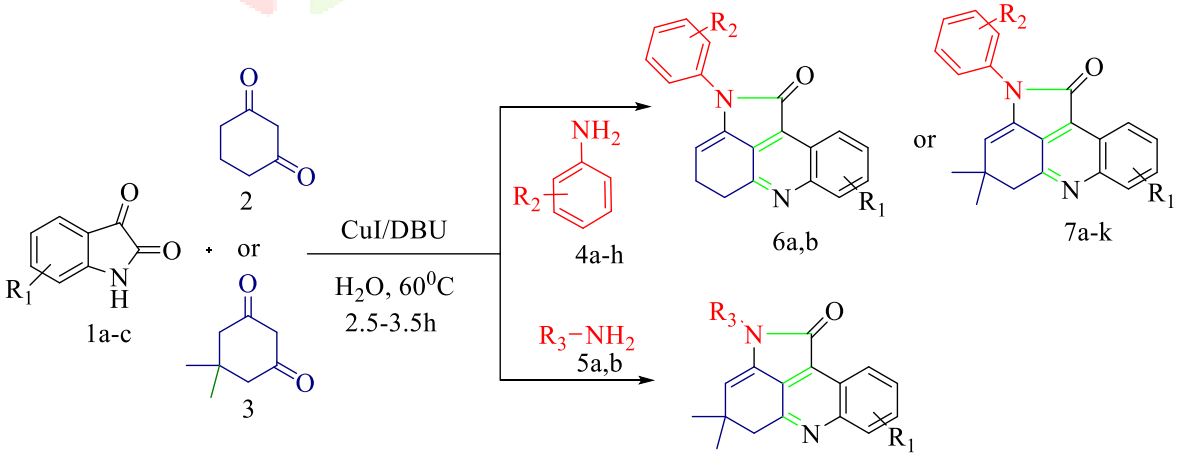
## ABSTRACT

Herein, CuI and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) have been employed as an efficient catalyst system to synthesize pyrrolo[2,3,4-kl]acridin-1-ones *via* ring-opening sequence or amidic C-N bond cleavage of isatin. It was found that this cost-competitive catalyst system could efficiently catalyse the reaction in only 2h at $60^0$C and a wide range of substrates were suitable for this reaction. Various target products were obtained in excellent yields. It was perceived that the catalyst system has a synergistic effect, copper(I) activatingthe carbonyl group and DBU triggering the activity of the amino group of amines for the reaction.




$R_1$ = H, Br, F, $NO_2$
$R_2$ = 4-OMe, 4-$CH_3$, H, 4-Br, 4-Cl, 4-F, 4-$NO_2$, 4-CHO
$R_3$ = $C_5H_{11}$, $C_6H_{13}$

***Keywords:*** Multicomponent, Thermal irradiation, Copper(I)/DBU Catalyst, Chemoselective synthesis, pyrrolo[2,3,4-*kl*]acridin-1-ones.

## INTRODUCTION

In recent years, the "greening" of chemical processes and industries around the world has become a major concern [1]. Numerous ancient artificial methodologies have varied applications but they fail to be in consonancewith green chemistry principles. Researchers and scientists are rapidly gravitating towards extremely eco-efficient and viable synthetic protocols, necessitating the development of biologically relevant heterocyclic nuclei using more environment friendly and cost-effective synthetic precursors, catalysts and solvents [2,3].

In modern times, multicomponent reactions (MCRs) are often an immensely usefulalternative to sequential, time-consuming, multistep synthesis.MCRsinvolve one-pot reactions that employ three or morestarting materials and incorporate majority of the atoms from the starting materials in the final product, regardless of the mechanisms involved.MCRs are frequently tagged with descriptive terms like atom economy, efficiency and sustainability [4].Such reactionsencourage diversity-oriented synthesis and are facile to implement. They may be considered to be beneath the umbrella of green chemistry due to the fact that they display an exceptionally high atom efficiency [5]. The preparation of pyrrolo[2,3,4-kl]acridin by a multicomponent reaction (MCR) involving isatin, aniline and dimedone in the presence of acid catalysts has been used very often [6-8]. Herein we report an efficient method based on this MCR for the synthesis of pyrrolo[2,3,4-kl]acridin in the presence of base as a catalyst (Scheme 1). We areinterested in the modus development of multicomponent reactions for gaining access to privileged scaffolds [9].

Initially, acridine was primarily utilized in the production of dyes but its fluorescence and chemiluminescence capabilities led to a wide range of other applications [10,11]. For the first time in 1912, Ehrlich and Benda used acridines as antibacterial agents and the first medicinal use of such antibiotics happened in 1917 [12,13]. The interaction of acridine with various heterocycles is currently one of the most intriguing topics in medical research. It could lead to the development of new trypanocidal, antibacterial and antimalarial agents [14]. Because of its DNA affinity and intercalative capabilities (they can intercalate into DNA and disarray undesired biological activities [16]), the acridine scaffold is a promising pharmacophore for the development of anticancer medicines [15]. Further substantial biological activity of acridine has been documented against fungus [17],bacteria [18], Alzheimer's disease [19], parasites [20,21], viruses [22] and HIV/AIDS [23].

In addition, the pyrrole ring is found to be the nucleus of a number of bioactive natural products and novel medicinal molecules. Pyrrole-containing compounds have remarkablepharmacological properties such as being antioxidant, antimicrobial [24], antifungal, anti-HIV [25], exhibiting COX-2 inhibitory effect [26] etc. Because of their optical properties, they find use in optoelectronic tools [27].

A pyrroloacridine nucleus integrates both pyrrole and acridine moieties and thus enjoys the perks of both in a single nucleus, encouraging the creation of several biologically useful compounds. Pyroloacridine derivatives have anthelmintic and anticancer properties. Furthermore, pyrroloacridine compounds such as plakinidines A–C and alpkinidines are identified as tetracyclic cores in metabolites from marine sources [28].

