**Publications**


5. **Ramesh K. B.** Pasha M. A. Synthesis of nano ZnO and application as green catalyst in one-pot synthesis of Novel indole-4-hydroxy-chromen-2-ones; (Under communication)

6. **Ramesh K. B.** Pasha, M. A. One-Pot four-component synthesis of Biologically active tetrahydroquinolines using Silica Iodide as a heterogeneous and reusable catalyst; (Under communication)
Posters Presented in Conferences

1. Attended and presented a poster in “INDIAN SCIENCE CONGRESS ASSOCIATION”, organized by University of Mysore, Mysuru on 3–7, January 2016. (Preparation of nano ZnO and its application as a green catalyst in a one-pot three-component synthesis of novel indole-4-hydroxy-chromen-2-ones).

2. Attended and presented a poster in “FKCCI GREEN SUMMIT 2015”, conducted by the Ministry of Energy Resources, Govt. of Karnataka, held at the White Orchid Hotel, Bengaluru, 23–25 April, 2015. (Green synthesis, biological evaluation and molecular docking studies on some novel Triazoloquinazolinones).

3. Attended and presented a poster in “NATIONAL CONFERENCE ON PURE AND APPLIED CHEMISTRY (NACOPAC-2014)” organized by the Department of Studies in Chemistry, Manasagangotri, University of Mysore, Mysuru, on 29–31 December 2014. (Ultrasound-assisted One-pot three-component Synthesis of Triazoloquinazolinones using silica iodide as a heterogeneous catalyst).

4. Attended and presented a poster got the First Prize, in UGC sponsored state level seminar “ON MODERN TECHNIQUES IN CHEMICAL AND BIO-CHEMICAL ANALYSIS” (MTCBA-2014), organized by Department of Chemistry, A. V. Kanthamma College for Women, Hassan, on 10th September 2014 *Won the First Prize for Best Poster award for candidate (One-pot four-component synthesis of Biologically active Tetrahydroquinolines using Silica Chloride as a heterogeneous and reusable catalyst).

5. Attended and presented a poster in “32nd ANNUAL NATIONAL CONFERENCE OF INDIAN COUNCIL OF CHEMISTS” held at the Department of Studies in Chemistry, Karnataka University, Dharwad on 28–30th November 2013. (One-pot four-component synthesis of Polyhydroquinolines).

6. Attended and presented a poster in the in UGC sponsored national level seminar on “RECENT ADVANCES IN CHEMICAL BIOLOGY AN OVERVIEW (RACB-2013)” in the Department of post graduation Studies in Chemistry, Government Science College, Hassan, on 15–16th March 2013 (One-pot four-component synthesis of acridines).
Publications
Study on one-pot four-component synthesis of 9-aryl-hexahydro-acridine-1,8-diones using SiO$_2$–I as a new heterogeneous catalyst and their anticancer activity

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Ammonium acetate
Silica iodide
Anticancer activity

ABSTRACT

A simple, efficient and cost-effective method for the synthesis of 9-aryl-hexahydro-acridine-1,8-diones by a one-pot four-component cyclodehydration of dimedone, aromatic aldehydes and ammonium acetate as a nitrogen source in the presence of a new heterogeneous catalyst silica iodide (SiO$_2$–I) in EtOH at 80 °C is described. SiO$_2$–I was subjected to SEM–EDX and found to have iodo group bound to the catalyst. Some of the prepared acridine-diones were found to exhibit promising anti-cancer activity against HepG2 and MCF-7 cell lines.