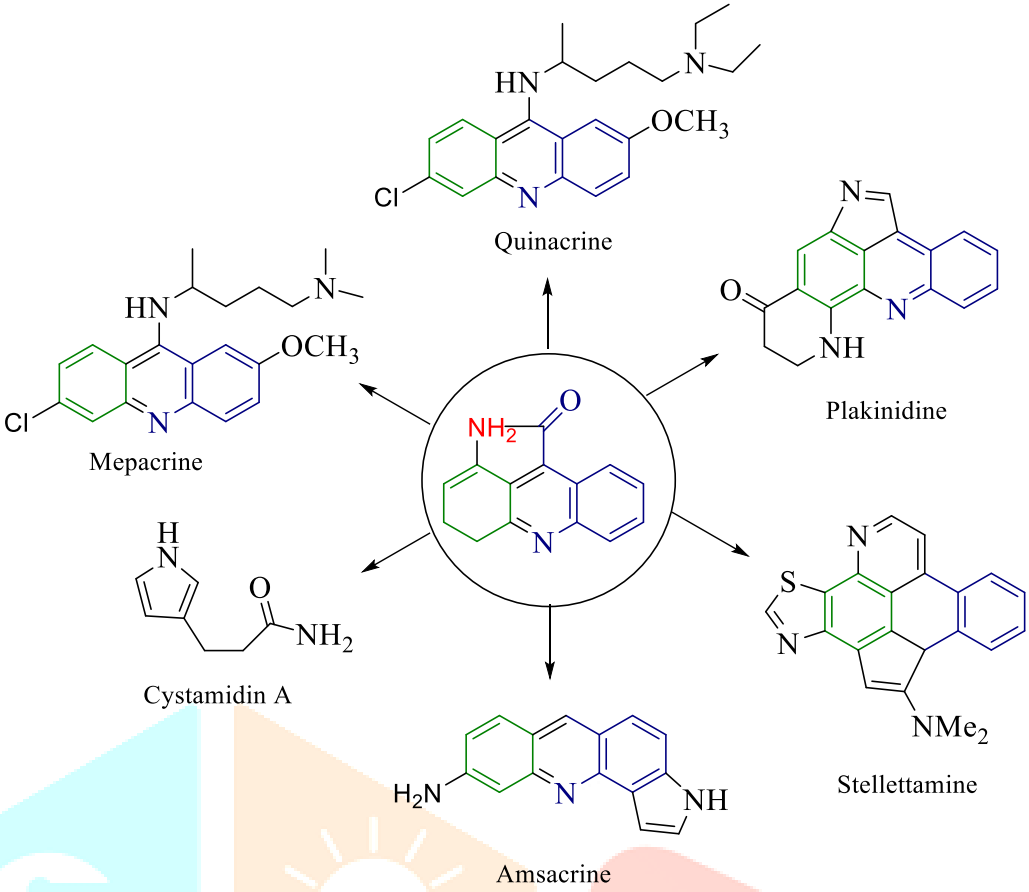


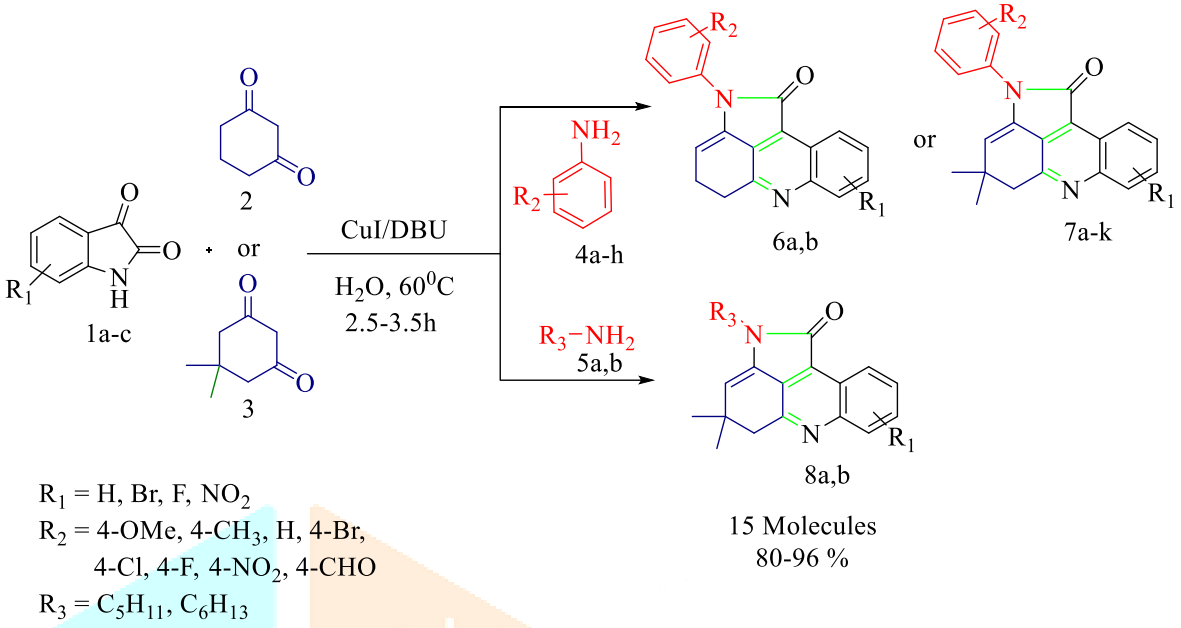

**Figure 1**. Examples of some bioactive pyrrolo[2,3,4-kl]acridin molecules

Despite the fact that various strategies for the synthesis of pyrrolo[2,3,4-kl]acridin are known in literature [6-8, 28-34],a large number of them suffer from one or more disadvantages such as the use of harsh reaction conditions, the inclusion of noxious metals or the use of expensive and not easily accessible exotic catalysts.

**Table 1.** Comparison of our proposed catalyst system with previously reported catalyst systems for thesynthesis of pyrrolo[2,3,4-kl]acridin-1-ones scaffolds.

| Sr. No. | Catalyst/catalyst amount | Reaction condition | References |
|---|---|---|---|
| 1 | Ag NPs/rGO/4 wt% | EtOH/MW | 28 |
| 2 | SMSNP-CA/ 20mg &CuI/ 10mol% | Reflux | 29 |
| 3 | [B(HSO4)3]/0.1 g | EtOH, reflux | 30 |
| 4 | [HMIm]HSO4/0.5 ml | $80^0$C | 31 |
| 5 | Meglumine/ 30 mol% | EtOH: $H_2O$ | 32 |
| 6 | BATA-MC/ 10 mol% | EtOH/ $100^0$C | 33 |
| 7 | (Na[Nd(pydc-OH)(H2O)4]3}[SiW12O40])/ HPA | $H_2O$/ $80^0$C | 34 |
| 8 | Fe3O4@SiO2–SO3H/0.01 g | Solvent free, 80 °C | 6 |
| 9 | Salicylic Acid/ 20 mol% | PEG 200/ $80^0$C | 7 |
| 10 | Lactic acid/35 mol% | Solvent free, 80 °C | 8 |
| 11 | CuI 20mol%/ DBU 20mol% | EtOH: $H_2O$ | This Work |

We developed a Chemoselective synthesis of pyrrolo[2,3,4-kl]acridin-1-ones using Copper(I)/DBU Catalyst, taking into account the tremendous biological activities of the desired scaffold and the environmental friendliness of the organocatalytic procedure.(**Scheme 1**).



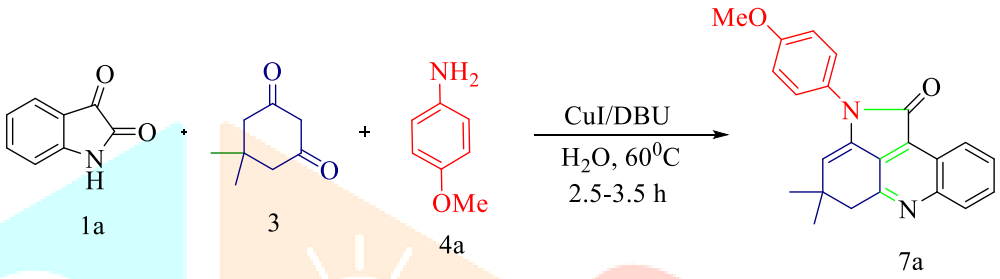

**Scheme 1:** Synthesis of pyrrolo[2,3,4-kl]acridin-1-ones

## RESULT AND DISCUSSION

In our preliminary attempt to find an efficient green route for the synthesis of thetarget compound, isatin (**1a,** 1 mmol), aniline (**4a**, 1 mmol) and dimedone (**3**, 1 mmol) were used to systematically study the influence of various parameters on the reaction outcome (Table 2). It was shown that in the absence of catalyst and base, the reaction did not occur (entry 1). Then the effect of catalyst was investigated at 60°C for 2h of reaction in$H_2O$. The product was not formed both in the absence of a base and also in the absence ofa copper catalyst (entries 2-3). To our delight, 96% NMR yield was obtained in the presence of 30 mol % of CuI catalyst and 20 mol % of DBU (entry 4). This suggests that CuI and DBU have excellent synergistic effect on catalysing the reaction. Encouraged by this result, we investigated the effect of varying quantities and different kinds of copper catalysts on the yield of product. For this purpose, copper catalysts such as CuCl, CuBr and CuCN were used in the reaction but the yields were not satisfactory (entries 5−7). Next, we optimised the amount of catalyst and we observed that 20 mol % of the catalyst is enough. This result indicates that CuI (20 mol %) is the most efficacious catalyst for the synthesis of the desired compound (entries 8,9). After the optimisation of the catalyst, we screened different kinds of bases under the same reaction conditions. Clearly, organic bases such as $Et_3N$ and 1,4-diazabicyclo[2.2.2]octane (DABCO) as well as inorganic bases such as $K_2CO_3$ and KOH were ineffective for the synthesis (entries 10-13). To our delight, when 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was used as base, the reaction proceeded smoothly and the product 7a was obtained in 96% yield (entry8). Next, we optimised the amount of DBU catalyst and observed that 20 mol % is optimum for the desired compound (entry 8, 14, 15). We then examined the effect of different solvents such as EtOH, EtOH: $H_2O$, THF, DCM, toluene, dioxane and DMSO (entries 16-22). Amongst them$H_2O$ was observed to be the most appropriate for the required transformation (entry 8).

Breslow, an organic chemist, first proposed the use of water as a solvent in 1980, claiming that the hydrophobic property of the solvent efficiently determines the rate of chemical reactions. In comparison to general organic solvents, water has unique and different physical properties such as a high dielectric constant, large cohesive energy, high specific heat and high surface tensionand its hydrophobic nature not only accelerates reaction rates but also increases reaction selectivity, even when the reactants are insoluble or sparingly soluble in the medium, making it the most impressive, convenient, and efficient for the desired transformation [35-37].The efficiency of the reaction also depended on reaction temperature. When the reaction temperature was reduced to 40°C, the yield of product was decreased to 21% (entry 24) but on increasing the temperature, no significant improvement was seen (entry 23).

**Table 2.** Results of screening the conditions[a]




| Entry | Catalyst | Base | Solvent | Temp($^0$C) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | ….c | ….d | $H_2O$ | 60 | NR |
| 2 | ….c | DBU (20 mol %) | $H_2O$ | 60 | NR |
| 3 | CuI (30 mol %) | …. | $H_2O$ | 60 | NR |
| 4 | CuI (30 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 96 |
| 5 | CuCl (30 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 20 |
| 6 | CuBr (30 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 45 |
| 7 | CuCN (30 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 62 |
| 8 | CuI (20 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 96 |
| 9 | CuI (10 mol %) | DBU (20 mol %) | $H_2O$ | 60 | 84 |
| 10 | CuI (20 mol %) | $Et_3N$ (20 mol %) | $H_2O$ | 60 | 80 |
| 11 | CuI (20 mol %) | DABCO (20 mol %) | $H_2O$ | 60 | 30 |
| 12 | CuI (20 mol %) | $K_2CO_3$ (20 mol %) | $H_2O$ | 60 | 35 |
| 13 | CuI (20 mol %) | KOH (20 mol %) | $H_2O$ | 60 | 52 |

| | | | | | |
|---|---|---|---|---|---|
| 14 | CuI (20 mol %) | DBU (30 mol %) | $H_2O$ | 60 | 96 |
| 15 | CuI (20 mol %) | DBU (10 mol %) | $H_2O$ | 60 | 86 |
| 16 | CuI (20 mol %) | DBU (20 mol %) | EtOH | 60 | 75 |
| 17 | CuI (20 mol %) | DBU (20 mol %) | EtOH: $H_2O$ | 60 | 82 |
| 18 | CuI (20 mol %) | DBU (20 mol %) | THF | 60 | NR |
| 19 | CuI (20 mol %) | DBU (20 mol %) | DCM | 60 | Trace |
| 20 | CuI (20 mol %) | DBU (20 mol %) | Toluene | 60 | 57 |
| 21 | CuI (20 mol %) | DBU (20 mol %) | Dioxane | 60 | Trace |
| 22 | CuI (20 mol %) | DBU (20 mol %) | DMSO | 60 | … |
| 23 | CuI (20 mol %) | DBU (20 mol %) | $H_2O$ | 80 | 96 |
| 24 | CuI (20 mol %) | DBU (20 mol %) | $H_2O$ | 40 | 72 |

[a]All reactions were carried out with **1a** (1 mmol), **4a** (1 mmol) and **3** (1 mmol) in different reaction conditions; [b]Isolated yields, r. t. = room temperature. [c]Absence of catalyst; [d]Absence of base.

## RECYCLABILITY

**Table 3**. Recyclability of DBU as a catalyst[a]

| Entry | Run | Yield[b] (%) |
|---|---|---|
| 1 | First | 96 |
| 2 | Second | 94 |
| 3 | Third | 92 |
| 4 | Fourth | 90 |

[a]All reactions were carried out with **1a** (1 mmol), **4a** (1 mmol) and **3** (1 mmol) in different reaction conditions; [b]Isolated yields.

Once the methodology for the synthesis of pyrrolo[2,3,4-kl]acridin-1-ones was idealized and its generality had been adequately demonstrated, we focused our attention towards exploring the possibility of recovery and recyclability of DBU utilizing the model reaction, under the optimized reaction conditions. Upon completion of the reaction, the reaction mixture was quenched with cold water and the compound was dissolved in ethyl acetoacetate while the catalyst was dissolved in water. The ethyl acetoacetate layer was isolated and the aqueous fraction was extracted with ethyl acetoacetate (3x3 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated in vacuo to give the crude product and the water fraction was then dried in vacuo and washed with a minimum amount of MeTHF to remove any trace of residual reagents/product and the pure recycled DBU so obtained was used for the next cycle. The recycled promoter could be reused multiple times without any perceivable loss of its activity. The recyclability of the catalyst prevents the alleged disadvantage of the high catalyst loading needed for this reaction.

## MECHANISM

A probable mechanistic pathway for the chemoselective synthesis of pyrrolo[2,3,4-kl]acridin-1-ones from the reaction between 2-aminothiazolo, aniline and dimedone has been proposed (**Fig. 2**).This mechanism is based on the results of our experiment and on literature [38-43].Initially, dimedone (1) is activated by CuI and simultaneously aniline (2) is deprotonated by DBU base. After that, dimedone (1) and aniline (2) react with each other to generate intermediate (A). Intermediate (A) converts into intermediate (B) in the presence of DBU with the elimination of water. Also,isatine (3) activated by CuI reacts with intermediate (B) to generate (C). Further, Compound (C) converts into (D) with the deprotonation of iminium ion. Compound (D) undergoes intramolecular cyclization to give compound (E) in the presence of DBU base. Now, compound (E) undergoes ring opening to convert into (F). CuI activated compound (F) again undergoes intramolecular cyclization and after elimination of water, affords compound (G). Finally, in the presence of DBU the desired product (7a) is formed.