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Multicomponent reactions (MCRs) have emerged as efficient and powerful strategies in the modern synthetic organic chemistry because synthesis of complex organic molecules from simple and readily available substrates can be achieved in a very fast and efficient manner without the isolation of any intermediates. MCRs contribute to the requirements of an environment friendly process by reducing the number of synthetic steps, energy consumption and waste production. Therefore, developing new MCRs and improvement of known MCRs are popular areas of research in the current synthetic organic chemistry. MCRs play a major role in several biological processes and proliferation of cancer cells. Cancer is one of the lethal diseases which can lead to human death. In most of the cases multi-drug resistance generally leads to the failure of chemotherapy; and most of the drugs used for the treatment of cancer are cytotoxic drugs which lack the site specific activity to cancer cells and lead to damage of the healthy cells. Many research groups have shown anticancer activity of different acridine analogs (Fig. 1), including compounds 1 and 2 on cancer cells.

Derivatives of acridine 3 and 4 (Fig. 2) showed good cytotoxic activity against human leukaemia cells.

Derivative of acridine such as 5 (Fig. 3) was found to be the most potent drug towards the metastatic breast cancer cells.

Acridines are an important class of organic compounds which find use as dyes, fluorescent materials for visualization of biomolecules, and in laser technology due to their useful spectroscopic properties. Acridines have also received significant attention from many pharmaceutical and organic chemists, essentially because of the broad spectrum of their biological and pharmaceutical properties, such as: antiviral, antibacterial, anti-nociceptive activities, as well as efficiency in photodynamic therapy and because of the anti-inflammatory activity. There are a few reports in the literature on the three-component Hantzsch-type condensation of aromatic aldehydes, amines and dimedone via the traditional heating in organic solvents under microwave irradiation and in ionic liquids leading to acridine. The main drawback of these methods is the inability to synthesize 9-aryl-hexahydro-acridine-1,8-diones, therefore, the development of simple, efficient, high-yielding and environment friendly methods and use of simple, readily available, recyclable, new heterogeneous catalysts for the preparation of acridines under mild conditions is in demand.

In recent years, the heterogeneous catalysis has developed considerable interest in the various disciplines of science including organic synthesis due to the prime advantage that, in most of the cases the heterogeneous catalysts can be recovered with only minor change in activity and selectivity so that they can be used in continuous flow reactions. Heterogeneous catalysts have many advantages over their homogeneous counterparts. Generally
heterogeneous catalysts are insoluble in common organic solvents, cause low corrosion, and show environmental acceptability. Also, the products can be easily separated from the reaction mixture and the catalyst is recoverable, and we have prepared a new heterogeneous catalyst-SiO₂-I form silica through its chloride and used successfully in the synthesis of acridines by a one-pot four-component reaction. Due to our interest in the synthesis of heterocyclic compounds,²³ and in continuation of our previous work on the application of reusable catalysts in organic reactions,²³ we, herein, report a new and an efficient synthesis of some novel and known 9-aryl-hexahydro-acridine-1,8-diones from two moles of dimedone, one mole of benzaldehyde and one mole of ammonium acetate as shown in the Scheme 1.

We have found that, the prepared acridine analogues show promising effect on cancer cell proliferation.

Materials and methods: All chemicals were commercially available and used without further purification, except liquid aldehydes which were distilled before use. All yields refer to isolated products after purification. Products were characterized by the IR, ¹H NMR, ¹³CNMR, Mass spectral and CHN analyses. Melting points were measured on a Raaga, Indian make melting point apparatus. NMR spectra were obtained on a 400 MHz and 100 MHz Bruker AMX instruments in CDCl₃ using TMS as a standard. ESI-MS analysis was carried out using ESI-Q-TOF instrument. Silica, silica chloride and silica iodide were characterized by SIRION high resolution Scanning Electron Microscope-Energy Dispersive X-ray spectroscopic (SEM–EDX) technique.

Preparation of silica iodide: Silica gel (20 g) was suspended in CH₂Cl₂ (50 mL), and SOCl₂ (20 mL) was added drop wise with continuous stirring at 26 °C. Evolution of HCl and SO₂ occurred instantaneously; after stirring for 1 h, the solvent was removed by distillation; and the residual solvent was removed under reduced pressure to get a dry solid of silica chloride (26.2 g). The solid SiO₂–Cl was washes with cold water and dried under vacuum. NaI (3 g) was first dissolved in a mixture of EtOH–H₂O (8:2, 10 mL), this silica chloride (6 g) was added, mixed well and filtered after 15 min, washed with cold water and dried under vacuum to get SiO₂–I (7.5 g).