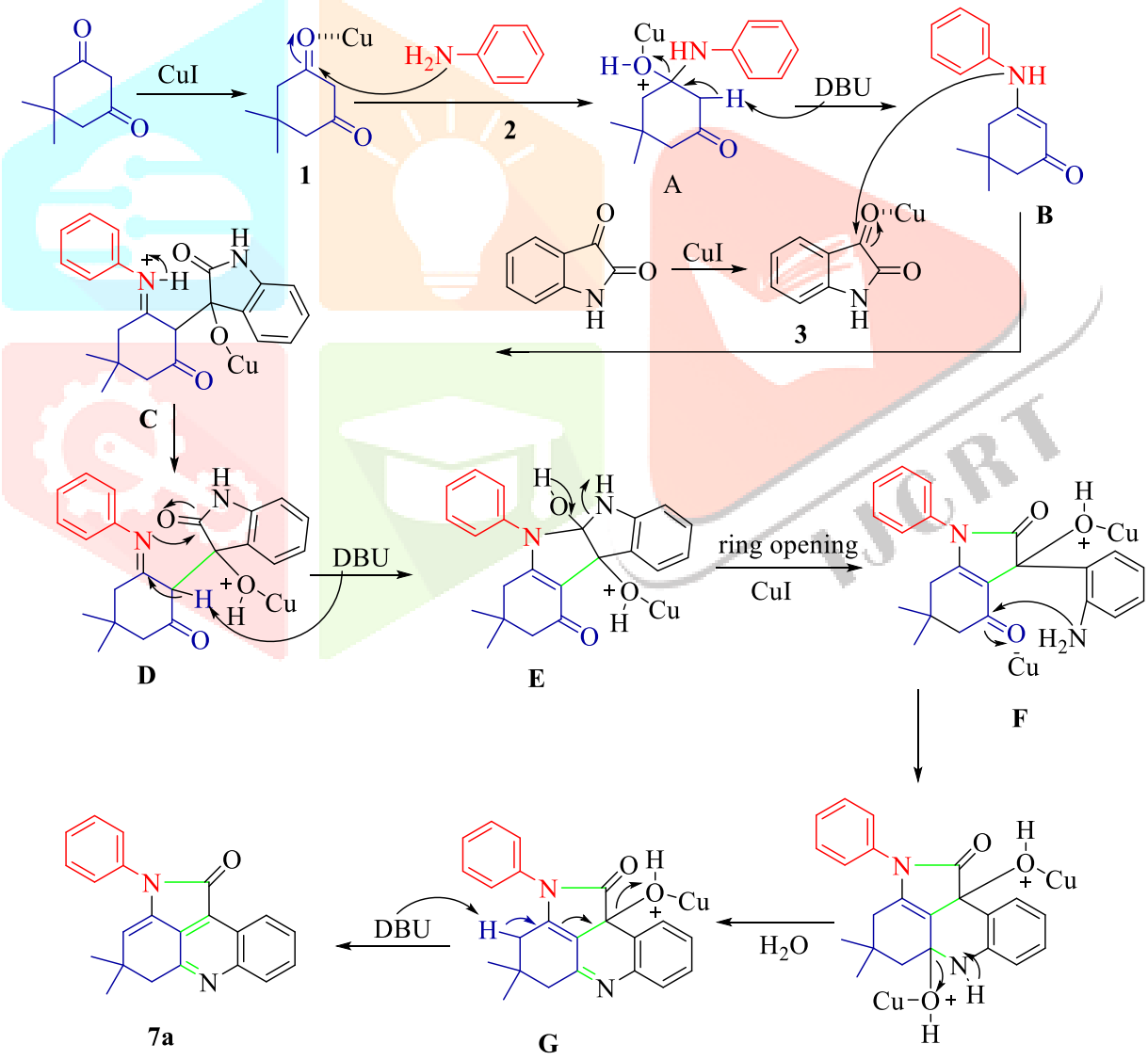
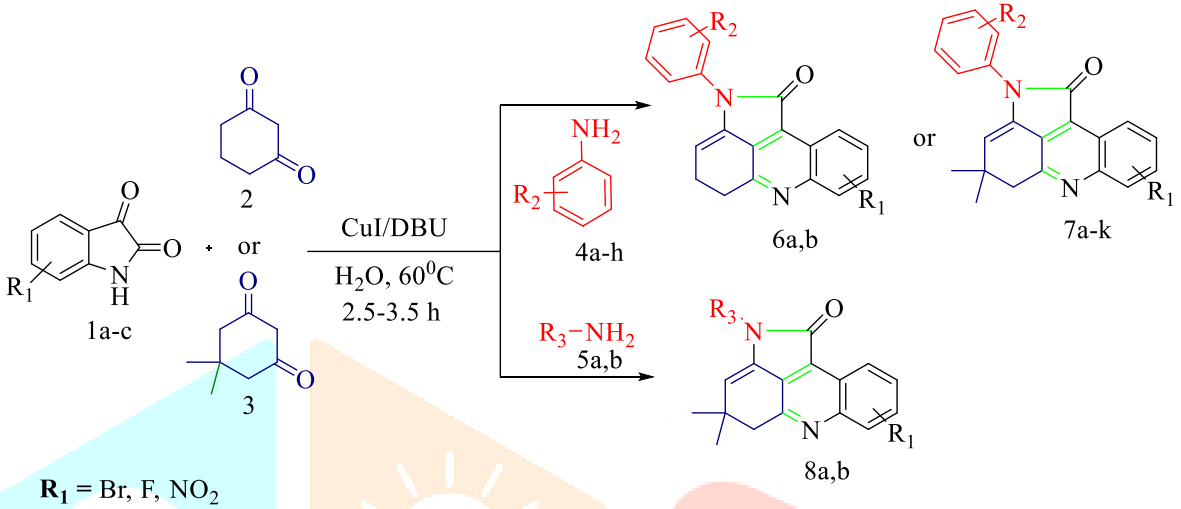