Detection of the iodide in silica iodide. Qualitative analysis. Test: 1. To detect the presence of iodide in the catalyst, 0.25 mg of silica iodide was transferred to a dry test tube; 0.25 mg of sodium metal was then introduced and heated till the test tube turned red-hot. After cooling the test tube, water (3 mL) was introduced and filtered to get the sodium fusion extract (SFE). SFE (1.5 mL) was then acidified with dil. HNO₃ and treated with AgNO₃ solution to get a pale yellow precipitate which was insoluble in aqueous ammonia to confirm the presence of iodide in the heterogeneous catalyst.²⁴

Test: 2. SFE (1.5 mL) was acidified with dil. HCl, carbon tetrachloride (0.3 mL) was then added and treated with chlorine water (1 mL) to get a violet globule which confirmed the presence of iodide in the heterogeneous catalyst.

Figure 4. SEM-EDX of (a) silica, (b) silica chloride and (c) silica iodide.
### Table 1
Effect of solvent on the synthesis of 9-phenyl-hexahydro-acridine-1,8-diones (4a):  
<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₃CN</td>
<td>83</td>
<td>5</td>
<td>4%</td>
</tr>
<tr>
<td>2</td>
<td>H₂O</td>
<td>98</td>
<td>5</td>
<td>55%</td>
</tr>
<tr>
<td>3</td>
<td>MeOH</td>
<td>65</td>
<td>4</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>EtOH</td>
<td>80</td>
<td>3</td>
<td>60%</td>
</tr>
<tr>
<td>5</td>
<td>CH₃Cl₂</td>
<td>40</td>
<td>6</td>
<td>Trace⁴</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>68</td>
<td>5</td>
<td>55%</td>
</tr>
<tr>
<td>7</td>
<td>Solvent-free</td>
<td>70</td>
<td>6</td>
<td>40%</td>
</tr>
</tbody>
</table>

* Isolated yield.  
⁴ TLC.

### Table 2
Influence of various catalysts on the synthesis of phenyl-hexahydro-acridine-1,8-diones (4a):  
<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amberlite IR120H</td>
<td>13</td>
<td>20%</td>
</tr>
<tr>
<td>2</td>
<td>ZnCl₂</td>
<td>11</td>
<td>30%</td>
</tr>
<tr>
<td>3</td>
<td>CeCl₃</td>
<td>12</td>
<td>35%</td>
</tr>
<tr>
<td>4</td>
<td>K₂CO₃</td>
<td>10</td>
<td>45%</td>
</tr>
<tr>
<td>5</td>
<td>NaF</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>SiO₂-Cl⁻</td>
<td>10</td>
<td>35%</td>
</tr>
<tr>
<td>7</td>
<td>SiO₂-CI⁻</td>
<td>5</td>
<td>70%</td>
</tr>
<tr>
<td>8</td>
<td>SiO₂-I⁻</td>
<td>2.5</td>
<td>90%</td>
</tr>
</tbody>
</table>

* 0.1 g.  
⁴ 10 mol %.  
⁴ Isolated yield.

### Table 3
Optimization of the amount of SiO₂-I  
<table>
<thead>
<tr>
<th>Entry</th>
<th>SiO₂-I (g)</th>
<th>Amount of NH₄OAc (mmol)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>40%</td>
</tr>
<tr>
<td>2</td>
<td>0.01</td>
<td>2</td>
<td>15</td>
<td>50%</td>
</tr>
<tr>
<td>3</td>
<td>0.05</td>
<td>2</td>
<td>10</td>
<td>55%</td>
</tr>
<tr>
<td>4</td>
<td>0.06</td>
<td>2</td>
<td>2</td>
<td>60%</td>
</tr>
<tr>
<td>5</td>
<td>0.08</td>
<td>2</td>
<td>2.5</td>
<td>70%</td>
</tr>
<tr>
<td>6</td>
<td>0.10</td>
<td>2</td>
<td>2.5</td>
<td>90%</td>
</tr>
<tr>
<td>7</td>
<td>0.15</td>
<td>2</td>
<td>2.5</td>
<td>90%</td>
</tr>
<tr>
<td>8</td>
<td>0.20</td>
<td>2</td>
<td>2.5</td>
<td>90%</td>
</tr>
<tr>
<td>9</td>
<td>0.25</td>
<td>2</td>
<td>2.5</td>
<td>90%</td>
</tr>
</tbody>
</table>

* Isolated yield.

### Scheme 2
A plausible mechanism for the formation of acridines.

From the above mentioned tests it was ascertained that iodide in present in silica iodide.

Quantitative analysis. Test: 1. SiO₂-I (1 g) was then taken in a 250 mL conical flask and titrated against 0.04 N Na₂S₂O₃ and found to have 0.33 milli-equivalent of iodide in it by the method developed by McDaniel.[25,26]

Test: 2 (SEM-EDX analysis). The SEM micrographs of silica and silica based catalysts viz., chloride and iodide are shown in Figure 4. SEM micrographs showed both chloride and iodide to have similar texture and that the iodide and chloride in these materials is uniformly dispersed on silica surface and both can be used as heterogeneous catalysts Figure 4(b and c). Also, we have determined the composition of the silica, silica chloride and silica iodide by EDX studies. The EDX plots are shown in Figure 4 (a, b and c) along with the SEM micrographs.
Table 4
SiO₂‐I catalyzed synthesis of acidines 4a‐k in ethanol at 80 °C

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehydes</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
<th>Found</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₅CHO</td>
<td>4a</td>
<td>2.5</td>
<td>90</td>
<td>249–251</td>
<td>258–260⁵⁶</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3-CNCH₂CH₃CHO</td>
<td>4b</td>
<td>2.8</td>
<td>87</td>
<td>215–218¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4-MeOCH₂CHO</td>
<td>4c</td>
<td>2.5</td>
<td>85</td>
<td>271–272¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4-ClC₆H₄CHO</td>
<td>4d</td>
<td>1.5</td>
<td>82</td>
<td>288–301</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4-NO₂C₆H₄CHO</td>
<td>4e</td>
<td>2</td>
<td>86</td>
<td>284–287</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3-Br-4-MeOCH₂CHO</td>
<td>4f</td>
<td>2</td>
<td>89</td>
<td>238–241¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>3-C₆H₄NO₂CH₂CHO</td>
<td>4g</td>
<td>2.6</td>
<td>79</td>
<td>210–213¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2,4-DH₂C₆H₄CHO</td>
<td>4h</td>
<td>2</td>
<td>85</td>
<td>210–215¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2-HO₂C₆H₄CHO</td>
<td>4i</td>
<td>2.5</td>
<td>74</td>
<td>223–225¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>2,4-(ClO₂)₂C₆H₄CHO</td>
<td>4j</td>
<td>2.3</td>
<td>83</td>
<td>291–296¹⁰</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>4-(CH₃)₂NHS₂H₄CHO</td>
<td>4k</td>
<td>2</td>
<td>80</td>
<td>281–283</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Isolated yield. All the synthesized products were characterized from their spectroscopic analytical data (IR, NMR, CHN, ESI-MS), except 4a which was compared on TLC with the authentic sample.

Mechanism: A probable mechanism for the formation of acidines involves the activation of aldehyde followed by the attack of enol form of the dimedone to give the intermediate I. The intermediate I may react with another molecule of dimedone to give II. Attack of ammonia formed from ammonium acetate gives III, and III may cyclise to give the acidine derivative IV which after the elimination of a molecule of water may give V. In the last step V may lose both the catalyst and another molecule of water to give acidines as shown in the Scheme 2.