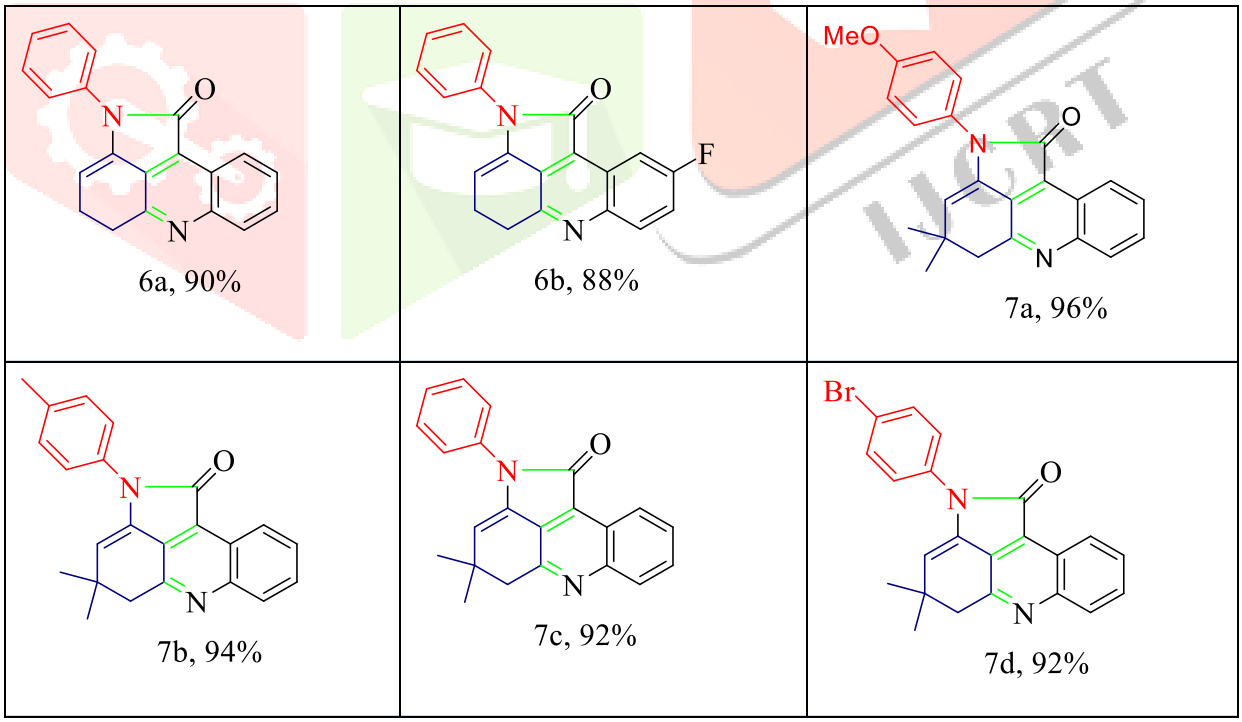

**Figure 2.** Plausible Mechanism for the synthesis of pyrrolo[2,3,4-kl]acridin

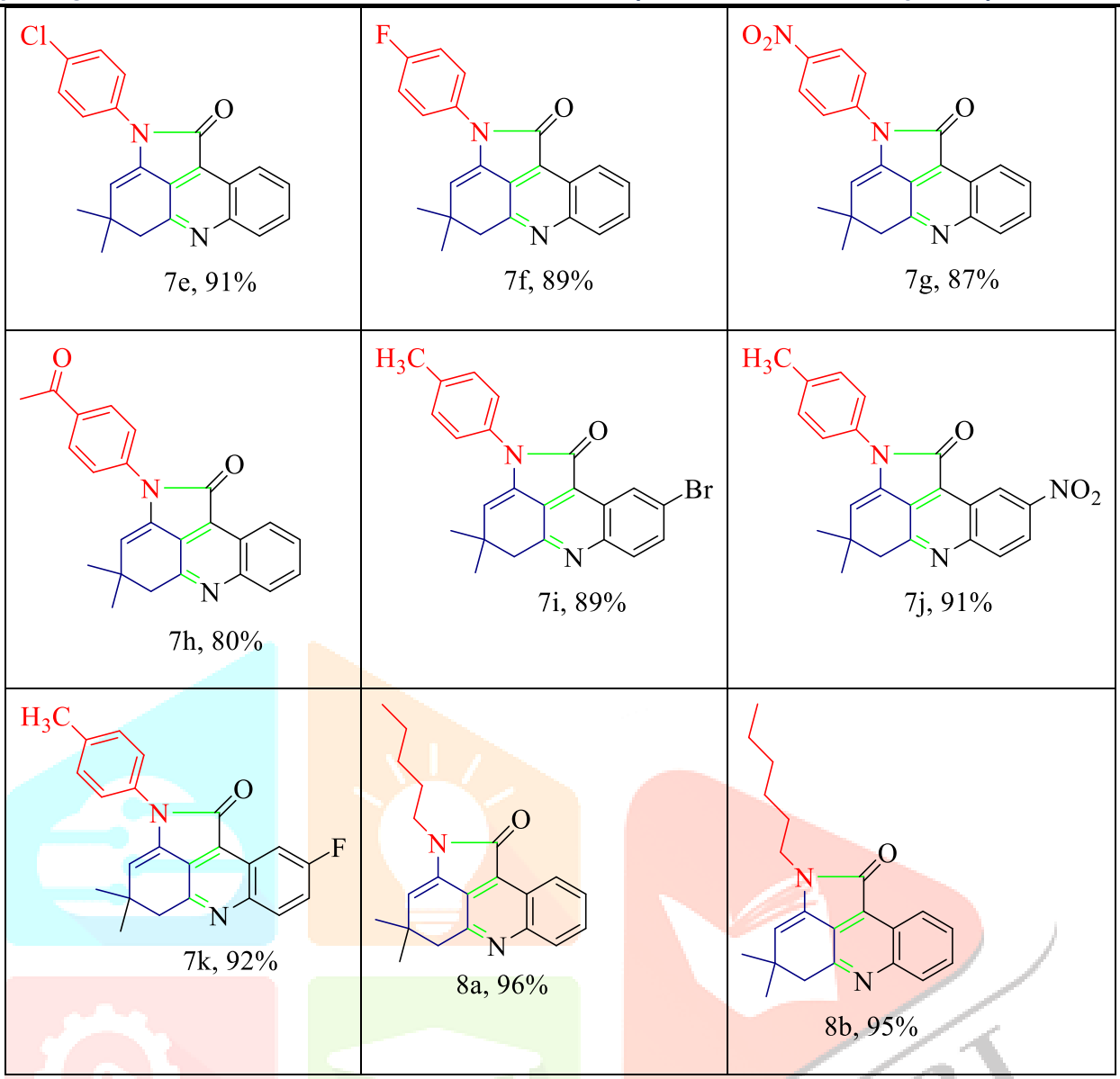
When the adaptability and recyclability of this approach was illustrated, the scope and limitation of the present synthetic strategy was examined for the synthesis of a series of pyrrolo[2,3,4-kl]acridin derivatives (Scheme 1). We first investigated a variety of anilines with various types of electron-donating and electron-

withdrawing groups that yielded good to excellent yields (80–96%) of theproducts (**6a-6b,7a-k, 8a-8b)**. The presence of electron-donating groups produced the best results while the presence of electron-withdrawing groups produced slightly lower yields. Notable results were obtained with aliphatic amines which provided high yields. When various substituted isatins were used, good yields of products were obtained.

**Table 4:** Substrate scope[a,b]






## CONCLUSION

To summarise, we have created a one-pot, three-component and environment friendly way to synthesize pyrrolo[2,3,4-kl]acridin from the reaction of dimedone, different anilines and isatins in the presence of Cu(I)/DBU as an inexpensive,recyclable and readily available catalyst with the goal of attaining green synthesis. The ease of work-up and purification, as well as the avoidance of any harmful organic solvent and the synthesis of the intended product in high yields without any bothersome by-products, are all distinctive features of this process.