We studied the effect of several solvents like acetonitrile, water, methanol, dichloromethane, and tetrahydrofuran on the reaction of two moles of dimedone, one mole of benzaldehyde and one mole of ammonium acetate. The reaction in tetrahydrofuran, water, acetonitrile afforded the product but yields were poor. The best results in terms of yield and reaction time were obtained with ethanol as a solvent (Table 1, entry 4). We, then decided to investigate the efficacy of SiO₂‐I for the synthesis of 4a under solvent‐free condition also, but, ended up getting the product in only 40% yield (entry 7). We studied the effect of different catalysts such as AmberliteIR120H, ZnCl₂, CeCl₃, K₂CO₃, NaI, SiO₂, SiO₂‐Cl and SiO₂‐I also on the preparation of 4a, and found that SiO₂‐I is best in terms of yield and duration of the reaction (Table 2, entry 8).

Further studies were carried out to optimize the amount of catalyst by using different amounts of SiO₂‐I (0.06, 0.08, 0.10, 0.15, 0.20 and 0.25 g) and the results of this study are presented in the Table 3. From this Table, it is clear that 0.1 g of SiO₂‐I afforded the product in 90% isolated yield (Table 3, entry 6). Increasing the amount of catalyst did not improve the yield (entries 7–9).

We then started our work by examining the possibility of an one‐pot four‐component reaction involving two molecules of dimedone (1, Scheme 1), one molecule of benzaldehyde (2) and a molecule of ammonium acetate (3) to get 9‐phenyl‐hexahydro‐acridine‐1,8‐dione (4a) in ethanol as a solvent in the presence of SiO₂‐I.

A mixture of 1, 2, and 3 (Scheme 1) in 1.5 mL ethanol was stirred in the presence of SiO₂‐I for 2–3 h at 80 °C to get 4a in 90% yield. Encouraged by this result, the reaction of various substituted arylaldehydes was taken up and the results of this study are presented in the Table 4. The data presented in Table 4 indicates that SiO₂‐I serves as an excellent catalyst for the synthesis of different substituted acidines in excellent yield in short reaction duration.

Study on reusability of SiO₂‐I catalyst: With an effort to make the present reaction much greener, the recovery and reusability of the catalyst was studied. After the completion of the reaction, the solid thus separated was filtered along with the catalyst. The residue containing the catalyst was washed with ether to get the solid SiO₂‐I which was then dried at 100 °C for 2 h and reused. The results of the study of the reusability of the catalyst are presented in the form of a graph in Figure 3. From Figure 3, it is clear that SiO₂‐I can be used successively for at least four runs after the first fresh run, after which the yield of the product dropped from 90% in the first fresh run to 67% in the fifth run. The yield of 4a was found to be 90%, 88%, 81%, 76% and 67%, respectively, for 1–5 cycles, the marginal decrease of yield in the first five cycles may be due to the loss of catalyst during the recovery.

Cell culture: HepG2 (Hepatocellular carcinoma cells) and MCF-7 (Human breast adenocarcinoma cells) cell lines were procured from National Centre for Cell Sciences (NCCS), Pune, India. The cells were cultured in minimum essential medium (MEM) growth medium supplemented with 10% heat inactivated Fetal bovine serum (FBS), penicillin (100 IU/mL), streptomycin (100 μg/mL) and amphotericin-B (5 μg/mL) in a humidified atmosphere of 5% CO₂ at 37 °C until confluent. The cells were trypsinized with TPVG solution (0.2% trypsin, 0.02% EDTA, 0.05% glucose in PBS). The cultures were grown in 25 cm² flat bottles and the studies were carried out in 96 wells plates.

MTT assay: Cells were plated in 96 wells plate (1 × 10⁴ cells/well) and cultured for 24 h at 37 °C in 5% CO₂ atmosphere to allow cell adhesion. After 24 h, when partial monolayer was formed, cells were treated with different concentration of standard drug (Doxorubicin) and sample compounds for 48 h. Microscopic examination was carried out and observations recorded every 24 h. After the treatment, the solutions in the wells were discarded and 50 μL of
freshly prepared MTT (2 mg/mL prepared in PBS) was added to each well. The plates were shaken gently and incubated for 3 h at 37°C in 5% CO₂ atmosphere. The supernatant was removed and the formazan crystals formed in the cells were solubilised by addition of 50 μL of iso-propanol. Finally, the absorbance was recorded using a Micro-plate reader (Bio-Tek, ELX-800 MS) at a wavelength of 540 nm.

%growth inhibition = control absorbance – test absorbance 
control absorbance 

The percentage growth was calculated using the standard formula and IC₅₀ values are shown in the Table 5.

The data presented in the Table 5 shows the IC₅₀ values and their comparison with the standard drug (Doxorubicin) on HepG-2 and MCF-7 cells. It is clear from this table that compounds 4b, 4f, 4i and 4j exhibited very good activity towards HepG2 cell lines and 4b, 4f, 4g and 4j showed comparatively better activity towards MCF-7 cell lines.

In conclusion a reliable, practical procedure and an alternative method for the synthesis of 9-aryl-hexahydro-acridine-1,8-diones has been developed. The method involves the use of silica iodide, a new heterogeneous catalyst which has made this method cost effective, as the catalyst can be recovered for at least five runs without loss of activity and the reaction involves simple workup procedure. The compounds 4b, 4f, 4i and 4j exhibited very good activity towards HepG2 cell lines and 4b, 4f, 4g and 4j showed greatly better activity towards MCF-7 cell lines which can be a plentiful source of potential anti-cancer drugs deserving further study. In our opinion the method is superior to all other previously reported methods 13, 14 of synthesis of 9-aryl-hexahydro-acridine-1,8-diones.

Acknowledgments

Mr. Ramesh K.B. gratefully acknowledges the UGC, New Delhi and the Bangalore University for a UGC-BSR fellowship. Authors also acknowledge the financial assistance by the VCST, Dept. of IT, BT and Science & Technology, Government of Karnataka for the CESEM Award Grant No. 24 (2010-2011). We also thank Mr. T.R. Lakshneesa of Dept. of Microbiology, Bangalore University for the biological assays of the prepared compounds.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bmcl.2014.06.047.
ESI-MS: [M+H] 395.1; 
Anal. Caled C_{36}H_{36}N_{2}O_{3}: C, 70.01; H, 6.64; N, 7.10; Found C, 69.31; H, 6.09; N, 6.29.

3-{2'-Bromo-4'-methoxyphenyl)-3,3,6,6-tetramethyl-2,4,5,7,9,10-hexahydroacridine-1,8-dione (4f):
Colorless solid, mp: 238–241 °C; IR (KBr, v cm⁻¹): 3369 (N–H), 1728 (C=O); ¹H NMR (400 MHz, CDCl₃): 8 6.95 (s, 6H, 2Me), 7.16 (t, 1H, J = 2.0 Hz), 7.68 (d, 1H, J = 8.8 Hz), 7.73 (d, 1H, J = 2.4 Hz), 8.28 (s, 1H, NH); ESI-MS: [M+H] 458.3.

Anal. Caled C₁₉H₁₄BrNO₅: C, 62.88; H, 6.16; N, 3.06; Found C, 62.46; H, 6.19; N, 3.0.

3-{2'-Ethoxyphenyl)-3,3,6,6-tetramethyl-2,4,5,7,9,10-hexahydroacridine-1,8-dione (4g):
Colorless solid, mp: 210–213 °C; IR (KBr, v cm⁻¹): 3110 (N–H), 1724 (C=O); ¹H NMR (400 MHz, CDCl₃): 8 7.05 (s, 6H, 2Me), 7.16 (t, 1H, J = 2.0 Hz), 7.73 (d, 1H, J = 8.8 Hz), 8.28 (s, 1H, NH); ESI-MS: [M+H] 394.2.