## EXPERIMENTAL SECTION

### General Remarks

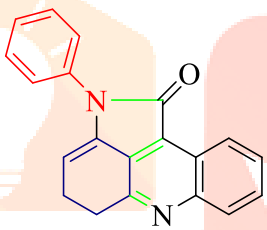
All chemicals were reagent grade and purchased from Sigma Aldrich, Alfa Aesar, Merck, Spectrochem and Qualigens and were used without purification. The reactions were monitored using pre-coated TLC plates of silica gel G/UV-254 of 0.25 mm thickness (Merck 60 F-254). NMR spectra were recorded on a Bruker Avance Neo 500FT spectrometer at 500 MHz ($^{1}$H) and 125 MHz ($^{13}$C) in $CDCl_3$ using TMS as an internal

reference. Mass Spectra (ESIMS) were obtained on Micromassquadro II spectrometer. Melting points were determined by open glass capillary method and were uncorrected.

**General Experimental Procedure**

In a 50ml round bottom flask equipped with a magnetic stirrer bar, isatin (**1a**, 1 mmol), dimedone (**3**, 1 mmol) and aniline (**4a**, 1 mmol) in the presence of catalyst CuI (20 mol%) and base DBU (20 mol%) were added and the resulting mixture was stirred at 60°C using $H_2O$ as solvent. After the completion of the reaction (monitored by TLC), the reaction mixture was quenched with cold water (3 ml) and the compound was dissolved in EtOAc. The EtOAc layer was separated and the aqueous fraction was extracted with EtOAc (3x3 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated in vacuo and the crude product was purified by silica gel chromatography (100-200 mesh silica gel; EtOAc/Hexane) to obtain the pure product (**6a-6b, 7a-7k, 8a-8b**). All the products are well known and have been characterized by the comparison of their spectra and melting point with those reported in literature [6-8,28-34].

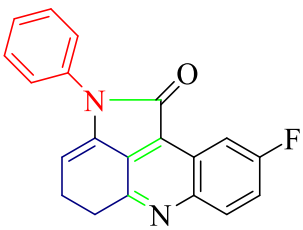
**SPECTRAL DATA OF SYNTHESIZED COMPOUNDS**




6a, 90%

**2-phenyl-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one (6a)**

Light brown solid, M.P. 295-297°C; IR (KBr $\nu$ $cm^{-1}$): 3385, 2977, 1715, 1528, 1263, 847, 787, 539; $^1H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 2.32 (d, 2H), 2.97 (d, 2H), 5.23 (s, 1H), 7.42-7.63 (m, 5H), 7.57 (t, 1H, J = 8.5 Hz), 7.69 (t, 1H, J = 8.5 Hz), 7.94 (d, 1H, J = 8.2 Hz), 8.03 (d, 1H, J = 8.2 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 21.3, 36.2, 105.3, 118.7, 122.8,125.1, 126.7, 128.0, 128.5, 130.7, 132.4, 133.6, 135.1, 139.5, 140.7, 148.3, 159.1, 165.7; ESI-MS *m/z*: 298.

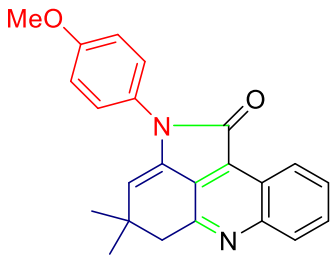



6b, 88%

**9-fluoro-2-phenyl-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one (6b)**

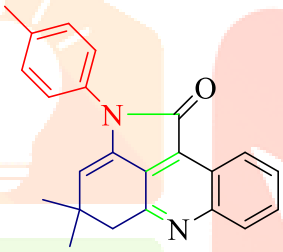
Red solid, M.P. 228-230°C; IR (KBr $\nu$ $cm^{-1}$): 3395, 2970, 1723, 1522, 1259, 856, 797, 551; $^1H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 2.34 (d, 2H), 3.02 (d, 2H), 5.27 (s, 1H),7.30 (d, 1H, J = 7.6 Hz), 7.45-7.67 (m, 5H), 8.07 (d, 1H, J = 7.6 Hz), 8.23 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 23.7, 37.5, 110.8, 118.5,

121.3,123.5, 125.6, 127.1, 129.3, 132.7, 135.4, 136.3, 138.6, 140.2, 147.2, 158.5, 160.5, 168.1; ESI-MS *m/z*: 316.



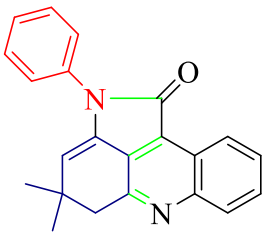

7a, 96%

**4,5-dihydro-2-(4-methoxyphenyl)-4,4-dimethylpyrrolo[2,3,4-kl]acridin-1(2H)-one(7a)** Light yellow coloured solid, M.P. 186-188°C; IR (KBr *v* $cm^{-1}$): 3379, 2957, 1709, 1515, 1254, 831, 775, 525; $^{1}H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 1.29 (s, 6H), 3.19 (s, 2H), 3.84 (s, 3H), 5.53 (s, 1H), 7.03 (d, 2H, J = 8.7 Hz), 7.38 (d. 2H, J = 8.7 Hz), 7.62 (t, 1H, J = 7.8 Hz), 7.72 (t, 1H, J = 7.8 Hz), 8.15 (d, 1H, J = 8.4 Hz), 8.69 (d, 1H, J = 8.1 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 31.5, 37.9, 41.7, 56.2, 113.8, 117.9, 123.1, 124.7, 125.9, 126.8, 127.0, 127.9, 128.1, 129.4, 129.9, 134.3, 150.2, 154.9, 159.2, 167.1; ESI-MS *m/z*: 356.




7b, 94%

**2-(4-Methylphenyl)-4,5-dihydro-4,4-dimethylpyrrolo[2,3,4-kl]acridine-1(2H)-one(7b)**Yellow powder, M.P. 221-223°C, IR (KBr *v* $cm^{-1}$): 3035, 2959, 1695, 1644, 1519, 1460, 1347, 1130, 813, 779; $^{1}H$ NMR (500 MHz, $CDCl_3$): (δ ppm); 1.38 (s, 6H), 2.41 (s, 3H), 3.29 (s, 2H), 5.58 (s, 1H), 7.36 (d, 2H J= 8.8 Hz), 7.40 (d, 2H J =8.8 Hz), 7.63 (t, 1H J= 7.4 Hz), 7.72 (t, 1H, J= 7.4 Hz), 8.23 (d, 1H, J =8.3), 8.74 (d, 1H, J =8.0 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): (δ ppm) 22.6, 32.1, 39.9, 41.9, 115.1, 121.8, 122.7, 125.7, 126.2, 126.9, 128.0, 129.3, 130.4, 130.8, 132.2, 133.9, 139.3, 146.7, 156.3, 167.6; ESI-MS *m/z*: 340.

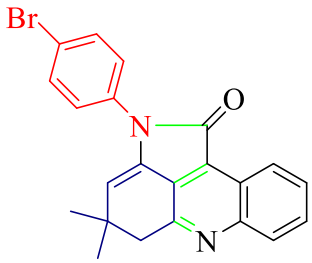



7c, 92%

**2-Phenyl-4,5-dihydro-4,4-dimethylpyrrolo[2,3,4-kl]acridine-1(2H)-one (7c).**

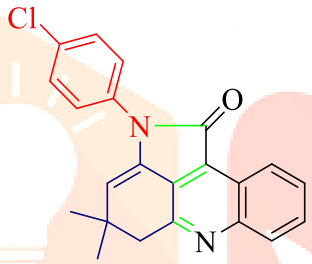
Light yellow solid, M.P. 198-201$^{0}$C; IR (KBr *v* $cm^{-1}$): 3036, 2947, 1700, 1655, 1529, 1458, 1345, 1102, 773; $^{1}H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 1.34 (s, 6H), 3.26 (s, 2H), 5.59 (s, 1H), 7.40 (d, 2H, J=6.4 Hz), 7.57 (t, 2H, J=6.8 Hz), 7.62 (t, 1H, J=7.6 Hz), 7.51-7.87 (m, 4H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 32.3,

35.0, 43.1, 117.9, 123.3, 124.0, 124.3, 124.9, 125.9, 126.3, 127.5, 129.1, 129.6, 134.0, 135.5, 138.7, 146.3, 150.4, 169.1; ESI-MS *m/z*: 326.



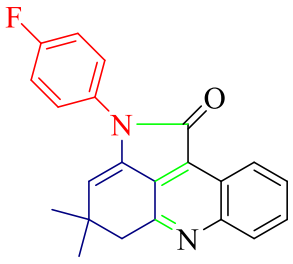

7d, 92%

**2-(4-Bromophenyl)-4,5-dihydro-4,4-dimethylpyrrolo[2,3,4-kl]acridine-1(2H)-one(7d)**Pale yellow solid, M.P. 190-192°C, IR (KBr *v* $cm^{-1}$): 3042, 2971, 1709, 1654, 1482, 1339, 1121, 1069, 812, 777; $^{1}H$ NMR (500 MHz, $CDCl_3$): (δ, ppm) 1.31 (s, 6H), 3.27 (s, 2H), 5.60 (s, 1H), 7.58 (d, 2H J =8.6 Hz), 7.63 (d, 2H, J =8.6 Hz), 7.61-7.92 (m, 4H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ ppm): 33.5, 35.7, 46.1, 120.2, 122.1, 123.7, 124.0, 125.9, 126.3, 127.1, 129.3, 132.2, 133.0, 133.7, 136.5, 139.7, 147.1, 155.9, 164.8; ESI-MS *m/z*: 405.




7e, 91%

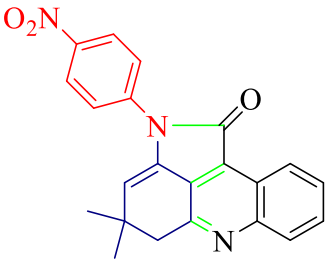
**2-(4-Chlorophenyl)-4,5-dihydro-4,4-dimethylpyrrolo[2,3,4-kl]acridine-1(2H)-one(7e)** Light yellow solid, M.P. 184-186°C, IR (KBr *v* $cm^{-1}$): 3061, 2960, 1710, 1655, 1492, 1348, 1086, 821, 771; $^{1}H$ NMR (500 MHz, $CDCl_3$): (δ ppm): 1.33 (s, 6H), 3.20 (s, 2H), 5.61 (s, 1H), 7.42 (d, 2H, J =8.8 Hz), 7.51 (d, 2H, J= 8.8 Hz), 7.62 (t, 1H, J =7.2 Hz), 7.73 (t, 1H, J= 7.2 Hz), 8.03 (d, 1H, J =8.4 Hz), 8.11 (d, 1H, J= 8.4 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): (δ ppm): 32.1, 39.8, 47.1, 120.2, 122.5, 123.2, 124.7, 125.1, 126.4, 127.5, 128.2, 129.3, 131.7, 133.1, 137.5, 145.7, 151.3, 154.6, 168.5; ESI-MS *m/z*: 360.




7f, 89%

**2-(4-Fluorophenyl)-4,4-dimethyl-4,5-dihydro-2H-pyrrolo[2,3,4-kl]acridin-1-one(7f)**

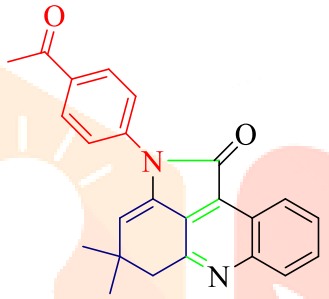
Yellow solid, M.P. 187-189 °C; IR (KBr *v* $cm^{-1}$): 3032, 2967, 1705, 1658, 1518, 1465, 1329, 1107, 797; $^{1}H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 1.28 (s, 6H), 3.11 (s, 2H), 5.64 (s, 1H), 7.48 (d, 2H, J = 7.8 Hz), 7.67 (d, 2H, J = 7.8 Hz), 7.68-8.02 (m, 4H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 33.0, 36.5, 47.1, 115.9, 121.5, 122.1, 123.7, 125.2, 126.5, 127.1, 129.7, 132.5, 134.3, 136.7, 139.2, 142.3, 147.6, 151.8, 167.5; ESI-MS *m/z*: 344.



7g, 87%

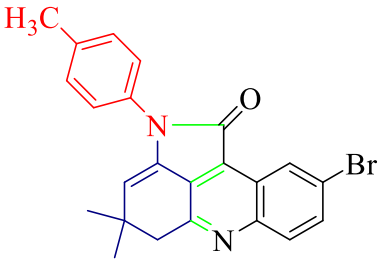
**2-(4-Nitrophenyl)-4,5-dihydro-4,4-dimethylpyrrolo[2,3,4-kl]acridine-1(2H)-one(7g)**

Light orange solid; M.P. 180-183°C; IR (KBr *v* $cm^{-1}$): 3047, 2962, 1720, 1667, 1556, 1542, 1343, 1136, 1062, 872, 793; $^{1}H$ NMR (500 MHz, $CDCl_3$): δ (ppm) 1.14 (s, 6H), 3.76 (s, 2H), 5.18 (s, 1H), 7.60 (t, 1H, J=7.2 Hz), 7.72 (t, 1H, J=7.2 Hz), 7.75 (d, 2H, J=8.0 Hz), 7.80 (d, 1H, J = 7.8 Hz), 7.95 (d, 1H, J = 7.8 Hz), 8.25 (d, 2H, J=8.0 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): 30.7, 32.5, 57.3, 115.1, 118.7, 122.4, 125.8, 126.7, 127.3, 128.6, 130.7, 133.8, 134.7. 136.8, 139.1, 141.7, 143.5, 147.9, 164.5; ESI-MS *m/z*: 371.



7h, 80%

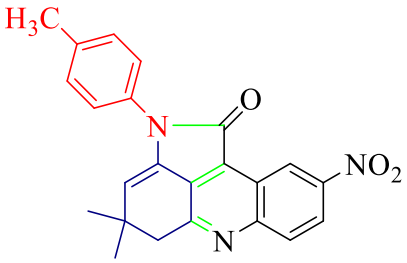
**2-(4-Acetylphenyl)-4,4-dimethyl-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one(7h)** Reddish yellow solid; M.P. 210-212ºC; IR (KBr *v* $cm^{-1}$): 2935, 1690, 1672, 1610, 1472, 1255, 785 $cm^{-1}$; $^{1}H$ NMR (500 MHz, $CDCl_3$): δ (ppm) 1.09 (s, 6H), 2.47 (s, 3H), 3.73 (s, 2H), 5.12 (s, 1H), 7.26 (d, 2H, J=7.6 Hz), 7.45 (t, 1H, J=6.8 Hz), 7.52 (t, 1H, J=6.8 Hz), 8.00 (d, 1H, J = 7.2 Hz), 8.05 (d, 1H, J = 6.4 Hz), 8.12 (d, 2H, J=7.6 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): 27.2, 29.7, 32.5, 56.3, 116.2, 120.8, 121.7, 123.6, 126.1, 128.4, 129.7, 130.2, 132.7, 133.8, 137.5, 138.4, 139.1, 142.7, 147.8, 165.7, 195.2; ESI-MS *m/z*: 368.