Anal. Caled C₁₉H₁₄NO₅: C, 76.30; H, 7.94; N, 3.56; Found C, 75.28; H, 7.09; N, 3.29.

3-{4'-Fluoro-2'-hydroxyphenyl)-3,3,6,6-tetramethyl-2,4,5,7,9,10-hexahydroacridine-1,8-dione (4h):
Colorless solid, mp: 210–215 °C; IR (KBr, v cm⁻¹): 3400 (O–H), 3190 (N–H), 1722 (C=O); ¹H NMR (400 MHz, CDCl₃): 8 6.98 (s, 6H, 2Me), 7.18 (t, 1H, J = 2.0 Hz), 7.64 (d, 1H, J = 8.8 Hz), 8.25 (s, 1H, NH), 8.34 (s, 1H, Ar-H); ¹³C NMR (400 MHz, CDCl₃): 8 217.6, 28.10, 28.29, 51.40, 72.75, 41.98, 50.30, 111.43, 116.20, 118.75, 124.67, 125.04, 128.00, 142.42, 151.44, 169.52; ESI-MS: [M+H] 384.3.

Anal. Caled C₁₉H₁₄NO₅: C, 72.04; H, 6.83; N, 3.65; Found C, 71.62; H, 6.05; N, 3.21.

ESI-MS: [M+H] 395.1; ¹H NMR (400 MHz, CDCl₃): 8 6.99 (s, 6H, 2Me), 7.02 (s, 1H, OH), 8.68 (s, 1H, CH), 8.79 (s, 1H, Ar-H); ¹³C NMR (400 MHz, CDCl₃): 8 27.6, 28.18, 28.59, 31.40, 32.75, 41.98, 50.30, 111.43, 116.20, 118.75, 124.67, 125.04, 128.00, 142.42, 151.44, 169.52; ESI-MS: [M+H] 384.3.

Anal. Caled C₁₉H₁₄NO₅: C, 72.04; H, 6.83; N, 3.65; Found C, 71.62; H, 6.05; N, 3.21.

3-{2'-Hydroxyphenyl)-3,3,6,6-tetramethyl-2,4,5,7,9,10-hexahydroacridine-1,8-dione (4i):
Colorless solid, mp: 222–225 °C; IR (KBr, v cm⁻¹): 3412 (O–H), 3156 (N–H), 1789 (C=O); ¹H NMR (400 MHz, CDCl₃): 8 0.99 (s, 6H, 2Me), 1.02 (s, 6H, 2Me), 2.33–2.54 (m, 8H, 4CH₂), 2.82 (s, 1H, OH), 4.68 (s, 1H, CH), 6.99–7.18 (m, 4H, Ar-H), 11.0 (s, 1H, N–H); ESI-MS: [M+H] 386.1.

Anal. Caled C₁₉H₁₄NO₅: C, 75.59; H, 7.45; N, 3.83; Found C, 75.43; H, 7.07; N, 3.20.

ESI-MS: [M+H] 395.1; ¹H NMR (400 MHz, CDCl₃): 8 6.92 (s, 6H, 2Me), 1.09 (s, 6H, 2Me), 1.95–2.50 (m, 8H, 4CH₂), 3.74 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.95 (s, 1H, NH), 4.73 (s, 1H, CH), 6.14 (d, 1H, J = 2.8 Hz, Ar-H), 6.45 (s, 1H, Ar-H), 6.85 (d, 1H, J = 8.4 Hz); ESI-MS: [M+H] 410.2.

Anal. Caled C₁₉H₁₄NO₅: C, 73.32; H, 7.63; N, 3.42; Found C, 72.04; H, 7.00; N, 3.19.

ESI-MS: [M+H] 392.2.

Anal. Caled C₁₉H₁₄NO₅: C, 76.49; H, 8.22; N, 7.14; Found C, 75.72; H, 7.04; N, 6.29.