7i, 89%

**9-bromo-4,4-dimethyl-2-(p-tolyl)-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one(7i)**

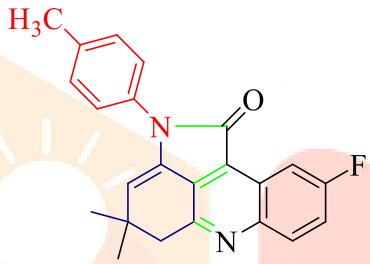
Yellow powder; M.P. 213-215ºC; IR (KBr *v* $cm^{-1}$): 2941, 1702, 1683, 1623, 1487, 1249, 796 $cm^{-1}$; $^{1}H$ NMR (500 MHz, $CDCl_3$): δ (ppm) 1.13 (s, 6H), 2.42 (s, 3H), 3.76 (s, 2H), 5.17 (s, 1H), 7.29 (d, 2H, J=8.0 Hz), 7.49 (d, 2H, J=8.0 Hz), 7.97 (d, 1H, J=7.2 Hz), 8.04 (d, 1H, J = 7.2 Hz), 8.92 (s, 1H, J = 7.0 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): 23.3, 28.5, 52.7, 117.8, 123.2, 124.1, 125.9, 127.3, 128.9, 130.1, 131.7, 133.2, 134.8, 136.4, 138.4, 140.7, 143.2, 146.3, 166.8; ESI-MS *m/z*: 418.



7j, 91%

**4,4-Dimethyl-9-nitro-2-p-tolyl-4,5-dihydro-2H-pyrrolo[2,3,4-kl]acridin-1-one(7j)**

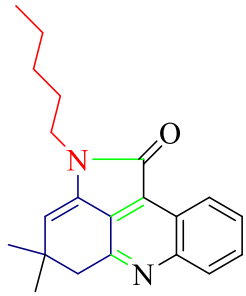
Yellow solid; M.P. 269-271°C; IR (KBr *v* $cm^{-1}$): 3025, 2948, 1719, 1641, 1512, 1536, 1442, 1372, 1123, 827; $^{1}H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 1.12 (s, 6H), 2.31 (s, 3H), 3.79 (s, 2H), 5.25 (s, 1H), 7.30 (d, 2H, J=8.0 Hz), 7.36 (d, 2H, J= 8.0 Hz), 7.65 (d, 1H, J= 7.8 Hz), 7.83 (d, 1H, J = 7.8 Hz), 8.62 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 22.5, 26.7, 33.6, 52.8, 115.1, 120.1, 123.5, 124.2, 125.7, 127.4, 128.9, 130.3, 132.5, 134.8, 137.1, 138.5, 140.8, 146.1, 162.7, 168.2; ESI-MS *m/z*: 385.



7k, 92%

**9-Fluoro-4,4-dimethyl-2-p-tolyl-4,5-dihydro-2H-pyrrolo[2,3,4-kl]acridin-1-one(7k)**

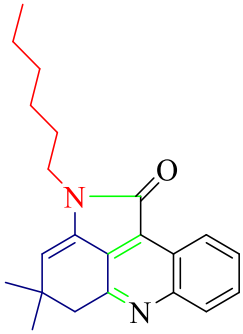
Yellow solid; M.P. 180-182°C; IR (KBr *v* $cm^{-1}$): 3043, 2972, 1721, 1655, 1513, 1467, 1341, 1138, 832;$^{1}H$ NMR (500 MHz, $CDCl_3$) (δ, ppm): 1.15 (s, 6H), 2.35 (s, 3H), 3.76 (s, 2H), 5.27 (s, 1H), 7.31 (d, 2H, J=8.2 Hz), 7.38 (d, 2H, J= 8.2 Hz), 7.63 (d, 1H, J= 7.2 Hz), 7.80 (d, 1H, J = 7.2 Hz), 8.70 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (δ, ppm): 23.7, 27.5, 32.3, 54.7, 117.2, 121.6, 122.1, 123.7, 125.8, 128.3, 129.7, 132.2, 134.8, 136.5, 138.5, 139.7, 142.6, 144.7, 167.2, 169.7; ESI-MS *m/z*: 358.



8a, 96%

**4,4-Dimethyl-2-pentyl-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one(8a)**

Yellow solid; M.P. 137-139ºC; IR (KBr *v* $cm^{-1}$): 2953, 1695, 1521, 1237, 1048, 785; $^{1}H$ NMR (500 MHz, $CDCl_3$): δ (ppm): 0.85 (t, 3H), 1.13 (s, 6H), 1.26-1.30 (m, 2H), 1.32-1.37 (m, 2H), 1.53-1.58 (m, 2H), 3.53 (t, 2H), 3.72 (s, 2H), 5.32 (s, 1H), 7.61 (t, 1H, J=7.4 Hz), 7.78 (t, 1H, J=7.4 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.12 (d, 1H, J=8.4 Hz); $^{13C}$ NMR (125 MHz, $CDCl_3$): 17.2, 25.6, 27.3, 30.5, 31.7, 33.4, 50.2, 54.7, 117.3, 121.7, 124.8, 127.6, 129.4, 135.6, 137.4, 139.2, 141.3, 152.7, 155.1, 169.7; ESI-MS *m/z*: 320.



8b, 95%

**2-Hexyl-4,4-dimethyl-4,5-dihydropyrrolo[2,3,4-kl]acridin-1(2H)-one(8b)**

Yellow solid; M.P. 149-151ºC; IR (KBr *v* $cm^{-1}$): 2947, 1683, 1535, 1245, 1053, 787 $cm^{-1}$; $^{1}H$ NMR (500 MHz, $CDCl_3$): δ (ppm): 0.86 (t, 3H), 1.10 (s, 6H), 1.24-1.29 (m, 2H), 1.33-1.36 (m, 2H), 1.50-1.54 (m, 2H), 1.53-1.56 (m, 2H), 3.57 (t, 2H), 3.69 (s, 2H), 5.35 (s, 1H), 7.58 (t, 1H, J=7.4 Hz), 7.74 (t, 1H, J=7.4 Hz), 8.07 (d, 1H, J=8.4 Hz), 8.10 (d, 1H, J=8.4 Hz); $^{13C}$ NMR (125 MHz, $CDCl_3$): 16.9, 24.7, 28.1, 31.4, 32.6, 35.7, 47.3, 55.4, 119.1, 122.8, 123.5, 126.1, 128.6, 130.3, 135.7, 136.3, 139.8, 143.6, 149.2, 157.5, 168.7; ESI-MS *m/z*: 334.

## SUPPORTING INFORMATION SUMMARY

General experimental, General procedure for the synthesis of pyrrolo[2,3,4-kl]acridin derivatives and Characterization data of products.

## ACKNOWLEDGEMENTS

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